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Picloram -
Revised Human Health and Ecological Risk Assessment
– Final Report

Prepared for:

USDA, Forest Service

Forest Health Protection

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

4A-TCP	2,3,5-trichloro-4-aminopyridine
ACGIH	American Conference of Governmental Industrial Hygienists
a.e.	acid equivalents
AEL	adverse-effect level
a.i.	active ingredient
ARS	Agricultural Research Service
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
GLEAMS	Groundwater Loading Effects of Agricultural Management Systems
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

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

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
MRL	minimum risk level
MSDS	material safety data sheet
MW	molecular weight
NAWQA	National Water Quality Assessment
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
PCBs	polychlorinated biphenyls
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SARA	Superfund Amendments and Reauthorization Act
SERA	Syracuse Environmental Research Associates
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
µ	micron
▸	greater than
≥	greater than or equal to

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

$<$	less than
$\leq$	less than or equal to
$=$	equal to
$\simeq$	approximately equal to
~	approximately

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

INTRODUCTION

Picloram is a herbicide used in the control a number of broadleaf weeds and undesirable brush. In the preparation of this risk assessment, literature searches of picloram were conducted in the open literature using PubMed, TOXLINE as well as the U.S. EPA CBI files. There is a very large body of literature on the environmental fate and toxicology of picloram and several reviews by U.S. EPA as well as other published reviews were used in the preparation of the current risk assessment. The U.S. EPA re-registration eligibility decision (RED) document also includes a summary of the product chemistry, mammalian toxicology, and ecotoxicology studies that were submitted by industry to the U.S. EPA as part of the registration process for this compound. Full text copies of key studies obtained and reviewed, and synopses of the information that can be disclosed from these studies are included in this document.

Technical grade picloram contains hexachlorobenzene as a contaminant and hexachlorobenzene is classified as a carcinogen. Because of the importance of and level of concern for this endpoint in humans, the human health risk assessment discusses the potential effects of hexachlorobenzene in some detail.

While this document discusses the studies required to support the risk assessments, it makes no attempt to re-summarize all of the information cited in the existing reviews. 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.

PROGRAM DESCRIPTION

Picloram is a herbicide used in the control of a number of broadleaf weeds and undesirable brush. Picloram is used in Forest Service programs almost exclusively for the control of noxious weeds. Very minor uses include rights-of-way management and general maintenance. Tordon K and Tordon 22K are the formulations of picloram currently available and used by the Forest Service. Both formulations are produced by Dow AgroSciences as a liquid containing the potassium salt of picloram (24.4% w/v). This is equivalent to a concentration of 2 lb a.e./gallon. The remaining 75.6% of the formulation consists of inerts, including a polyglycol. The U.S. EPA has placed the polyglycol on List 3 of the inerts that may be used in the formulation of pesticides. Very little additional information is available on this compound.

The most common methods of ground application for Tordon involve backpack (selective foliar) and boom spray (broadcast foliar) operations. The Forest Service does not typically use aerial applications for picloram. Nonetheless, Tordon is registered for aerial applications and aerial applications are included in this risk assessment in the event the Forest Service may wish to consider this application method. The labeled application rates for picloram range from 0.125 to 1 lb a.e./acre. Typically, the Forest Service uses rates in the lower part of this range and some applications may be below the lower range of the labeled rate. For this risk assessment, the typical rate of 0.35 lb a.e./acre with a lower range of 0.1 lb a.e./acre is use to reflect Forest Service practice. An upper range of 1 lb a.e./acre is used to assess the consequences of using the

highest labeled rate should the Forest Service need to consider this option.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification – The toxicity of picloram to experimental mammals has been very well-characterized. Most of the studies have been conducted in support of the registration of picloram and are summarized in the U.S. EPA re-registration eligibility decision document. Picloram has a low order of acute toxicity, with acute oral LD_{50} values in the range of 3000 to 5000 mg/kg body weight. Picloram can cause irritation to the eyes. Although picloram is not a strong skin irritant, repeated dermal exposures may lead to skin sensitization.

In chronic toxicity studies, the most sensitive effect for picloram in mammals involves effects on the liver. The current U.S. EPA RfD is based on a two-year feeding study in male and female Fischer rats in which picloram acid was administered at dietary concentrations that resulted in daily doses of 20, 60, and 200 mg/kg/day. The only statistically significant observations included an increase in liver size and an alteration in the staining properties of centrilobular hepatocytes in the 60 and 200 mg/kg/day dose groups. Dogs appear to be somewhat more sensitive to picloram than rats. In a six month feeding study in which male and female beagle dogs were administered picloram at levels that resulted in average daily doses of 0, 7, 35, and 175 mg/kg/day, the two higher dose levels resulted in increase in absolute and relative liver weight in two males and changes in liver enzyme activity.

Although technical grade picloram has been subject to several chronic bioassays for carcinogenicity and none of the bioassays have shown that picloram has carcinogenic potential, technical grade picloram does contain hexachlorobenzene, a compound that has shown carcinogenic activity in three mammalian species and has been classified as a potential human carcinogen by the U.S. EPA. Thus, this effect is considered both qualitatively and quantitatively in this risk assessment.

Exposure Assessment –Exposure assessments are conducted for both workers and members of the general public for the typical application rate of 0.35 lb/acre. The consequences of using the maximum application rate, 1 lb/acre, are discussed in the risk characterization. For both workers and members of the general public, the upper ranges of all acute exposures are below 1 mg/kg and most exposures are much lower. The highest modeled exposure is about 0.7 mg/kg and is associated with the consumption of contaminated water by a child following an accidental spill of picloram into a small pond. The upper ranges of non-accidental acute exposure scenarios for members of the general public are associated with doses from about 0.00002 to 0.07 mg/kg. The highest dose estimates for non-accidental exposure scenarios are associated with the consumption of contaminated vegetation or fish. Exposures from dermal contact or drinking contaminated water are likely to be much lower.

General exposure assessments for workers are in the range of exposures modeled for the general public. For workers, three types of application methods are modeled: directed ground, broadcast ground, and aerial. Central estimates of exposure span a relatively narrow range: 0.005 to 0.008 mg/kg. The upper ranges of exposures are also similar for the different groups of workers: 0.03

to 0.05 mg/kg/day. All of the accidental exposure scenarios for workers involve dermal exposures. Because picloram is not readily absorbed across the skin, 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.

Hexachlorobenzene is a contaminant in technical grade picloram. The average concentration of hexachlorobenzene in technical grade picloram is 8 ppm and the maximum concentration is 50 ppm. For all exposure assessments detailed in this risk assessment, the average concentration of 8 ppm is used. The impact of the 50 ppm level is detailed in the risk characterization. Hexachlorobenzene is ubiquitous and persistent in the environment. The major sources of general exposure for the public to hexachlorobenzene involve industrial emissions, proximity to hazardous waste sites, and the consumption of contaminated food. Virtually all individuals are exposed to hexachlorobenzene and virtually all individuals have detectable concentrations of hexachlorobenzene in their bodies. Based on current concentrations of hexachlorobenzene in environmental media and food, daily doses of hexachlorobenzene (i.e., background levels of exposure) are in the range of 0.000001 (1×10^{-6}) mg/kg/day. Based on the amount of hexachlorobenzene in picloram and the amount of picloram used in Forest Service programs, the use of picloram by the Forest Service will not substantially contribute to any wide-spread increase of ambient levels of hexachlorobenzene. Nonetheless, the potential impact of local contamination is considered for workers as well as for several acute and chronic exposure scenarios for members of the general public. For both workers, the upper range of longer term exposure scenarios result in dose estimates of about 2×10^{-7} mg/kg/day to 4×10^{-7} mg/kg/day, below general background levels of exposure by about a factor of 2 to 5. For members of the general public, the upper range of longer term exposure scenarios are about 1×10^{-10} mg/kg/day to 2×10^{-8} mg/kg/day, below general background levels of exposure by about a factor of 50 to 10,000. The upper range of estimated doses associated with acute exposure scenarios for both workers and members of the general public are about 0.002 mg/kg/day, higher than background levels of exposure by about a factor of 2000.

Dose-Response Assessment – The Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.2 mg/kg/day for picloram. This RfD is based on a chronic rat NOAEL of 20 mg/kg/day and an uncertainty factor of 100. In the same study, the LOAEL was 60 mg/kg/day and the effect noted was a change in the staining properties of liver cells. No frank signs of toxicity were seen at this or higher dose levels. This NOAEL for chronic toxic effects is below the NOAELs for reproductive effects. Thus, doses at or below the RfD will be below the level of concern for reproductive effects.

The contamination of technical grade picloram with hexachlorobenzene can be quantitatively considered to a limited extent. The U.S. EPA has derived an RfD and cancer potency parameter for hexachlorobenzene. Based on the levels of contamination of technical grade picloram with these compounds and the relative potencies of these compounds to picloram, this contamination is not significant in terms of potential systemic toxic effects. This assessment, however, does not impact the potential carcinogenicity associated with hexachlorobenzene and this risk, based on the U.S. EPA's cancer potency parameter, is quantitatively considered in the risk

characterization.

Risk Characterization – Typical exposures to picloram do not lead to estimated doses that exceed a level of concern. For workers, no exposure scenarios, acute or chronic, exceeds the RfD even at the upper ranges of estimated dose. 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 picloram into a very small pond. Even this exposure scenario results in only a small excursion above the chronic 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. Thus, based on the available information and under the foreseeable conditions of application, there is no route of exposure or scenario suggesting that workers or members of the general public will be at any substantial risk from longer-term exposure to picloram.

Irritation and damage to the eyes can result from exposure to relatively high levels of picloram (i.e., placement of picloram directly onto the eye) and repeated exposures to picloram can lead to skin sensitization. From a practical perspective, eye irritation and skin sensitization are likely to be the only overt effects as a consequence of mishandling picloram. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling and application of picloram.

Based on the standard assumptions used in this and other Forest Service risk assessments, the contamination of picloram with hexachlorobenzene does not appear to present any substantial cancer risk even at the upper ranges of plausible exposure. Administratively, the Forest Service has adopted a cancer risk level of one in one-million (1÷1,000,000) as a trigger that would require special steps to mitigate exposure or restrict and possibly eliminate use. Based on relatively conservative exposure assumptions and at the typical application rate of 0.35 lb a.e. picloram/acre, the highest cancer risk is about 0.7 in one-million – i.e., for workers involved in broadcast ground spray. At the upper range of the application rate – i.e., 1 lb a.e./acre – this risk would scale to 2 in one-million. This is not, however, an appropriate approach for risk scaling because it would assume that the same worker applies picloram at an atypically high application rate over a lifetime. For members of the general public, the highest cancer risk is estimated at 0.1 in one-million at the typical application rate of 0.35 lb a.e./acre. Scaled to an application rate of 1 lb/acre, the cancer risk would be about 0.3 in one-million.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification – The toxicity of picloram is relatively well characterized in experimental mammals but few wildlife species have been assayed relative to the large number of nontarget species that might be potentially affected by the use of picloram. Within this admittedly substantial reservation, picloram appears to be relatively non-toxic to terrestrial animals but is moderately toxic to aquatic animals, particularly fish.

The assessment of the toxicity of picloram to nontarget terrestrial animals is based almost exclusively on toxicity studies using experimental mammals (i.e., the same studies used in the human health risk assessment). Acute oral LD_{50} values for picloram are in the range of 3000 to

5000 mg/kg body weight and NOAEL from chronic studies range from 7 mg/kg/day to 20 mg/kg/day. Some additional studies are available on birds, bees, and snails that generally support the characterization of picloram as relatively non-toxic to terrestrial animals. This assessment is supported by field studies that reported no detectable effects on mammalian or avian diversity after the application of picloram.

Picloram is a pyridine herbicide that acts as a plant growth regulator. This is to say that picloram mimics naturally occurring plant auxins or hormones in a manner that leads to uncontrolled and abnormal growth. These effects can in turn lead to gross signs of toxicity or death. The toxicity of picloram to terrestrial plants has been assayed in relatively standardized studies of seed emergence, seed germination, and post-emergence applications that have been submitted to the U.S. EPA to support the registration of picloram. Picloram is more toxic to broadleaf plants than grains or grasses. The lowest reported adverse effect (the EC_{25} for the inhibition of seed emergence in soybeans) for the potassium salt of picloram is 0.000014 kg or about 0.000012 lb a.e./acre. The highest reported NOEC in any of the terrestrial plant bioassays is about 0.4 lb a.e./acre for seedling emergence in corn.

The acute and chronic toxicity of picloram to aquatic animals has been assayed in various species of fish and invertebrates. Acute (96-hour) LC_{50} value for trout range from 0.8 mg/L to 19.3 mg/L. Bluegill sunfish and fathead minnows, common test species used in aquatic toxicity studies, appear to be less sensitive to picloram, with LC_{50} values ranging from about 15 mg/L to 55 mg/L. Two sets of longer-term (egg and fry) studies are available in trout and the results of these studies are not consistent. Studies accepted by the U.S. EPA indicate a NOEC of 0.55 mg/L in rainbow trout. An earlier series of studies of using lake trout indicate a NOEC of <0.035 mg/L. Limitations in the this earlier series of studies include the failure to use an acetone control and the failure to measure concentrations in the test solutions. An early life-stage study in the fathead minnow, yielded a NOEC of 0.71 mg a.e./L, very similar to the NOEC reported in trout. This study, however, was conducted on the triisopropanolamine salt of picloram rather than the potassium salt.

In *Daphnia*, an aquatic invertebrate commonly used in aquatic toxicity studies, the reported acute (48-hours) LC_{50} value is 68.3 (63–75) mg/L. Chronic studies in the same species using reproductive or developmental parameters identified a no-effect level at 11.8 mg/L and a lowest effect level at 18.1 mg/L. Thus, it appears that trout are more sensitive than daphnids to both the acute and chronic effects of picloram.

As with aquatic animals, the toxicity of picloram to aquatic plants varies substantially among different species. Based on the available toxicity bioassays, the most sensitive species is *Navicula pelliculosa*, a freshwater diatom, with an EC_{50} for growth of 0.94 mg a.e./L and a NOEC of 0.23 mg a.e./L. The least sensitive aquatic plants appear to be from the genus *Chlorella* (another group of freshwater algae), with EC_{50} values greater than 160 mg a.e./L. Macrophytes appear to have a sensitivity that is in the upper range of that seen in algae, with a reported EC_{50} of 164 mg a.e./L in 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 indirect 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 85 mg/kg under typical exposure conditions and up to about 859 mg/kg under more extreme conditions. Substantially lower doses are anticipated from the consumption of contaminated vegetation: up to about 6 to 9 mg/kg under typical conditions with an upper range of 17 to 27 mg/kg. 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 vertebrate from the consumption of contaminated vegetation are in the range of 0.00006 to 3 mg/kg/day. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, 0.000005 mg/kg/day to 0.0002 mg/kg/day. Based on general relationships of body size to body volume, larger vertebrates will be exposed to lower doses and smaller animals, such as insects, to much higher doses than small vertebrates under comparable exposure conditions. Because of the apparently low toxicity of picloram 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 rates considered in this risk assessment, 0.35 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 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 picloram 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 picloram is 0.05 (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 picloram is 0.001 (0.0001 to 0.004) 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 for chronic exposure is based on a NOAEL of 7 mg/kg/day from a 6-month dog feeding study. For acute exposures, a NOAEL of 34 mg/kg/day is used based on a teratogenicity study in rabbits. For birds, short term feeding studies are used to estimate an acute NOAEL of 1,500 mg/kg body weight. No adequate data are available on chronic toxicity in birds and the chronic NOAEL of 7 mg/kg/day derived for mammals is used to characterize risk. Relatively little data is available on terrestrial invertebrates and a standard LD_{50} value of >1000 mg/kg in bees is used to characterize risk in terrestrial invertebrates.

For assessing the potential consequences of exposures to nontarget plants via runoff, a NOEC of 0.000012 lb a.e./acre is used for sensitive species and a NOEC of 0.4 lb a.e./acre is used for tolerant species. For assessing the impact of drift, bioassays on vegetative vigor are used with a NOEC of 0.00021 lb a.e./acre for sensitive species and a NOEC of 0.062 lb a.e./acre for tolerant species.

Soil microorganisms may display detectable responses to picloram at relatively low concentrations and true NOEC values for effects on microorganisms are not available. For this risk assessment, a soil concentration of 1 ppm is used as benchmark dose and the potential consequences of soil contamination by picloram is considered further in the risk characterization.

The general dose-response assessment for aquatic species is characterized by substantial variability within different groups (fish, invertebrates, and plants) but few substantial difference among the different groups. In general, sensitive species have NOECs or LC_{50} values in the 0.2 to 4 mg/L range and tolerant species have NOECs or LC_{50} values in the 10 to over 100 mg/L range. Trout appear to be the most sensitive animal species, with acute LC_{50} values as low as 0.8 mg/L. The dose response assessment for aquatic species is complicated by a very low reported LOEC, 0.035 mg/L in lake trout. This is an older study that was not designed to meet current standards. Nonetheless, this study is well documented and is not discounted. A relatively low LOEC of 0.1 mg/L has also been reported in one species of macrophyte. The observed effect was a transient delay in flowering with no inhibition of growth.

Risk Characterization – Picloram is a herbicide and the most likely damage to nontarget species will involve terrestrial plants. As is the case with any herbicide, the likelihood of damage to nontarget plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential nontarget species. Sensitive plant species could be adversely affected by the off-site transport of picloram under a variety of different scenarios depending on local site-specific conditions that cannot be generically modeled. If picloram is applied in the proximity of sensitive crops or other desirable sensitive plant species, site-specific conditions and anticipated weather patterns will need to considered if unintended damage is to be avoided. More tolerant plant species are not likely to be affected unless they are directly sprayed or subject to substantial drift. A detectable inhibition of the activity of soil microorganisms is also likely at application rates used in Forest Service programs. These changes could lead to an increase in the persistence of picloram in soil and/or a more general decrease in microbial activity. That this inhibition would be associated with

detectable changes in soil productivity or other undesirable gross effects is much less certain. The potential for adverse effects on other terrestrial nontarget animal species appears to be remote. The weight of evidence suggests that no adverse effects in terrestrial animals are plausible using typical or even very conservative worst case exposure assumptions.

There is substantial variability in the toxicity of picloram to aquatic species. While this variability adds uncertainty to the dose-response assessment, it has no substantial impact on the risk characterization. None of the hazard indices for fish, aquatic invertebrates, or aquatic plants reach a level of concern.

The risk characterization for both terrestrial and aquatic species is limited by the relatively few animal and plant species on which data are available compared to the large number of species that could potentially be exposed. This limitation and consequent uncertainty is common to most if not all ecological risk assessments.

1. INTRODUCTION

Two commercial formulations of picloram, Tordon K and Tordon 22K, are used by the Forest Service in vegetation management programs. The USDA Forest Service has conducted previous risk assessments on picloram as part of environmental impact statements (USDA 1989a,b,c) and has prepared a herbicide background statement on picloram (USDA 1989d). In addition, the USDA Forest Service had a risk assessment prepared on picloram in 1999 (SERA 1999). The present document provides an update to the 1999 risk assessment for human health effects and ecological effects to support an assessment of the environmental consequences of using picloram in future Forest Service programs.

This is a technical support document and it addresses some specialized technical areas. Nevertheless an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2001). Some of the more complicated terms and concepts are defined, as necessary, in the text.

In the preparation of this risk assessment, literature searches of picloram were conducted in the open literature using PubMed, TOXLINE as well as the U.S. EPA CBI files. There is a very large body of literature on the environmental fate and toxicology of picloram. In addition to the herbicide background statement on picloram (USDA 1989d), the toxicology and environmental fate of picloram have been reviewed by the U.S. EPA (U.S. EPA 1992a,b; U.S. EPA 1994; U.S. EPA 1995a,b; U.S. EPA 1998a; U.S. EPA 1999) as well as the USDA (USDA 1995; ExToxNet 1996a). An additional review of picloram has been published by Cox (1998) and a review and reevaluation of data supporting the ecological risk assessment of picloram has been submitted to the U.S. EPA (Havens and Peacock 1995). The U.S. EPA (1995a) re-registration eligibility decision (RED) document also includes a summary of the product chemistry, mammalian toxicology, and ecotoxicology studies that were submitted by industry to the U.S. EPA as part of the registration process for this compound. Full text copies of key studies (n=64) were kindly provided by the U.S. EPA Office of Pesticide Programs. The CBI studies were reviewed, and synopses of the information that can be disclosed from these studies are included in this document.

While this document discusses the studies required to support the risk assessments, it makes no attempt to re-summarize all of the information cited in the existing reviews. 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 picloram 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 picloram 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.

Most of the calculations are relatively simple, and the very simple calculations are included in the body of the document. Some of the calculations, however, are cumbersome. For those calculations, a set of worksheets is included as an attachment to the risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on nontarget organisms. The worksheets are included at the end of this risk assessment and further documentation for these worksheets are included as Attachment 1. As detailed in Attachment 1, two versions of the worksheets are available: one in a word processing format and one in a spreadsheet format. 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.

Technical grade picloram contains hexachlorobenzene as a contaminant and hexachlorobenzene is classified as a carcinogen. Because of the importance of and level of concern for this endpoint in humans, the human health risk assessment discusses the potential effects of hexachlorobenzene in some detail and a separate subset of worksheets for hexachlorobenzene are provided at the end of this document. Again, these worksheets are provided in both a word processing format and one in a spreadsheet format.

2. PROGRAM DESCRIPTION

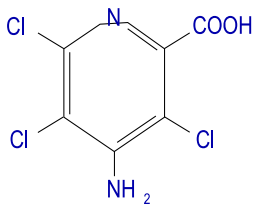
2.1. OVERVIEW

Picloram is a herbicide used in the control of a number of broadleaf weeds and undesirable brush. Picloram is used in Forest Service programs almost exclusively for the control of noxious weeds. Very minor uses include rights-of-way management and general maintenance. Tordon K and Tordon 22K are the formulations of picloram currently available and used by the Forest Service. Both formulations are produced by Dow AgroSciences as a liquid containing the potassium salt of picloram (24.4% w/v). This is equivalent to a concentration of 2 lb a.e./gallon. The remaining 75.6% of the formulation consists of inerts, including a polyglycol. The U.S. EPA has placed the polyglycol on List 3 of the inerts that may be used in the formulation of pesticides. Very little additional information is available on this compound.

The most common methods of ground application for Tordon involve backpack (selective foliar) and boom spray (broadcast foliar) operations. Mist blower application of picloram is not permitted. The Forest Service does not typically use aerial applications for picloram. Nonetheless, Tordon is registered for aerial applications and aerial applications are included in this risk assessment in the event the Forest Service may wish to consider this application method. The labeled application rates for picloram range from 0.125 to 1 lb a.e./acre. Typically, the Forest Service uses rates in the lower part of this range and some applications may be below the lower range of the labeled rate. For this risk assessment, the typical rate of 0.35 lb a.e./acre with a lower range of 0.1 lb a.e./acre is used to reflect Forest Service practice. An upper range of 1 lb a.e./acre is used to assess the consequences of using the highest labeled rate should the Forest Service need to consider this option.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Picloram is the common name for 4-amino-3,5,6-trichloropicolinic acid:



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

The only formulations of picloram used by the Forest Service are Tordon K and Tordon 22K, both of which are produced by Dow AgroSciences. Both of these are formulated as a liquid containing the potassium salt of picloram (24.4% w/v). This is equivalent to a concentration of 2 lb a.e./gallon. The remaining 75.6% of the formulation consists of inerts. The identity of all inerts 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 (Lanman 1996a,b,c). 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.

Some inerts - i.e., those listed under SARA Title III, Section 313 - are specified on the product material safety data sheets and can be publicly disclosed. On the MSDS's for Tordon K and Tordon 22K, one inert is listed as polyglycol, with a CAS No. 069029-39-6 (C&P Press 2003). On the U.S. EPA list of inerts used in pesticides (U.S. EPA/OPP 2003), the polyglycol is listed as polyoxypropylene mono(disec-butylphenyl) ether and classified as a List 3 inert. List 3 inerts designate those inerts for which the available toxicology data are insufficient to classify the the compound as of toxicologic concern (List 1), possible toxicologic concern (List 2), or of minimal concern (List 4)(U.S. EPA/OPP 2003). Additional information on this and other adjuvants is presented in Section 3.1.14.

Technical grade picloram contains hexachlorobenzene as a contaminant (U.S. EPA 1995b). Nominal or average concentrations of hexachlorobenzene are 8 ppm and the maximum concentration of hexachlorobenzene currently in technical grade picloram is 50 ppm (McMaster 1999). The impact of this contaminant and other impurities on the human health risk assessment is detailed in Section 3.1.15.

Both of the Tordon formulations are labeled for the control of a variety of broadleaf weeds, woody plants, and vines in non-crop areas. Only Torodon K is registered specifically for forestry. Tordon 22 is registered for rights-of-way and other non-cropland uses such as along road sites and fence rows (C&P Press 2003). When Tordon K is used in forest planting sites, periods of 6 to 12 months after treatment are recommended before the planting of conifers. A cautionary note on the product label indicates that legume seedlings may not grow for two years after treatments. Recommended adjuvants include non-ionic surfactants. In aerial and some ground broadcast applications, thickening agents are also recommended to reduce drift (C&P Press 2003).

2.3. APPLICATION METHODS

The most common methods of ground application for Tordon 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 acre/hour with a plausible range of 0.25–1.0 acre/hour.

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). The Tordon formulations may not be applied with a mist-blower.

Both Tordon formulations are registered for aerial applications (C&P Press 2003). Although this is not an application method that the Forest Service will typically employ for picloram, this method is covered by this risk assessment in the event that the Forest Service may need to consider aerial applications. Aerial applications may be made using helicopters. Tordon 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.

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. Application rates may be expressed in various units such as gallons of formulation per acre (used in most product labels), lb a.i. per acre (designating the amount of the potassium salt of picloram), or lb a.e. per acre (designating the amount of the picloram acid equivalents). Unless otherwise specified, all application rates and other expressions of amounts are based on acid equivalents.

Application rates of ¼ to 2 quarts Tordon/acre are recommended on the product labels and no more than 2 quarts Tordon/acre may be applied in a single growing season (C&P Press 2003). The application rates of ¼ to 2 quarts Tordon/acre are equivalent to 0.0625–0.5 gallons Tordon per acre. Given that there is 2 lbs picloram a.e./gallon in the Tordon formulations, these rates correspond to 0.125 to 1 lb picloram a.e./acre.

The use of picloram in Forest Service Programs for fiscal year 2001, the most recent year for which data are available, is summarized in Table 2-2. Picloram is used currently in Forest Service Programs primarily almost exclusively in noxious weed control (99.92%). Other minor uses (totaling about 0.1% of total use) include recreations improvement and rights-of-way management. Based on the total amount used and number of acres treated, the application rates are about 0.2 lb/acre for noxious weed control, 0.5 lb/acre for recreation improvement, and 0.25 lb/acre for rights-of-way management.

For this risk assessment, the typical application rate will be taken as 0.35 lb a.e./acre. This is about the average value of all individual applications conducted by the Forest Service in 2001 (0.3432 lbs/acre). It should be noted that this is greater than the arithmetic average of about 0.2 lbs/acre for all applications combined – i.e., the total pounds applied divided by the total acres treated.

The range of application rates will be taken as 0.1 lb a.e./acre to 1 lb a.e./acre to reflect plausible ranges that the Forest Service may use. The lower range of the application is essentially

arbitrary. Lower application rates have been reported and these reports may involve spot applications conducted sporadically over a relatively large area. The upper range of the application rate will be taken as 1 lb/acre, the maximum labeled rate. The worksheets that accompany this risk assessment are based on the typical application rate of 0.35 lb/acre rather than the full range of application rates. The consequences of varying application rates within the range of 0.1 to 1 lb/acre is considered in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

For forestry applications, mixing volumes of 5 to 25 gallons of water per acre are recommended for aerial applications. Recommended mixing volumes for ground applications range from 10 to 100 gallons of water per acre (C&P Press 2003). For this risk assessment, the extent to which a picloram formulation is 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 picloram in the applied spray). The higher the concentration of picloram, the greater the risk. For this risk assessment, the lowest dilution will be taken at 5 gallons/acre, the minimum recommended for aerial applications. The highest dilution (i.e., that which results in the lowest risk) will be based on 100 gallons of water per acre, the highest application volume recommended for ground applications. The typical dilution rate will be taken as 30 gallons/acre, approximately the geometric mean of the range recommended for ground applications [$(10\times100)^{0.5}=31.6$].

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. Forest Service analysts may use different input variables such as application rate, rainfall or slope to recalculate values in the attached worksheets in order to assess any differences in potential human health or ecological risks for site-specific projects.

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.] As illustrated in Figure 2-1 and detailed further in Table 2-3, the heaviest used of picloram occurs in the northern central regions: Region 1 (Northern) Region 2 (Rocky Mountain), and Region 4 (Inter-mountain) with a lesser amount used in Region 6 (Pacific Northwest). Only very small quantities of picloram are used in the Region 9 (Eastern) and Region 8 (Southeastern).

Picloram is used extensively in agriculture. A summary of the agricultural use of picloram is presented in Figure 2-3 (USGS 1998). These use statistics are for 1992, the most recent year for which data are available. As indicated in this figure, over 1,700,000 lbs of picloram are applied to crops annually, primarily to pasture, with minor uses including hay, wheat, grains, flax, oats, and barley. Picloram is used for agriculture in the same areas in which the use by the Forest Service is predominant. In addition, substantial amounts of picloram are used in the south central and south western areas of the United States. As noted in Table 2-3, the total annual use

of picloram by the Forest Service for 2001 is about 12,900 lbs, which is 0.76 percent of the agricultural use. While the use of picloram by the Forest Service is not trivial, this use is less than that of agricultural uses by a factor of over 130. Thus, there is no basis for asserting that Forest Service programs will substantially contribute to general concentrations of picloram nationally. The potential for local contamination of environmental media by the use of picloram in Forest Service programs is discussed in detail in the human health risk assessment (Section 3) and the ecological risk assessment (Section 4).

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview. The toxicity of picloram to experimental mammals has been very well-characterized. Most of the studies have been conducted in support of the registration of picloram and are summarized in the U.S. EPA re-registration eligibility decision document. Picloram has a low order of acute toxicity, with acute oral LD_{50} values in the range of 3000 to 5000 mg/kg body weight. Picloram can cause irritation to the eyes. Although picloram is not a strong skin irritant, repeated dermal exposures may lead to skin sensitization.

In chronic toxicity studies, the most sensitive effect for picloram in mammals involves effects on the liver. The current U.S. EPA RfD is based on a two-year feeding study in male and female Fischer rats in which picloram acid was administered at dietary concentrations that resulted in daily doses of 20, 60, and 200 mg/kg/day. The only statistically significant observations included an increase in liver size and an alteration in the staining properties of centrilobular hepatocytes in the 60 and 200 mg/kg/day dose groups. Dogs appear to be somewhat more sensitive to picloram than rats. In a six month feeding study in which male and female beagle dogs were administered picloram at levels that resulted in average daily doses of 0, 7, 35, and 175 mg/kg/day, the two higher dose levels resulted in increase in absolute and relative liver weight in two males and changes in liver enzyme activity.

Although technical grade picloram has been subject to several chronic bioassays for carcinogenicity and none of the bioassays have shown that picloram has carcinogenic potential, technical grade picloram does contain hexachlorobenzene, a compound that has shown carcinogenic activity in three mammalian species and has been classified as a potential human carcinogen by the U.S. EPA. Thus, this effect is considered both qualitatively and quantitatively in this risk assessment.

3.1.2. Mechanism of Action. While the mechanism of action of picloram in plants is well understood (Section 4.1.2.4), any specific mechanism of action in humans or experimental animals is unclear. As discussed in Section 3.1.5, the most sensitive effect of picloram in mammals appears to involve effects on the liver. At physiologic pH, picloram will be predominantly in the anion (acid) form and the liver does have a non-specific anion active transport system (Moslen 1996). It seems unlikely, however, that this has a substantial impact on the sensitivity of the liver to picloram because other organs, particularly the kidney, also have extremely efficient anion active transport systems (Goldstein and Schnellmann. 1996). The liver also has a major involvement in the metabolism of many chemicals, both naturally occurring and synthetic. Picloram, however, is not metabolized substantially by the liver or other organ (Section 3.1.15) and thus there is not basis for asserting that metabolic activation could account for the apparent sensitivity of the liver to picloram.

3.1.3. Kinetics and Metabolism. The oral absorption kinetics of picloram in humans has been studied by Nolan et al. (1984), who administered picloram in about 100 mL of grape juice to six

male caucasian volunteers at doses of 0.5 and 5.0 mg/kg. The compound was taken orally in grape juice and the investigators report that picloram has a bitter taste that is not masked by grape juice. The average body weights of the volunteers was 78.5 kg. Thus, the concentrations of picloram in the grape juice were about 392.5 mg/L (0.5 mg/kg × 78.5 kg ÷ 0.1L) and 3925 mg/L (5 mg/kg × 78.5 kg ÷ 0.1L). Taste thresholds for picloram in water or other liquids have not been encountered in the literature. The absorption and elimination kinetics of picloram in the human volunteers was described by a two compartment model and the average oral first order absorption rate coefficient was about 2 $hour^{-1}$. The elimination kinetics of picloram by humans follows a two-compartment model with halftimes of about 1 and 19 hours. Over 75% of the administered picloram was eliminated after 6 hours and over 90% of the administered dose was eliminated after 72 hours (Nolan et al. 1984).

Biphasic elimination kinetics have been observed in rats, dogs, and cattle (U.S. EPA 1992b). Based on the plateau principle (e.g., Goldstein et al. 1974; O'Flaherty 1981), the concentration at infinite time (C_∞) relative to the concentration after the first treatment (C_0) may be calculated as:

$$C_\infty \div C_0 = 1 \div (1 - e^{-k\,\Delta t})$$

where, k is the elimination rate in units of reciprocal time and Δt is the time interval between treatments. The terminal halftime of 40 hours reported by Nolan et al. 1984 corresponds to an elimination rate of 0.017 $hours^{-1}$ [$k = \ln(2) \div t_{1/2}$]. Assuming an exposure interval of 1 day (24 hours), the maximum accumulation of picloram in humans would be expected to be about a factor 3:

$$1 \div (1 - e^{-0.017 \times 24\ \text{hours}}) = 2.94$$

Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared to an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies in animals. Thus, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which picloram is likely to be absorbed from the surface of the skin. Two types of dermal exposure scenarios are considered: immersion and accidental spills. As detailed in SERA (2001), the calculation of absorbed dose for 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. 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 dermal absorption of picloram in humans was also studied by Nolan et al. (1984). A dose of 2 mg/kg was applied to the back of each volunteer (over about a 1000 cm^2 area) and the volunteers were instructed to shower 12 to 14 hours after application. An average proportion (P) of 0.0018 of the applied dose was excreted by 6 human volunteers over a 72 hour period (Nolan

et al. 1984, Table 1, column 3). Among the 6 volunteers, proportion of the dose excreted in the urine ranged from 0.0004 to 0.0048. As with the oral absorption kinetics, Nolan et al. (1984) used a two compartment model to describe the elimination kinetics of picloram. Unlike the study of the oral absorption kinetics, however, the low dermal absorption of picloram prevented the direct estimate of the kinetic parameters from the dermal phase of the study and the group average kinetic parameters for excretion from the oral study were used to estimate dermal absorption rates.

Nolan et al. (1984) report an average first-order dermal absorption rate 0.056 $hour^{-1}$ with a range of 0.031 $hour^{-1}$ to 0.075 $hour^{-1}$ (Nolan et al. 1984, Table 1, column 6). These values, however, are not consistent with the reported recovery of picloram in the urine. Under the assumption of first-order absorption, the proportion absorbed (*P*) at time *t* is:

$$P = 1\text{-}e^{-kt}$$

Assuming rapid urinary excretion, as noted in the oral phase of the Nolan et al. (1984) study, a dermal absorption rate of 0.056 $hour^{-1}$ over a 13 hour exposure period – i.e., the central point in the showering interval – the proportion absorbed would be 0.51 or about 50%. As noted above, however, the average proportion recovering in the urine was only 0.0018 of the applied dose or about 0.2%. The reason for the discrepancy between the dermal absorption rates and the urinary recovery reported by Nolan et al. (1984) is not apparent.

By rearrangement of the above equation, an alternative absorption rate can be estimated as:

$$k = -\ln(1\text{-}P)/t$$

where *P* is the proportion absorbed and *t* is the period of exposure (e.g., Goldstein et al. 1974, p. 302). Thus, if 0.0018 of the administered dose is recovered in the urine following a 13 hour period of exposure, the first order dermal absorption rate can be estimated at about 0.00014 $hour^{-1}$:

$$ka = -\ln(1 - 0.0018)/13 \text{ hours} = 0.00014 \text{ hours}^{-1}$$

Taking the range of the proportions of the applied dose recovered in the urine, 0.0004 to 0.0048 (Nolan et al. 1984, Table 1, column 3), the range of dermal absorption rates may be calculated as 0.00003 $hour^{-1}$ to 0.0004 $hour^{-1}$.

By comparison, the first-order dermal absorption rate estimated from the molecular weight and octanol-water partition coefficient of picloram is 0.0013 $hour^{-1}$ with a range of 0.00051 to 0.0035 $hour^{-1}$ (Worksheet B03). The central estimate is higher than the value based on the Nolan et al. (1984) data by about a factor of about 9 [0.0013 $hour^{-1}$ ÷ 0.00015 $hours^{-1}$ = 8.66].

For this risk assessment, the estimates based on the study by Nolan et al. (1984) are used. The Nolan et al. (1984) study appears to have been properly conducted and there is no basis for using the much higher estimated dermal absorption rates from Worksheet B03.

3.1.4. Acute Oral Toxicity. Standard acute toxicity studies, required by the U.S. EPA for pesticide registration, have been conducted as are summarized in U.S. EPA (1995b). These studies have been obtained and reviewed in the preparation of this risk assessment. U.S. EPA (1995b) cites an LD_{50} value in excess of 5000 mg/kg for male rats for picloram acid (Jeffrey 1987a) as well as the potassium salt of picloram as Tordon K salt liquor, an intermediate in the manufacture of picloram (Jeffrey et al. 1987e). Female rats appear to be somewhat more sensitive, with LD_{50} values of 4012 mg/kg (95% CI 3091-6654 mg/kg) for picloram acid (Jeffrey 1987a) and 3536 mg/kg for the potassium salt of picloram, again as Tordon K salt liquor (Jeffrey et al. 1987e). Based on the Tordon 22K formulation, however, there is no apparent difference in sensitivity between male and females rats, with no mortality or signs of toxicity over a two-week observation period at an acute dose of 5,000 mg/kg, expressed as the formulation (Jeffrey et al. 1987g).

In a review, Cox (1998) interpreted to the data of Hayes et al. (1986) as suggesting that the acute mammalian toxicity is approximately 5-fold lower for female rats and several fold lower for male rats (LD_{50} values of 690 mg/kg and 950 mg/kg, respectively). These results, however, were based on tests using doses of unneutralized potassium picloram solution (pH>11) (Hayes et al. 1986). U.S. EPA (1992b) concluded that the relatively low LD_{50} values obtained by Hayes et al. (1986) compared to the results of other investigators "*is probably due in part to the extreme alkalinity of the dosing solution*" (U.S. EPA 1992b, page V-3).

3.1.5. Subchronic or 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) and immune system (Section 3.1.7), development or reproduction (Section 3.1.8), and carcinogenicity or mutagenicity (Section 3.1.9). This section encompasses the remaining signs of general and non-specific toxicity.

Although some subchronic dermal toxicity studies have been conducted on picloram (Section 3.1.11), most of the subchronic and chronic toxicity studies on picloram have involved oral exposures. While these studies are summarized in the RED (U.S. EPA 1995b), more detailed summaries are given in various U.S. EPA reports that document the RfD for picloram (U.S. EPA 1992c, 1994, 1999).

The most sensitive effect for picloram in mammals involves effects on the liver. The current U.S. EPA RfD (Section 3.3.2) is based on a two-year feeding study in male and female Fischer rats (50 rats/sex/dose) in which picloram (acid) was administered at dietary concentrations that resulted in daily doses of 20, 60, and 200 mg/kg/day (Landry et al. 1986). Interim sacrifices

(10 rats/sex/dose) were made at 6-months and 1-year. At the end of the two-year exposure, the only statistically significant observations included an increase in liver size and an alteration in the staining properties of centrilobular hepatocytes in the 60 and 200 mg/kg/day dose groups. Both of these effects were more pronounced in males than in females. Increased liver weights as well as slight increases in the size and pallor of centrilobular hepatocytes were also seen in the 6-month and 12-month interim sacrifices. While the U.S. EPA has classified 60 mg/kg/day as the LOAEL for this study (U.S. EPA 1992b, 1999), the U.S. EPA/OPP RfD workgroup (U.S. EPA 1994) "*...felt that the LOAEL might have been higher*". In other words, while effects were seen at 60 mg/kg/day, the magnitude and severity of these effects were not regarded with substantial concern by the workgroup.

Similar effects on the liver have been noted in a 6-month dog feeding study (Barna-Lloyd et al. 1982). In this study, male and female beagle dogs were administered picloram (acid) in the diet at levels that resulted in average daily doses of 0, 7, 35, and 175 mg/kg/day. At the two higher dose levels, increases were noted in absolute and relative liver weight in two males and changes in liver enzyme activity were noted at the highest dose level. Additional effects included decreased food consumption and decreased body weight gain. As discussed further in Section 3.3.2, this study served as the based for the previous U.S. EPA RfD on picloram.

As reviewed in some detail by U.S. EPA (1992b), increased liver weight as well as changes in the appearance of the liver have also been observed in studies in mice as well as other studies in rats and dogs. There is very little evidence, however, that picloram is likely to impact other organs. At very high doses (i.e., 370 and 740 mg/kg/day) 80-week dietary exposures to picloram induced a number of different gross effects in rats including dermatitis accompanied by changes in hair coats and alopecia, diarrhea, abdominal distention, discolored urine, and vaginal bleeding. Pathological changes were also noted in the parathyroid, thyroid, and testes but not at frequencies that were statistically significantly different from control animals.

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 picloram. At high doses that produce a broad spectrum of toxicologic effects, clinical signs of acute picloram poisoning include ataxia, tremors, convulsions, and weakness (U.S. EPA 1992b). These reports, however, do not implicate picloram as a direct neurotoxicant.

No studies designed specifically to detect impairments in motor, sensory, or cognitive functions in animals or humans exposed picloram have been reported in the open literature or in the listing of studies submitted to the U.S. EPA to support the registration an re-registration of picloram.

Specifically, the U.S. EPA/OPTS (2003) has standard protocols for a number of types of neurotoxicity studies including a neurotoxicity screening battery (Guideline 870.6200), acute and 28-day delayed neurotoxicity of organophosphorus substances (Guideline 870.6100). Neither of these types of studies have been conducted on picloram and the U.S. EPA/OPP (1995b) specifically states that such studies are not required. This is not surprising, since the undertaking of such studies on a substance such as picloram, for which the clinical and experimental toxicology experience provides no reason to suspect a direct neurotoxic potential, would be highly unusual.

3.1.7. Effects on Immune System. There is very little direct information on which to assess the immunotoxic potential of picloram. The only studies specifically related to the effects o picloram on immune function are skin sensitization studies conducted on picloram (Section 3.1.11). While these studies provide support for asserting that picloram may cause skin sensitization, they provide no information useful for directly assessing immune suppressive potential of picloram.

A commercial formulation of picloram and 2,4-D, Tordon 202C, has been shown to inhibit immune function in mice (Blakley 1997). The design of this study does not permit the determination of which agent caused the immune response or whether the immune response was attributable to a toxicologic interaction of the two herbicides. This formulation is not used in Forest Service programs.

3.1.8. Effects on Endocrine System. In terms of functional effects that have important public health implications, effects on endocrine function would be expressed as diminished or abnormal reproductive performance. This issue is addressed specifically in the following section (Section 3.1.9). Mechanistic assays are generally used to assess the potential for direct action on the endocrine system (Durkin and Diamond 2002). Picloram, however, has not been tested for activity as an agonist or antagonist of the major hormone systems (e.g., estrogen, androgen, thyroid hormone). Thus, all inferences concerning the potential effect of triclopyr on endocrine function must be based on inferences from standard toxicity studies.

A two-generation reproduction study of picloram (K salt) in CD rats reported no endocrine effects at doses as high as 1000 mg/kg/day (Breslin et al. 1991, as reviewed by U.S. EPA 1995b). Endocrine effect endpoints examined in this study included reproductive outcomes, histopathological examination of tissues. In this study, renal effects and increased body weight gain were observed at 1000 mg/kg/day (i.e., the maximum tolerated dose was tested). Of the other studies reviewed in this risk assessment, no evidence for picloram producing direct effects on the endocrine system was found. As noted above, however, picloram has not been specifically tested for activity as an agonist or antagonist of the major hormone systems.

3.1.9. Reproductive and Teratogenic Effects. The potassium salt of picloram has been tested for teratogenic in rats and rabbits and reproductive effects in rats. None of these studies have

been published in the open literature and all were submitted to U.S. EPA (1992b, 1995b; 1999) in support of the registration or reregistration of picloram.

In an oral gavage study with the potassium salt of picloram, doses of 0, 34, 172, and 344 mg a.e./kg/day were administered to New Zealand rabbits from days 6 to 18 of gestation (John et al. 1984). No effects were noted on offspring at the highest dose tested. The only effects noted on the dosed adults was decreased body weight, which occurred at 172 mg a.e./kg/day with a NOAEL of 34 mg a.e./kg/day. Another gavage teratology study on the potassium salt of picloram has been conducted in rats at doses of 0, 30, 150, 298 mg a.e./kg/day on days 6-15 of gestation (Schroeder 1990). The only effect seen in this study was excessive salivation in dams at 298 a.e./kg/day with a corresponding NOAEL of 150 mg a.e./kg/day. No adverse reproductive effects were noted. Other teratology studies summarized in various reviews by U.S. EPA (1992b, 1995b; 1999) involve salts or esters of picloram that are not used in Forest Service programs. In addition to these teratology studies, a two-generation reproduction study has been conducted on picloram acid. In this study, male and female rats were administered picloram in the diet at levels corresponding to doses at 0, 20, 200, or 1000 mg/kg/day. Histopathological effects on the kidney as well as other signs of kidney damage were noted at 1000 mg/kg/day. There were, however, no effects on reproductive performance (Breslin et al. 1991).

As with potential effects on the immune system (Section 3.1.7), there may be greater concern for mixtures of picloram and 2,4-D. Tordon 202c, a commercial formulation of picloram and 2,4-D, has been associated with adverse reproductive effects in mice (Blakley et al. 1989a,b,c). More recently, Oakes et al. (2002b) reported a statistically significant reduction in absolute and relative testicular weight (17% and 26%, respectively) in male Sprague Dawley rats exposed to Tordon 75D (75 g a.e./L picloram and 300 g a.e./L 2,4-D) by gavage 5 days/week for 9 weeks. The reduction in testicular weight occurred in the absence of adverse reproductive effects (Oakes et al. 2002a). The dose of Tordon 75D associated with a statistically significant reduction in testicular weight was 37.5 mg/kg, the NOAEL was 18.7 mg/kg (Oakes et al. 2002b). Exposure to Tordon 75D did not result in any evidence of male-mediated birth defects (Oakes et al. 2002a). Again, this formulation of 2,4-D and picloram is not used in Forest Service programs.

3.1.10. Carcinogenicity and Mutagenicity. Picloram has been tested for mutagenicity in a number of different test systems and has been assayed for carcinogenic activity in rats and mice. A review and detailed evaluation of the mutagenicity assays on picloram by U.S. EPA (1992b) concluded that:

> No compelling evidence of a mutagenic effect in relevant biological systems was uncovered. Although picloram at a single reported dose was mutagenic in *S. coelicolor*, the weight of evidence from well-conducted microbial (Ames test), mammalian cell, and *Drosophila* mutagenicity studies tends to support the conclusion that picloram does not possess mutagenic activity (U.S. EPA 1992b, pp. V19 to V20).

Some additional studies have reported mutagenic activity in assays using higher plants. Mohammed and Ma (1999) reported dose dependent increase in *Tradescantia* micronucleus formation. Tomkins and Grant (1976) reported that picloram treatment produced a statistically significant increase in the frequency of chromosome aberration in *Pastinaca sativa* growing in normal field conditions.

The Health Effects Division Carcinogenicity Peer Review Committee of the U.S. EPA Office of Pesticides has reviewed the carcinogenicity data on picloram acid as well as the potassium salt of picloram and has classified these agents as Group E (no evidence of carcinogenicity) based on the lack of carcinogenic activity in rats and mice (U.S. EPA 1999).

In the past, some commercial preparations of picloram were formulated as the isooctyl ester of picloram. The compound used to produce this ester (ethylhexyl phthalate) is a potential carcinogen (U.S. EPA 1994). Formulations of picloram as the ethylhexyl ester are not used by the Forest Service.

Technical grade picloram is contaminated with hexachlorobenzene, a compound classified as a potential carcinogen by the U.S. EPA (1997). A recent review of the extensive toxicity data on hexachlorobenzene is available from ATSDR (2002). As discussed further in Section 3.1.15.1, the risk of cancer from this contaminant is considered both qualitatively and quantitatively in this risk assessment.

3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes). As part of the herbicide registration process, standardized tests for skin and eye irritation as well as dermal sensitization are required and have been summarized in the RED for picloram (U.S. EPA 1995b). These data suggest that picloram exposure produces substantial, but temporary eye injury (Berdasco 1990a; Jeffrey 1987d). Both picloram acid and the potassium salt of picloram, which is contained in the formulations used by the Forest Service, are classified as moderate eye irritants (Category III) but as non-irritant to the skin (Category IV).

Tordon 22K (Gilbert 1996c) as well as a formulation mixture of picloram and 2,4-D (Tordon 101 M, Gilbert 1996a) noted transient skin irritation in standard acute dermal studies . Haut and Bell (1997) reported that Tordon 22K (20.6% picloram) produced a delayed hypersensitivity reaction in Hartley guinea pigs (8/10 animals exhibited a positive response after 48 hours). Haut and Bell (1997) used 0.4 mL of a 75% solution of Tordon 22K in water, during induction phase, and 0.4 mL of 50% solution of Tordon 22K in water, during the challenge phase. Other delayed hypersensitivity testing with lower concentrations of picloram (acid) in combination with 2,4-D found no dermal sensitization (Jeffrey 1987b; Gilbert 1996b; Berdasco 1990c).

3.1.12. Systemic Toxic Effects from Dermal Exposure. The toxicity studies summarized in the RED for picloram (U.S. EPA 1995b) indicate that dermal exposure to 2000 mg/kg picloram acid or the potassium salt of picloram was not associated with any signs of systemic toxicity in rabbits based on standard acute/single application bioassays with 14-day observation periods. In

general, dermal LD_{50} values are higher than oral LD_{50} values (e.g., Gaines 1969). Since the reported acute oral LD_{50} values of picloram are all 5000 mg/kg or greater, the lack of toxic effects at dermal doses of up to 2000 mg a.e./kg/day in New Zealand White rabbits (Jeffrey 1987c) is to be expected. In a test of Tordon K salt liquor (38.8% a.i., 33.4% a.e.) in New Zealand rabbits, no signs of toxicity were observed over a 2-week period after the application of 2000 mg/kg formulation (about 668 mg a.e./kg)(Jeffrey et al. 1987f). Similarly, no signs of toxicity were observed in New Zealand White rabbits after a dose of 2000 mg/kg Tordon 22K (20.36% a.e.), equivalent to about 407 mg a.e./kg (Jeffrey et al. 1987).

In addition to the acute dermal studies, a 21-day dermal toxicity assay of the potassium salt of picloram has been conducted in New Zealand white rabbits at doses of 0, 65, 217, and 650 mg a.e./kg/day, five days/week, for three weeks. No systemic toxic effects were observed (U.S. EPA 1995b). Another 21-day repeat dermal exposure study of XRM-5179 (mixture containing 2.86 % picloram and 10.71% 2,4-D) found localized dermal irritation but no signs of systemic toxicity were noted based on clinical signs, body weights, clinical pathology, organ weights, gross pathology, or histology (Mizzell et al. 1990).

3.1.13. Inhalation Exposure. Picloram is relatively non-volatile (Table 2-2). Acute aerosol inhalation toxicity data from tests of Tordon 22K (24.1% picloram acid) in Fisher 344 rats reported no deaths among 10 rats (5/sex) that were exposed to 8.11 mg Tordon 22K/L (equivalent to 1.95 mg/L picloram acid) respirable air for 4 hours (MMAD = 1.74 m). No clinical signs were noted during exposure or during the two-week post exposure period, body weights were not significantly different from unexposed controls, and no gross abnormalities were noted on necropsy (McGuirk and Cieszlak 1996). These results are consistent with an earlier report of no toxic effects resulting from acute inhalation exposure to aerosolized picloram acid (Streeter et al. 1987a). Streeter et al. (1987a) exposed F344 rats (5/sex) to a time-weighted average concentration of 35.1 mg/m^3 picloram acid for 4 hours (the highest aerosol concentration attainable; MMAD = 7.96 μ, GSD = 3.59). All animals appeared normal during the two-week post exposure observation period, with one rat showing porphyrin staining around its nares on day 2. Body weights were not significantly different from unexposed controls, and no gross abnormalities were noted on necropsy (Streeter et al. 1987a). Tordon K salt liquor (38.8% a.i., 33.4% a.e.) caused a transient decrease in body weight in male rats after a four hour exposure to a concentration of 1.63 mg/L as formulation (0.54 mg a.e./L). No significant decrease in body weight were noted in female rats (Streeter et al. 1987b). Similarly, inhalation exposure to a nominal concentration of 18.3 mg/L Tordon 22 K (with a TWA exposure concentration of 0.65 mg/L) resulted in only transients decreases in body weight in male and female rats (Streeter et al. 1988).

3.1.14. Adjuvants. As indicated in Section 2, the commercial formulation of picloram used by the Forest Service is in the form of the potassium salt of picloram. Both of the Tordon formulations also contain Polyglycol 26-2 (CAS No. 069029-39-6) (C&P Press 1998). This compound is classified by the U.S. EPA (2003) as a List 3 inert. In other words, there is insufficient information to categorize this compound as either hazardous (Lists 1 or 2) or

non-toxic (List 4). Notwithstanding this classification, surfactants are surface active agents that can disrupt cellular membranes and lead to a number of different adverse effects (e.g., Warisnoicharoen et al. 2003). In an *in vitro* study on oxidative phosphorylation in submitochondrial particles derived from a marine algae, Oakes and Pollak (1999) noted that a commercial preparation of 2,4-D and picloram that contained Polyglycol 26-2 as well as Polyglycol 26-2 both inhibited oxidative function in the submitochondrial preparations at a concentration of about 0.01%. While this study clearly indicates that Polyglycol 26-2 will impact mitochondrial function *in vitro*, the implications for potential effects in humans at plausible levels of exposure are not apparent.

Other inerts used in Tordon K and Tordon 22K have been publicly disclosed by Northwest Coalition for Alternatives to Pesticides (http://www.pesticide.org/FOIA/picloram.html). These include emulsified silicone oil (CAS No. 63148-62-9), ethoxylated cetyl ether (CAS No. 9004-95-9), and potassium hydroxide (CAS No. 1310-58-3). All of these compounds are classified by U.S. EPA (2003) as List 4B, inerts of minimal concern. Potassium hydroxide is a GRAS (generally recognized as safe) compound and is approved as an indirect food additive (Clydesdale 1997). Both formulations also contain water as an inert.

The limited toxicity data on formulations of picloram do not suggest any substantial differences between the toxicity of the formulations and the toxicity of picloram when expressed in units of acid equivalents. Dow Chemical Co. (1970) specifically compared the acute oral toxicity of picloram (98.5% a.e.) to a Tordon formulation (22% a.e.). The acute oral LD_{50} in rats for the formulation was 8.2 mg a.e./kg and the corresponding LD_{50} for the formulation is given as approximately 10 mg a.e./kg (Dow Chemical Co. 1970).

3.1.15. Impurities and Metabolites. Virtually no chemical synthesis yields a totally pure product. Technical grade picloram, as with other technical grade products, undoubtedly contains some impurities. To some extent, concern for impurities in technical grade picloram is reduced by the fact that the existing toxicity studies on picloram 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.

An exception to this general rule involves carcinogens, most of which are presumed to act by non-threshold mechanisms. Because of the non-threshold assumption, any amount of a carcinogen in an otherwise non-carcinogenic mixture may pose a carcinogenic risk. This is the situation with picloram. As indicated in Section 2, technical grade picloram contains hexachlorobenzene. Nominal or average concentrations of hexachlorobenzene are 8 ppm and the maximum concentration is 50 ppm. The U.S. EPA has classified hexachlorobenzene as a probable human carcinogen for which the data are adequate to consider risk quantitatively (U.S. EPA 1997). While a detailed review of hexachlorobenzene is beyond the scope of this risk assessment, adequate information is available on hexachlorobenzene to quantify the carcinogenic risk associated with the use of picloram (ATSDR 2002). This is detailed further in Section 3.3.

As with contaminants, the potential effect of metabolites on a risk assessment is often encompassed by the available *in vivo* toxicity studies under the assumption that the toxicologic consequences of metabolism in the species on which toxicity studies are available will be similar to those in the species of concern (i.e., humans). Uncertainties in this assumption are encompassed by using an uncertainty factor in deriving the RfD (Section 3.3) and may sometimes influence the selection of the study used to derive the RfD.

As reviewed by U.S. EPA (1992b), the metabolism of picloram has been studied in several mammalian species and there is no indication that picloram is extensively metabolized. In the environment, however, picloram may undergo decarboxylation by microorganisms, photolysis, or pyrolysis and this may impact the assessment of the toxicity to some nontarget species (Section 4.1.2.5). There are no studies, however, on the toxicity of this environmental metabolite to mammals.

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 0.35 lb/acre. The consequences of using the maximum application rate, 1 lb/acre, are discussed in the risk characterization. For both workers and members of the general public, the upper ranges of all acute exposures are below 1 mg/kg and most exposures are much lower. The highest modeled exposure is about 0.7 mg/kg and is associated with the consumption of contaminated water by a child following an accidental spill of picloram into a small pond. The upper ranges of non-accidental acute exposure scenarios for members of the general public are associated with doses from about 0.00002 to 0.07 mg/kg. The highest dose estimates for non-accidental exposure scenarios are associated with the consumption of contaminated vegetation or fish. Exposures from dermal contact or drinking contaminated water are likely to be much lower.

General exposure assessments for workers are in the range of exposures modeled for the general public. For workers, three types of application methods are modeled: directed ground, broadcast ground, and aerial. Central estimates of exposure span a relatively narrow range: 0.005 to 0.008 mg/kg. The upper ranges of exposures are also similar for the different groups of workers: 0.03 to 0.05 mg/kg/day. All of the accidental exposure scenarios for workers involve dermal exposures. Because picloram is not readily absorbed across the skin, 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.

Hexachlorobenzene is a contaminant in technical grade picloram. The average concentration of hexachlorobenzene in technical grade picloram is 8 ppm and the maximum concentration is 50 ppm. For all exposure assessments detailed in this risk assessment, the average concentration of 8 ppm is used. The impact of the 50 ppm level is detailed in the risk characterization. Hexachlorobenzene is ubiquitous and persistent in the environment. The major sources of general exposure for the public to hexachlorobenzene involve industrial emissions, proximity to hazardous waste sites, and the consumption of contaminated food. Virtually all individuals are exposed to hexachlorobenzene and virtually all individuals have detectable concentrations of hexachlorobenzene in their bodies. Based on current concentrations of hexachlorobenzene in environmental media and food, daily doses of hexachlorobenzene (i.e., background levels of exposure) are in the range of 0.000001 (1×10^{-6}) mg/kg/day. Based on the amount of hexachlorobenzene in picloram and the amount of picloram used in Forest Service programs, the use of picloram by the Forest Service will not substantially contribute to any wide-spread increase of ambient levels of hexachlorobenzene. Nonetheless, the potential impact of local contamination is considered for workers as well as for several acute and chronic exposure scenarios for members of the general public. For both workers, the upper range of longer term exposure scenarios result in dose estimates of about 2×10^{-7} mg/kg/day to 4×10^{-7} mg/kg/day, below general background levels of exposure by about a factor of 2 to 5. For members of the general public, the upper range of longer term exposure scenarios are about 1×10^{-10} mg/kg/day to 2×10^{-8} mg/kg/day, below general background levels of exposure by about a factor of 50 to 10,000. The upper range of estimated doses associated with acute exposure scenarios for both

workers and members of the general public are about 0.002 mg/kg/day, higher than background levels of exposure by about a factor of 2000.

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 worker as well as members of the general public are detailed in the worksheets on picloram that accompany this risk assessment [WPWS 03-43-16-01]. Detailed documentation for these worksheets is presented in presented in SERA WSD 01-2.04, *Documentation for Worksheets Version 2.04 - Human Health and Ecological Risk Assessments*, dated February 25, 2003. A copy of this documentation 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 picloram 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 picloram 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 0.35 lbs a.e./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. 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).

The specific assumptions used for each application method are detailed in worksheets C01a (directed foliar), C01b (broadcast foliar), and C01c (aerial). In these 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 ranges for the amounts handled per day are calculated as the product of the range of acres treated per day and the application rate. Similarly, the central estimate of the daily absorbed dose is calculated as the product of the central estimate of the exposure rate and the central estimate of the amount handled per day. The ranges of the

daily absorbed dose are calculated as the range of exposure rates and the range for the amounts handled per day. The lower and upper limits are similarly calculated using the lower and upper ranges of the amount handled, acres treated per day, and worker exposure rate.

Two studies (Lavy et al. 1987; Libich et al. 1984) have been conducted on workers handling picloram that permit an estimate of worker exposure rates in terms of absorbed dose (mg/kg body weight per lb a.e. handled) and both of these studies were used to develop the exposure estimates given in SERA (2001). By far the most detailed study on worker exposure to picloram is that conducted by Lavy et al. (1987). In this study, the uptake of 2,4-D, picloram, and dichlorprop was assayed in four groups of forestry workers using four different application methods: backpack, injection bar, hypohatchet, and hack-and-squirt. In addition, for each method, uptake was studied under standard work practices (referred to as T1 in this publication) and work practices involving special precautions (referred to as T2 in this publication). The special precautions involved the use of new gloves for mixing and application, improved personal hygiene, and exposure avoidance. Absorption of the herbicides was assayed using 5 day complete urine collections. In another study, Libich et al. (1984) studied the exposure of herbicide applicators involved in electric power transmission rights-of-way maintenance to 2,4-D, dichlorprop, and picloram. Absorbed dose was estimated from daily urine sampling rather than total urine collection. Two application methods were examined: spray guns mounted on vehicles and mist blowers connected to a back pack. The spray guns were mounted either on trucks—for roadside spraying—or all terrain vehicles (ATV's)—for spraying less accessible areas. The herbicides used were Tordon 101, a formulated 4:1 mixture of 2,4-D and picloram (463 g/L) and a 1:1 mixture of 2,4-D and dichlorprop (480 g/L). For spray gun applications, the commercial product was diluted with 100 parts water. For the backpack application, the product was diluted with 16 parts water. A limitation in the comparison of this study with the study by Lavy et al. (1987) is that Libich et al. (1984) do not specify the amount of product handled. 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).

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.

As summarized in Section 3.1.11, picloram can produce substantial but transient eye injury and both picloram acid and the potassium salt of picloram are classified as moderate eye irritants. 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 picloram is not available. Thus, the Kp for picloram is estimated using the algorithm from U.S. EPA/ORD (1992), which is detailed in Worksheet A07b. The application of this algorithm to picloram, 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. As summarized in Section 3.1.3, the first-order dermal absorption rates are taken from the study by Nolan et al. (1984): an average value of 0.00014 $hour^{-1}$ with a range of 0.00003 $hour^{-1}$ to 0.0004 $hour^{-1}$. These values are included in Worksheet B05 rather than the values calculated in Worksheet B03, which are based on molecular weight and the $k_{o/w}$ for picloram.

For both scenarios, it is assumed that the contaminated skin is effectively cleaned after 1 hour and the mg of absorbed dose is divided by body weight (kg) to yield an estimated dose in units of mg chemical/kg body weight.

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 picloram. 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 E02. 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 (see 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 picloram. 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 A04.

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 picloram 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 picloram in ambient water are acute/accidental exposure from an accidental spill and longer-term exposure to picloram 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 picloram 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 picloram in a small pond is estimated to range from about 0.3 mg/L to 6 mg/L with a central estimate of about 1 mg/L (Worksheet D05).

The other acute exposure scenario for the consumption of contaminated water involves runoff into a small stream. Two monitoring studies are available in which picloram has been detected in ambient water shortly after the application of picloram at a known amount (Davis and Ingebo 1973; Michael and Neary 1993). Michael and Neary (1993) summarize monitoring data on the concentrations of picloram in surface water after the application of picloram by injection, broadcast ground, and broadcast aerial applications. Normalized for application rate, the reported peak concentrations of picloram in water were about 2 µg/L to 50 µg/L per lb/acre applied (Table 3-1). The injection data is also summarized in Michael et al. (1994) and the ground and aerial application data are detailed further in Neary et al. (1993). Both the ground and aerial broadcast application involved pellet formulations and the ground application involved a 140 meter buffer. In another study using an application rate of 10.4 kg/ha (9.3 lb/acre), the maximum concentration noted in stream water draining from the watershed was 370 µg/L, which occurred after a 6.4 cm (about 2.5 inches) rainfall (Davis and Ingebo 1973). This is equivalent to 40 µg/L per lb/acre (370 µg/L÷9.3 lb/acre). In a study by Watson et al. (1989), no picloram was detected in streams, at a limit of detection of 0.5 µg/L, after the application of picloram at rates of 0.28 kg a.e./ha (about 0.25 lb/acre) or 1.12 kg a.e./ha (1 lb/acre) in areas with loam or sandy loam soil.

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. Consequently, for this component of the exposure assessment, the monitored levels in ambient water are compared to modeled estimates 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 (2003).

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 picloram 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 (2003). 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 10 µg/L to nearly 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.

The modeled maximum concentrations are generally consistent with the available monitoring data. As noted above, the WCR of 40 µg/L per lb/acre reported by Davis and Ingebo (1973) occurred after a rainfall of about 2.5 inches. In terms of the GLEAMS modeling, in which rainfall is assumed to occur every tenth day, 2.5 inches of rain corresponds to an annual rainfall rate of about 90 inches. As noted in Table 3-3, the modeled maximum concentrations range from about 10 µg/L to 184 µg/L. The water contamination rates derived from Michael and Neary (1993) – i.e., about 2 ppb to 50 µg/L per lb/acre applied (Table 3-1) – are in the range of modeled concentrations for rainfall rates of 15 inches to 50 inches per year. The GLEAMS modeling is also consistent with the study by Watson et al. (1989), in which no picloram was detected in streams at a limit of detection of 0.5 µg/L after the application of picloram at a rate of 0.25 lb/acre in loam and 1 lb/acre in sandy loam soil. At the former site (0.25 lb/acre), a total of 431 mm of rain (about 17 inches) occurred over 1 year after application. As indicated in Table 3-3, the expected maximum concentration in the stream at 20 inches per year would be 0.6 µg/L (2.47 µg/L per lb/acre× 0.25 lb/acre) and the average expected concentration would be only about 0.015 µg/L (0.06 µg/L per lb/acre× 0.25 lb/acre). Thus, even if a sample was taken immediately after a rain, the expected concentration would be very close to the limit of detection. Watson et al. (1989) provide details on rainfall at the 1 lb/acre site (sandy loam) but indicate that only 3 mm of rain (about 0.01 inch) fell on day 3 after application and that there was insufficient "...rain to leach picloram into soil or sand" by day 7 after application. In addition, Watson et al. (1989)

indicate that this site was more heavily covered by a canopy of vegetation that may have further reduced soil percolation and subsequent contamination of the adjacent stream.

The GLEAMS scenarios do not specifically consider the effects of accidental direct spray. For example, the steam 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 × 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 runoff or percolation are generally in excess of 10 µg/L and then encompass the potential effects of accidental direct spray.

For the 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 somewhat higher than the maximum concentration at an annual rainfall rate 200 inches for clay soil and about four times the concentration of the upper range of values derived from the data in Table 3-1 (Michael and Neary 1993). 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 – i.e., annual rainfall of 15 inches.

3.2.3.4.2. LONGER-TERM EXPOSURE – The scenario for chronic exposure to picloram 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, as well as NAWQA monitoring data.

The National Water Quality Assessment (NAWQA) of the U.S. Geological Survey (USGS) has involved a large scale monitoring effort to characterize pesticides in surface and ground water. A detailed description of the USGS program may be obtained at http://water.usgs.gov/nawqa/index.html. In brief, the USGS has monitored concentrations of a large number of pesticides, including picloram, in over 50 major river basins and aquifers. The monitoring data are given separately for streams and ground water for three types of sites: agricultural land use areas, urban areas, and major aquifers or large rivers of streams. Detailed data for rivers and streams covering a period from 1992 to 1998 are available at http://ca.water.usgs.gov/pnsp/ and corresponding data for ground water are available at http://ca.water.usgs.gov/pnsp/pestgw/. A subset of the data covering a period from 1992 to 1996 is available at http://ca.water.usgs.gov/pnsp/allsum/#t1. Over the period from 1992 to 1998, picloram was detected in streams at a maximum concentration of 0.01 µg/L. The frequency of detection is extremely low . Picloram was not detected in any of the agricultural stream sites or in 31 large rivers and streams and was found in only 1 or 573 samples from 22 urban streams. Higher concentrations have been found in ground water, with a maximum concentration of 3.91 µg/L. Again, the frequency of detection is very

low: 0.17% of for agricultural land use wells with a maximum concentration of 2.2 µg/L, 0.5% for urban land use wells with a maximum concentration of 3.91 µg/L, and 0.14% for major aquifers with a maximum concentration of 0.17 µg/L.

The the NAWQA data and the GLEAMS modeling are not directly comparable. The NAWQA data may be viewed as general exposure levels that are not directly associated with a fixed application while the GLEAMS modeling is an effort to characterize, at least generically, concentrations that might be expected after applications associated with Forest Service programs. Nonetheless, the maximum concentration monitored in NAWQA, 0.01 µg/L, suggests that applications of picloram near streams may result in average yearly concentrations that are substantially higher – i.e., about 0.1 to 1 µg/L – than those generally found in the environment. On the other hand, while the application of GLEAMS does not specifically model groundwater, the average modeled concentrations in lakes – i.e., about 0.6 to 5 µg/L from Table 3-4 – are reasonably consistent with the maximum concentrations reported in NAWQA for groundwater – i.e., about 2 to 4 µg/L.

For this risk assessment, the typical WCR is taken as 1 µg/L or 0.001 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 4 µg/L or 0.004 mg/L per lb/acre. This is the highest average concentration modeled from sandy soil and is identical to the highest concentration in groundwater from NAWQA. 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 near the limit of detection 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).

Bidlack (1980a) attempted to measure the bioconcentration factor of ^{14}C-picloram in bluegill sunfish over a 28 day exposure period at concentrations of 0.1 and 1 mg/L in water. Only trace amounts of ^{14}C were recovered in fish and Bidlack (1980a) concluded that the bioconcentration factor of picloram is less than one. Similar results were obtained with channel catfish in an

aquatic microcosm study (Bidlack 1980b). Thus, the bioconcentration factor for picloram appears to be substantially less than one (USDA 1989d; U.S. EPA 1995b). For this risk assessment a bioconcentration factor of 1 L/kg is used. This assumption will over-estimate exposure but 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 picloram 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 (U.S. EPA 1996), 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 picloram 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 picloram 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 picloram 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 picloram (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 picloram 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 form the vegetation half-time of 8 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, $\mathbf{C_t}$, can be calculated based on the initial concentration, $\boldsymbol{C_0}$, as:

$$\mathbf{C_t = C_0 \times e^{-kt}}$$

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

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

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.

3.2.4. Hexachlorobenzene. As mentioned in Section 2.2, technical grade picloram is contaminated with hexachlorobenzene. The average concentration of hexachlorobenzene in technical grade picloram is 8 ppm and the maximum concentration is 50 ppm. For all exposure assessments detailed in this risk assessment, the average concentration of 8 ppm is used. The impact of the 50 ppm level is detailed in the risk characterization.

As discussed in Section 3.1.15, the potential effect of a contaminant on a risk assessment is often encompassed by the available *in vivo* toxicity studies under the assumption that the toxicologic consequences of the contaminant is encompassed by the use of technical grade material – in this case picloram containing hexachlorobenzene. This rationale cannot be applied to hexachlorobenzene, however, because hexachlorobenzene is both more persistent than picloram and because hexachlorobenzene is classified as a carcinogen (Section 3.1.15). Thus, in order to quantitatively consider the potential cancer risk from hexachlorobenzene posed by the use of technical grade picloram in Forest Service programs, separate exposure assessments are required for hexachlorobenzene. Summaries of the exposure assessments for workers and members of the general public are the hexachlorobenzene worksheets that accompany this risk assessment (Supplement 2). All worksheets mentioned in this section refer those in Supplement 2.

The following discussion of the exposure assessments for hexachlorobenzene focuses on aspects of the exposure assessments that differ substantially from those used for picloram.

3.2.4.1. Dermal Absorption – No studies have been encountered on the dermal absorption rate of hexachlorobenzene in humans. In a study using rats, Koizumi (1991) estimated a first-order dermal absorption rate coefficient of 0.0014 $hour^{-1}$. Based on empirical relationships of molecular weight and the octanol-water partition coefficient to human dermal absorption rates, central estimate of the first-order dermal absorption rate coefficient for hexachlorobenzene is 0.022 $hour^{-1}$ with a range of about 0.0047 to 0.1 $hour^{-1}$ (Supplement 2, Worksheet B03). While a case could be made for using the lower dermal absorption rate from Koizumi (1991) because it is based on an experimental measurement, the higher first-order dermal absorption rates from Supplement 2, Worksheet B03, are used in the exposure scenarios involving first-order dermal absorption for both workers (Worksheets C03a, C03b) and members of the general public (D01a, D01b, and D02). This approach is taken because of uncertainties in the application of absorption rate data from rats for exposure assessments in humans.

As with first-order dermal absorption, no measurements of dermal permeability (K_p in cm/hr) in humans have been encountered for hexachlorobenzene. As with picloram, the K_p for hexachlorobenzene is estimated using the algorithm from U.S. EPA/ORD (1992), which is detailed in Worksheet A07b and applied to hexachlorobenzene in Worksheet B04 of Supplement 2.

3.2.4.2. Acute Exposures – For all of the worker exposure assessments as well as the acute exposure assessments for members of the general public, the exposure estimates follow the same general methods used for the picloram exposure assessments, as detailed in Sections 3.2.2 and 3.2.3. The major differences in the exposure assessments for picloram and hexachlorobenzene involve lipophilicity and water solubility. Picloram is highly water soluble (430mg/L, Table 2-1). Consequently, picloram does not partition substantially into fatty tissue ($K_{o/w}$ of about 84 or less) and thus dermal absorption, binding to soil, and bioconcentration of picloram are low compared to hexachlorobenzene.

Hexachlorobenzene, on the other hand, is highly lipophilic. The $K_{o/w}$ of hexachlorobenzene is about 1,500,000 and the water solubility of hexachlorobenzene is only about 0.006 mg/L. Thus, hexachlorobenzene may be readily absorbed across the skin, will bind tightly to most soils, and will bioconcentrate in fish (ATSDR 2002). Although the amount of hexachlorobenzene in technical grade picloram is relatively low, the potential for human exposure, in terms of the proportion of the exposure dose that might be absorbed, is higher than that for picloram itself.

Because of the extremely high lipophilicity and low water solubility of hexachlorobenzene, one adjustment considered in the acute exposure assessments concerns the impact of water solubility on the dermal spill scenarios. As detailed in hexachlorobenzene Worksheets B01 and B02, the calculation of the concentration of a compound, either a herbicide or contaminant, in a solution that is applied in the field is dependent on the concentration of the compound in the formulation as well as the dilution rates for the formulation recommended by the manufacturer. For hexachlorobenzene, the range of concentrations in a field solution based on these rates can be calculated as 0.0000034 mg/mL to 0.000067 mg/mL (Worksheet B01). The upper range exceeds

the water solubility of hexachlorobenzene, which is 0.006 mg/L or 0.000006 mg/mL. Thus, following the dermal exposure guidelines proposed by U.S. EPA (1992a), the functional exposure to hexachlorobenzene would be based on the water solubility of hexachlorobenzene rather than the maximum nominal concentration. For this risk assessment, however, the nominal concentrations are used. This approach is taken both to remain protective and because the presence of adjuvants in the Tordon formulations may increase the solubility of hexachlorobenzene in the formulations and this may result in a higher water solubility of hexachlorobenzene in dilute aqueous solutions of the formulation – i.e., as in an accidental spill.

For acute exposure scenario involving an accidental spill into a small pond (Worksheets D05), both the central estimated and upper range of the concentration of hexachlorobenzene in the field solution also exceed the nominal concentration of hexachlorobenzene in water. As with the dermal exposure scenarios, and for the same reasons, these concentrations are used in the exposure assessment.

As with picloram, both the acute and chronic scenarios for the consumption of fish contaminated with hexachlorobenzene (Worksheets D07 and D10) require estimates of a bioconcentration factor (i.e., the concentration in fish divided by the concentration in water). As reviewed in ATSDR (2002), reported bioconcentration factors in fish range from about 2,000 to 20,000. For this risk assessment, the upper range of these bioconcentration factors is used in the chronic exposure scenarios. The application of a bioconcentration factor of 20,000 to the acute exposure scenario for contaminated fish (hexachlorobenzene D07) is a protective assumption. All of the bioconcentration factors reported in ATSDR (2002) involved exposure periods of at least one month. As detailed by Calabrese and Baldwin (1993, pp. 12–22), the kinetics of bioconcentration in fish are essentially identical to standard pharmacokinetic zero-order absorption and first-order elimination models (e.g., Goldstein et al. 1974). Consequently, for compounds that are extensively bioconcentrated, such as hexachlorobenzene, the levels in fish after one day will reflect bioconcentration factors that are typically much less than those seen after long-term exposures. Thus, for the acute exposure scenarios, the lower range of the bioconcentration factors reported in ATSDR (2002) is used – i.e., a BCF of 2000 L/kg.

3.2.4.3. General Considerations for Chronic Exposures – Hexachlorobenzene is ubiquitous and persistent in the environment. The major sources of general exposure for the public to hexachlorobenzene involve industrial emissions, proximity to hazardous waste sites, and the consumption of contaminated food. Virtually all individuals are exposed to hexachlorobenzene and virtually all individuals have detectable concentrations of hexachlorobenzene in their bodies (ATSDR 2002). Based on current concentrations of hexachlorobenzene in environmental media and food, daily doses of hexachlorobenzene (i.e., background levels of exposure) are in the range of 0.000001 mg/kg/day (ATSDR 2002). The major source of hexachlorobenzene release to the environment is from the manufacture of chlorinated solvents which accounts for an annual release of 70,343 to 241,311 kg (154,000 to 532,000 pounds). The presence of hexachlorobenzene as a contaminant in all pesticides containing hexachlorobenzene as a contaminant results in the release of about 17,366 kg/year (38,285 lbs/year) (ATSDR 2002). As

detailed below, only a small fraction of this amount is associated with the use of picloram in Forest Service programs.

The use of picloram by the Forest Service is currently about 13,000 lbs/year (Table 2-3) or about 5,900 kg/year [13,000 lbs × 0.4536 kg/lb = 5896.8 kg]. Given an average concentration of 8 ppm hexachlorobenzene in technical grade picloram, the amount of hexachlorobenzene released to the environment as a result of Forest Service programs using picloram is about 0.05 kg:

$$5900 \text{ kg} \times 0.000008 = 0.0472 \text{ kg}.$$

This amount represents a factor of about one in 350,000 (17,366÷0.05 = 347,320) relative to the amount of hexachlorobenzene released as a contaminant in all pesticides and a fraction of about 1 in 1.4 million (70,343 ÷ 0.05) to 1 in 4.8 million (241,311 ÷ 0.05) compared to the amount released from the manufacture of contaminated solvents. Thus, the use of picloram by the Forest Service will not substantially contribute to any wide-spread increase of ambient levels of hexachlorobenzene.

While the use of picloram by the Forest Service will not result in any general increase in environmental levels of hexachlorobenzene, this does not demonstrate that localized contamination would be insignificant. In order to better assess the potential impact of local contamination, three chronic exposure scenarios are considered quantitatively: contaminated vegetation, contaminated water, and contaminated fish.

3.2.4.4. Chronic Exposures Involving Contaminated Vegetation – Immediately after direct foliar application to vegetation, hexachlorobenzene will volatilize relatively rapidly from the surface of the vegetation and relatively little will be absorbed and available for longer-term exposures. Once hexachlorobenzene is absorbed into the soil column, however, it is relatively persistent, with reported half times in soil ranging from 3 to 6 years (ATSDR 2002). Thus, the primary concern for chronic exposures to contaminated vegetation is soil contamination with subsequent uptake by plants. This type of scenario requires estimates of long-term levels in soil as well as bioconcentration factors for terrestrial plants. The highest bioconcentration factor for the uptake of hexachlorobenzene from soil into plants is 19 (ATSDR 2002). This BCF was measured in the edible portion of carrots and is used directly for this exposure assessment (Worksheets D03 and D04). As illustrated in these worksheets, this bioconcentration factor is multiplied by the concentration of hexachlorobenzene in soil to estimate the concentration of hexachlorobenzene in the plant. The remaining methods for estimating daily dose are identical to those used for picloram.

GLEAMS is used to estimate the concentration of hexachlorobenzene in soil. As with picloram, GLEAMS simulations were conducted over a wide range of annual rainfall rates in three types of soil: clay, loam, and sand. The chemical and site specific parameters used in the GLEAMS simulations are summarized in Table 3-5. The basic pond and stream scenarios are very similar to the scenarios used for picloram except that a root zone of 12 inches is used for

hexachlorobenzene rather than the 60 inch root zone used for picloram. Most loss of hexachlorobenzene is due to runoff rather than percolation and use of a shallower root zone favors runoff (Knisel and Davis 2000, p. 28). Because of the shallow root zone, only two soil horizons are used, the top 1 inch and the remaining 11 inches. While hexachlorobenzene is extremely persistent in soil once it has become incorporated into the soil, hexachlorobenzene will rapidly volatilize from the soil surface and the relatively short halftime for the upper soil horizon is based on the study by Beall (1976) in which a very rapid decrease in hexachlorobenzene in the upper soil layer (0-2 cm or about 1 inch) was attributed to volatilization. The much longer halftimes for deeper soil layers is taken from a range of soil halftimes reported by ATSDR (2002).

The concentrations of hexachlorobenzene in soil from the GLEAMS simulations are summarized in Table 3-6. As with the corresponding tables for picloram, the concentrations are expressed as contamination rates – concentrations associated with an application rate of 1 lb/acre. Adjustments to these concentrations are made in the worksheets in which they are used.

The maximum concentrations in soil are independent of rainfall and reflect initial concentrations in soil immediately after application. Differences among soils are not remarkable. For the acute exposure assessment involving the consumption of contaminated vegetation (Worksheet D03), the highest concentration, 0.67 ppm, is used uniformly. This has no impact on the characterization of risk.

For the longer-term exposure scenario (Worksheet D04), the central estimate of the soil contamination rate is taken as 0.026 mg/kg soil per lb/acre. This is near the simulated values for all soil types over a wide range of rainfall rates. The upper range is only modestly higher, 0.031 mg/kg soil per lb/acre simulated for sandy soil at annual rainfalls of 200 or 250 inches. The lower range is taken as 0.007 mg/kg soil per lb/acre, the simulated value for clay at an annual rainfall of 250 inches.

For comparison, Beall (1976) monitored hexachlorobenzene in the top sandy loam at a concentration of about 0.1 mg/kg after the application of hexachlorobenzene. Although Beall (1976) does not specify an application rate in units of quantity per unit area, such as lb/acre, Beall specifies that the hexachlorobenzene was applied to yield an initial concentration of 10 mg/kg soil in the top 5 cm of soil. With this information, an approximate application rate can be calculated. A 1 cm^2 soil surface that is 5 cm deep has a volume of 5 cm^3. The soil type used in the Beall (1976) study is specified as sandy loam but detailed soil characteristics are not provided in the publication. Taking a bulk density of 1.6 g/cm^3 for sandy loam soil (Knisel and Davis 2000, p. 46), a 5 cm^3 volume of soil would weigh 0.008 kg:

$$5\ cm^3 \times 1.6 g/cm^3 = 8\ g = 0.008\ kg.$$

To achieve a nominal concentration of 10 mg hexachlorobenzene/kg soil, the amount applied to a 1 cm^2 surface of soil would be :

$$0.008 \text{ kg} \times 10 \text{ mg HCB/kg soil} = 0.08 \text{ mg} = 80 \text{ µg}.$$

The application rate can be calculated as 80 µg/cm^2 or about 7.1 lbs/acre (1.0 lb/acre = 11.21 µg/cm2):

$$80 \text{ µg/cm}^2 \div (11.21 \text{ µg/cm}^2 \div 1 \text{ lb/acre}) = 7.136 \text{ lbs/acre}.$$

Thus, the soil contamination rate from the study by Beall (1976) is about 0.014 mg/kg per lb/acre [0.1 mg/kg ÷ 7.136 lbs/acre], only about a factor of 2 less than the average concentration modeled in GLEAMS and within the range of variability in the GLEAMS simulations.

3.2.4.5. Exposures Involving Contaminated Streams and Ponds – Immediately after application of a pesticide that is contaminated with hexachlorobenzene to soil or plants, there is not likely to be any immediate contamination of water attributable to the hexachlorobenzene in the contaminated pesticide. Nonetheless, because of the persistence of hexachlorobenzene, it will remain in the soil and could be transferred to surface waters where most of the hexachlorobenzene will be bound to sediments or bioconcentrated in aquatic organisms (ATSDR 2002).

No monitoring studies have been encountered that permit a direct estimate of the amount of hexachlorobenzene that would be found in ambient water as a result of applying a herbicide contaminated with hexachlorobenzene. Nonetheless, there are ample monitoring data to indicate that hexachlorobenzene can, over time, be transported to water either by runoff or by volatilization with subsequent redeposition in rainwater. Because hexachlorobenzene binds tightly to and is relatively immobile in soils, hexachlorobenzene is not likely to percolate through soils and directly contaminate ground water (ATSDR 2002). While volatilization may be an important route of environmental transport, volatilized hexachlorobenzene will be rapidly dispersed and transported over a relatively wide area. Although this will contribute to general background levels of hexachlorobenzene, the amounts of hexachlorobenzene released in Forest Service programs will not substantially contribute to background levels of hexachlorobenzene (Section 3.2.4.2). Consequently, for this risk assessment, the contamination of ambient water is based on estimates of hexachlorobenzene runoff from contaminated soil.

Based on the GLEAMS simulations described in the previous section, concentrations in streams and ponds at various annual rainfall rates and soils are summarized in Tables 3-7 and 3-8. The greatest concentrations of hexachlorobenzene will be from runoff sediment from clay, with lesser concentrations from loam or sand. For acute exposures, a peak concentration rate of 90 µg/L per lb/acre is used as the central estimate for water in a contaminated stream. This is about the maximum concentration from clay at an annual rainfall of 100 inches (Table 3-7). The upper range is taken as 300 µg/L per lb/acre, somewhat above the highest concentration from clay at an annual rainfall of 250 inches. The lower range is set somewhat arbitrarily at 1 µg/L per lb/acre, in the range of concentrations that could be expect from runoff from clay in arid regions. These

values are entered into Worksheet B06 and used in all exposure scenarios involving acute exposures to hexachlorobenzene associated with drinking water from a stream.

Longer-term concentrations in streams (Table 3-7) are estimated to be somewhat higher than those in lakes or ponds (Table 3-8). This is because the stream scenario assumes a rocky stream bed and ignores binding to sediment. For this risk assessment, the longer term concentrations are based on the simulations for a stream. The central estimate is taken as 0.5 µg/L per lb/acre, about the simulated concentration from clay at an annual rainfall of 100 inches as well as the the simulated concentration from loam at an annual rainfall of 250 inches. The longer-term concentration is taken as 1 µg/L per lb/acre, somewhat above the simulated concentration from clay at an annual rainfall of 250 inches. The lower limit is again somewhat arbitrarily set at 0.03 µg/L per lb/acre. These values are entered into Worksheet B06 and used in all exposure scenarios involving longer term exposures to hexachlorobenzene associated with drinking water from a stream.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.2 mg/kg/day for picloram. This RfD is based on a chronic rat NOAEL of 20 mg/kg/day and an uncertainty factor of 100. In the same study, the LOAEL was 60 mg/kg/day and the effect noted was a change in the staining properties of liver cells. No frank signs of toxicity were seen at this or higher dose levels. This NOAEL for chronic toxic effects is below the NOAELs for reproductive effects. Thus, doses at or below the RfD will be below the level of concern for reproductive effects.

The contamination of technical grade picloram with hexachlorobenzene can be quantitatively considered to a limited extent. The U.S. EPA has derived an RfD and cancer potency parameter for hexachlorobenzene. Based on the levels of contamination of technical grade picloram with these compounds and the relative potencies of these compounds to picloram, this contamination is not significant in terms of potential systemic toxic effects. This assessment, however, does not impact the potential carcinogenicity associated with hexachlorobenzene and this risk, based on the U.S. EPA's cancer potency parameter, is quantitatively considered in the risk characterization.

3.3.2. Existing Guidelines for Picloram. The most recent RfD for picloram is 0.2 mg/kg/day, a value derived by the U.S. EPA's Office of Pesticide Programs (U.S. EPA 1994). This RfD is based on a NOAEL of 20 mg/kg/day from a two-year rat feeding study (Landry et al. 1986), discussed in Section 3.1.5, with an uncertainty factor of 100. At doses of 60 and 200 mg/kg/day, changes in the staining properties of liver cells, but no frank signs of toxicity, were noted. This RfD is also cited in the RED for picloram (U.S. EPA 1995b) as well as proposed pesticide tolerances for picloram (U.S. EPA 1999).

An earlier RfD of 0.07 mg/kg/day is listed on IRIS (U.S. EPA 1992c). This RfD is based on a no-observed-effect level (NOEL) of 7 mg/kg/day from a 6-month dog feeding study (Barna-Lloyd et al. 1982), also discussed in Section 3.1.5, and this RfD also was derived using an uncertainty factor of 100. While the U.S. EPA (1994) does not specifically discuss the rationale for adopting the higher RfD of 0.2 mg/kg/day, the two-year rat study was probably preferred because it is a lifetime study whereas a 6-month dog feeding study is substantially less than lifetime. In addition, dogs are generally considered a poor animal model because of a decreased ability to secrete weak acids via the kidney.

The U.S. EPA (1999) has not derived an acute exposure limit for picloram. In discussing the available acute toxicity data, the U.S. EPA (1999) has concluded that:

> *No toxicological effect that could be attributable to a single oral exposure was identified, and therefore picloram is not expected to present an acute dietary hazard* (p. 421, Section C.1.i.).

This statement appears to be based primarily on a review of the acute toxicity studies submitted to the U.S. EPA as part of the registration process. No information has been encountered in the published literature that would contradict EPA's assertion. Nonetheless, it is likely that higher doses could be tolerated after a single acute exposure than would be tolerated in chronic exposures.

A surrogate acute toxicity value could be derived from the available data. For example, the reproductive NOAEL values for picloram range up to 400 mg/kg/day, a factor of 20 above the lifetime NOAEL used to derive the chronic RfD. The lack of an acute RfD, however, has a relatively minor impact on this risk assessment. As discussed in Section 3.4, the only acute exposure scenario that results in a modest increase above the RfD involves the accidental spill into a small pond (3.2.3.4.1). Thus, no surrogate acute toxicity value is proposed in this risk assessment.

3.3.3. Existing Guidelines for Hexachlorobenzene.

3.3.3.1. Systemic Toxicity – The U.S. EPA RfD for hexachlorobenzene is 0.0008 mg/kg/day. This RfD is based on a 130-week feeding study in male and female rats that also included a 90-day exposure to offspring. The U.S. EPA judged the NOAEL for liver effects at a dose of 0.08 mg/kg/day with a LOAEL at 0.29 mg/kg/day. The LOAEL was characterized by U.S. EPA (1997) as "an increase ($p<0.05$) in hepatic centrilobular basophilic chromogenesis" in the offspring of the chronically exposed rats. As with picloram and for the same reasons as with picloram, the U.S. EPA used an uncertainty factor of 100 to derive the RfD of 0.0008 mg/kg/day.

ATSDR (2002) has derived an acute MRL for hexachlorobenzene of 0.008 mg/kg/day, a factor of 10 above the chronic RfD derived by U.S. EPA. The Office of Drinking Water of the U.S. EPA has derived a maximum contaminant level of 0.001 mg/L of drinking water and a maximum short term health advisory of 0.05 mg/L of drinking water (U.S. EPA 1998a).

3.3.3.2. Carcinogenic Potency – In addition to systemic toxicity, hexachlorobenzene has been shown to cause tumors of the liver, thyroid and kidney in three species of rodents—mice, rats, and hamsters (ExToxNet 1996a; U.S. EPA 1997). Based on a two-year feeding study in rats, the U.S. EPA (1997) derived a cancer slope factor for lifetime exposures of 1.6 $(mg/kg/day)^{-1}$. The recent review of hexachlorobenzene by ATSDR (2002) reports no new data that would impact this estimate of the cancer potency factor.

Cancer risk over a lifetime (P) is calculated as the product of the daily dose (d) over a lifetime and the potency parameter (β):

$$P = d\,\beta$$

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

$$d = P \div \beta$$

Thus, the lifetime daily dose of hexachlorobenzene associated with a risk of one in one-million (1÷1,000,000 or 0.000001) is 0.000000625 mg/kg/day:

$$d_{(mg/kg/day)} = 0.000001 \div (1.6\ (mg/kg/day)^{-1}).$$

As noted in Section 3.1, picloram is not classified as a carcinogen. While it can be argued that the technical grade picloram used in the standard bioassays encompasses any toxicologic effects that could be caused by hexachlorobenzene, this argument is less compelling for carcinogenic effects because, for most cancer causing agents, the cancer risk is viewed as a non-threshold phenomenon (i.e., zero risk is achieved only at zero dose).

The potency factor of 1.6 $(mg/kg/day)^{-1}$ is intended to be applied to lifetime daily doses. As summarized in Section 3.2, many of the exposure assessments used in this risk assessment involve much shorter periods of time. Following the approach recommended by U.S. EPA (1997, p. 35), this risk assessment assumes that the average daily dose over a lifetime is the appropriate measure for the estimation of cancer risk.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. Typical exposures to picloram do not lead to estimated doses that exceed a level of concern. For workers, no exposure scenarios, acute or chronic, exceeds the RfD even at the upper ranges of estimated dose. 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 picloram into a very small pond. Even this exposure scenario results in only a small excursion above the chronic 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. Thus, based on the available information and under the foreseeable conditions of application, there is no route of exposure or scenario suggesting that workers or members of the general public will be at any substantial risk from longer-term exposure to picloram.

Irritation and damage to the eyes can result from exposure to relatively high levels of picloram (i.e., placement of picloram directly onto the eye) and repeated exposures to picloram can lead to skin sensitization. From a practical perspective, eye irritation and skin sensitization are likely to be the only overt effects as a consequence of mishandling picloram. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling and application of picloram.

Based on the standard assumptions used in this and other Forest Service risk assessments, the contamination of picloram with hexachlorobenzene does not appear to present any substantial cancer risk even at the upper ranges of plausible exposure. Administratively, the Forest Service has adopted a cancer risk level of one in one-million (1÷1,000,000) as a trigger that would require special steps to mitigate exposure or restrict and possibly eliminate use. Based on relatively protective exposure assumptions and at the typical application rate of 0.35 lb a.e. picloram/acre, the highest cancer risk is about 0.7 in one-million – i.e., for workers involved in broadcast ground spray. At the upper range of the application rate – i.e., 1 lb a.e./acre – this risk would scale to 2 in one-million. This is not, however, an appropriate approach for risk scaling because it would assume that the same worker applies picloram at an atypically high application rate over a lifetime. For members of the general public, the highest cancer risk is estimated at 0.1 in one-million at the typical application rate of 0.35 lb a.e./acre. Scaled to an application rate of 1 lb/acre, the cancer risk would be about 0.3 in one-million.

3.4.2. Workers. A quantitative summary of the risk characterization for workers associated with exposure to picloram is presented in Worksheet E02 (Supplement 1). The quantitative risk characterization is expressed as the hazard quotient, which is the ratio of the estimated doses from Worksheet E01 to the chronic RfD for picloram, 0.2 mg/kg/day (Section 3.3.2). As indicated in Section 2, the hazard quotients in Worksheet E02 are based on the typical application rate of 0.35 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 1 lb a.e./acre, the highest application rate contemplated by the Forest Service, the level of concern would be 0.35.

Under typical conditions of exposure, none of the exposure scenarios approach a level of concern. Even at the upper limits of exposure which are based on the worst-case exposure assumptions, the hazard indices do not exceed unity for the general worker exposures. In addition, level of concern of 0.35 for the highest application rate is not exceeded, although the upper range of exposures for workers involved in broadcast ground spray leads to a hazard quotient of 0.3, which approaches the level of concern for an application rate of 1 lb a.e./acre. Nonetheless, it should be noted that using the highest application rate to assess chronic risks is implausible in that it assumes that a worker would repeatedly apply picloram at the highest application rate. As indicated in Section 2, this is not likely given the application rates typically used in Forest Service programs.

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 that the upper ranges. 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 picloram that are regarded as unacceptable so long as reasonable and prudent handling practices are followed.

As discussed in Section 3.1.11, picloram can cause irritation and damage to eyes and skin sensitization. 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 picloram. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of picloram.

3.4.3. General Public. The quantitative hazard characterization for the general public associated with exposure to picloram 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 chronic RfD of 0.2 mg/kg/day for both acute and chronic 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 picloram even if the level of concern is set to 0.35 – i.e., that associated with the maximum application rate that will be used in Forest Service programs.

For the acute/accidental scenarios, none of the central estimates representing typical exposure conditions exceed the RfD. 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 by a factor of 3. It does not seem likely that this exposure would result in any frank adverse effects. As noted in Section 3.3.2, the chronic NOAEL of 20 mg/kg/day used to derive the chronic RfD is a factor of about 20 below reported NOAELs from shorter term exposures.

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 picloram, considerations of multiple exposure scenarios has little impact on the risk assessment. For example, typical levels of exposure for a woman 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 0.088 (0.0004 + 0.0006 + 0.02 + 0.007 + 0.06). Similarly, for all of the chronic exposure scenarios, the addition of all possible pathways lead to hazard quotients that are substantially less than unity. Some acute exposure scenarios could be constructed at the upper limits of exposure that could lead to modest excursions about the RfD but compounding several different upper range assessments would constitute an implausible series of events.

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 picloram. As discussed in Sections 3.1 and 3.3.2, the likely critical effect of picloram in humans cannot be identified clearly. In animals, the most sensitive effect of picloram involves changes in the staining characteristics of liver cells. These effects, however, were only noted in one study and are not consistent among species or even between different studies in the same species. Thus, it is unclear if individuals with pre-existing diseases of the liver would be particularly sensitive to picloram exposures, although individuals with any severe disease condition could be considered more sensitive to many toxic agents.

3.4.5. Connected Actions. As noted in Section 3.1.3, a commercial formulation of picloram and 2,4-D, Tordon 202C, has been shown to inhibit immune response in mice (Blakley 1997). The effects of mixtures of picloram, alachlor, and atrazine compared to the activity of each chemical given alone have been characterized in both 90-day drinking water studies (10 ppm in water) and 90-day gavage studies (100 mg/kg in corn oil) using mice (Chaturvedi 1993). Again, the design of this study does not permit a quantitative characterization of interactions of these three pesticides. Nonetheless, exposures to picloram were associated with increased weights of the spleen, kidney, and liver.

3.4.6. Cumulative Effects. As noted above, this risk assessment specifically considers the effect of repeated exposure in that the chronic RfD is used as an index of acceptable exposure. Consequently, repeated exposure to levels below the toxic threshold should not be associated with cumulative toxic effects.

3.4.7. Hexachlorobenzene.

3.4.7.1. Workers – Summaries of the exposure assessments and risk characterization for workers are given in the hexachlorobenzene worksheets that accompany this risk assessment (Supplement 2). Worksheet E01 summarizes the exposure assessment for workers and is analogous to the corresponding worksheet for picloram. Worksheet E02 summarizes the risk characterization for workers.

Unlike picloram, the toxicity data on hexachlorobenzene allows for separate dose-response assessments for acute and chronic exposures. For acute exposures, the hazard quotients are based on ATSDR's short-term MRL of 0.008 mg/kg/day (ATSDR 2002). For chronic exposures, the hazard quotients are based on the chronic RfD from U.S. EPA of 0.0008 mg/kg/day.

For general worker exposures, the hazard quotients associated with hexachlorobenzene (Worksheet E02) are approximately four orders of magnitude below the corresponding hazard quotients for picloram. Similarly, hazard quotients associated with accidental scenarios are consistently lower for hexachlorobenzene than the corresponding scenarios for picloram. Thus, for the reasonably diverse exposure scenarios covered in this risk assessment, the amount of hexachlorobenzene in technical grade picloram is not toxicologically significant.

The cancer risks presented in Worksheet E02 are presented as the estimated exposure divided by the lifetime dose associated with a cancer risk of 1 in one million. Thus, the interpretation of these quotients is identical to that of hazard quotients for toxicity – i.e., if the hazard quotient is below unity, the cancer risk is below 1 in one million. As indicated in Worksheet E02, none of the cancer risks in workers exceed 1 in one million.

As indicated in Section 3, all of these risk characterizations are based on the typical or average 8 ppm concentration of hexachlorobenzene in technical grade picloram. Particularly for chronic exposures in which workers would be exposed over several years to hexachlorobenzene in many different batches of picloram, the use of the average concentration appears to be a much more reasonable approach than the use of the upper limit.

While there are substantial uncertainties involved in any cancer risk assessment, the verbal interpretation of the numeric risk characterization derived in this risk assessment is relatively simple. Using the assumptions and methods typically applied in Forest Service risk assessments, there is no plausible basis for asserting that the contamination of picloram with hexachlorobenzene will result in any substantial risk of cancer in workers applying picloram under normal circumstances.

While the chronic cancer potency could be scaled linearly and the cancer risk associated with short term exposures could be calculated, this sort of extrapolation is highly uncertain and, more importantly, ignores the normal background exposures to hexachlorobenzene from other sources. For example, background levels of exposure to hexachlorobenzene are in the range of 0.000001 mg/kg/day or 1×10^{-6} mg/kg/day (Section 3.2.4.3). As summarized in Worksheet E01, even the

upper range worker exposure values are below this background dose – i.e., in the range of 2 to 4×10^{-7} mg/kg/day. As discussed in the next section, the upper range of the longer term exposure scenarios for the general public are substantially below the background dose – i.e., about 1×10^{-10} to 6×10^{-8}. Thus, there is no basis for asserting that the presence of hexachlorobenzene in picloram will impact substantially cancer risk under conditions characteristic of applications made in Forest Service programs.

3.4.7.2. General Public – Summaries of the acute exposure assessments and risk characterization for the general public are given in the hexachlorobenzene worksheets that accompany this risk assessment and parallel those for the risk characterization for workers discussed in the previous section: Worksheet E03 summarizes the exposure assessments and Worksheets E04a, E04b, and E04c summarize the risk characterizations.

Worksheet E04a presents the hazard quotients for the general public associated with the acute exposure scenarios. As with the corresponding worksheet for workers, the hazard quotients for acute exposure are based on the short-term MRL of 0.008 mg/kg/day and the hazard quotients for chronic exposures are based on the U.S. EPA RfD of 0.0008 mg/kg/day.

All exposure scenarios result in hazard quotients that are below unity (i.e., the level of exposure is below the RfD for chronic exposures and below the MRL for acute exposures). In addition, all of the acute exposure scenarios result in hazard quotients that are substantially below the corresponding hazard quotient for picloram. The highest acute hazard quotient for hexachlorobenzene is 0.1, the upper range of the hazard quotient associated with the consumption of contaminated fish by subsistence populations.

As with worker exposures, none of the hazard quotients for cancer risk levels of 1 in 1-million exceed unity. As noted in Section 3.2.4.3, the typical background exposure to hexachlorobenzene is about 0.000001 or 1×10^{-6} mg/kg/day (ATSDR 2002). As indicated in hexachlorobenzene Worksheet E03, the highest longer-term exposure rate associated with Forest Service programs is 6.48×10^{-8} mg/kg/day – i.e., the upper range of exposure for the consumption of contaminated fish by subsistence populations. This is below the typical background exposure by a factor of about 15.

The simple verbal interpretation of this risk characterization is that, in general, the contamination of picloram with hexachlorobenzene does not appear to pose a risk to the general public. This is consistent with the conclusions reached by the U.S. EPA (1995b).

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. The toxicity of picloram is relatively well characterized in experimental mammals but few wildlife species have been assayed relative to the large number of nontarget species that might be potentially affected by the use of picloram. Within this admittedly substantial reservation, picloram appears to be relatively non-toxic to terrestrial animals but is moderately toxic to aquatic animals, particularly some species of fish.

The assessment of the toxicity of picloram to nontarget terrestrial animals is based almost exclusively on toxicity studies using experimental mammals (i.e., the same studies used in the human health risk assessment). Acute oral LD_{50} values for picloram are in the range of 3000 to 5000 mg/kg body weight and NOAEL from chronic studies range from 7 mg/kg/day to 20 mg/kg/day. Some additional studies are available on birds, bees, and snails that generally support the characterization of picloram as relatively non-toxic to terrestrial animals. This assessment is supported by field studies that reported no detectable effects on mammalian or avian diversity after the application of picloram.

Picloram is a pyridine herbicide that acts as a plant growth regulator. This is to say that picloram mimics naturally occurring plant auxins or hormones in a manner that leads to uncontrolled and abnormal growth. These effects can in turn lead to gross signs of toxicity or death. The toxicity of picloram to terrestrial plants has been assayed in relatively standardized studies of seed emergence, seed germination, and post-emergence applications that have been submitted to the U.S. EPA to support the registration of picloram. Picloram is more toxic to broadleaf plants than grains or grasses. The lowest reported adverse effect (the EC_{25} for the inhibition of seed emergence in soybeans) for the potassium salt of picloram is 0.000014 kg or about 0.000012 lb a.e./acre. The highest reported NOEC in any of the terrestrial plant bioassays is about 0.4 lb a.e./acre for seedling emergence in corn.

The acute and chronic toxicity of picloram to aquatic animals has been assayed in various species of fish and invertebrates. Acute (96-hour) LC_{50} value for trout range from 0.8 mg/L to 19.3 mg/L. Bluegill sunfish and fathead minnows, common test species used in aquatic toxicity studies, appear to be less sensitive to picloram, with LC_{50} values ranging from about 15 mg/L to 55 mg/L. Two sets of longer-term (egg and fry) studies are available in trout and the results of these studies are not consistent. Studies accepted by the U.S. EPA indicate a NOEC of 0.55 mg/L in rainbow trout. An earlier series of studies of using lake trout indicate a NOEC of <0.035 mg/L. Limitations in the use of this earlier series of studies include the failure to use an acetone control and the failure to measure concentrations in the test solutions. An early life-stage study in the fathead minnow, yielded a NOEC of 0.71 mg a.e./L, very similar to the NOEC reported in trout. This study, however, was conducted with the triisopropanolamine salt of picloram rather than the potassium salt.

In *Daphnia*, an aquatic invertebrate commonly used in aquatic toxicity studies, the reported acute (48-hours) LC_{50} value is 68.3 (63–75) mg/L. Chronic studies in the same species using reproductive or developmental parameters identified a no-effect level at 11.8 mg/L and a lowest effect level at 18.1 mg/L. Thus, it appears that trout are more sensitive than daphnids to both the acute and chronic effects of picloram.

As with aquatic animals, the toxicity of picloram to aquatic plants varies substantially among different species. Based on the available toxicity bioassays, the most sensitive species is *Navicula pelliculosa*, a freshwater diatom, with an EC_{50} for growth of 0.94 mg a.e./L and a NOEC of 0.23 mg a.e./L. The least sensitive aquatic plants appear to be from the genus *Chlorella* (another group of freshwater algae), with EC_{50} values greater than 160 mg a.e./L. Macrophytes appear to have a sensitivity that is in the upper range of that seen in algae, with a reported EC_{50} of 164 mg a.e./L in duckweed.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals – As detailed in Section 3.1 (Hazard Identification for the human health risk assessment), the toxicity of picloram to experimental mammals is well characterized and these data are relevant to the assessment of effects in wildlife species. Two issues, however, are unique to the ecological risk assessment for mammalian species: the NOAEL for acute exposures and differences in chronic NOAELs for different mammalian species.

Picloram has a 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, reported acute oral LD_{50} values in rats range from 690 mg/kg (Hayes et al. 1986) to >5000 mg/kg in male rats (Jeffrey 1987a). The lower end of this ranged involved exposures to unneutralized potassium picloram solution (pH>11) and the atypically high toxicity relative to other studies is probably due to the extreme alkalinity of the test solution (U.S. EPA 1992b). In terms of practical significance, these acute LD_{50} values are several orders of magnitude higher than any plausible exposures and have no practical impact on the risk assessment.

As noted in the human health risk assessment (Section 3.3), the U.S. EPA (1999) has not derived an acute exposure limit for picloram because:

> *No toxicological effect that could be attributable to a single oral exposure was identified, and therefore picloram is not expected to present an acute dietary hazard* (p. 421, Section C.1.i.).

For the current risk assessment, however, the failure to define an acute NOAEL limits the interpretation of potential risks associated with many of the acute exposure scenarios developed for mammals (Section 4.2). As discussed further in the dose-response assessment, the reproduction studies in experimental mammals (Section 3.1.9) can be used to estimate acute exposures that are not likely to result in adverse effects in mammals.

In the human health risk assessment, a NOAEL of 20 mg/kg/day is used as the basis for the RfD (Section 3.3.2). This NOAEL is from a two-year feeding study in male and female Fischer rats (50 rats/sex/dose) in which picloram (acid) was administered at dietary concentrations that resulted in daily doses of 20, 60, and 200 mg/kg/day (Landry et al. 1986). The dose of 60 mg/kg/day was considered an LOAEL but the severity of the effect – i.e., changes in liver weight and appearance – were considered marginal by the U.S. EPA (U.S. EPA 1994). Typically, the NOAEL used for the RfD is applied directly to the ecological risk assessment for mammalian species. However, as detailed in Section 3.1.5, a LOAEL of 35 mg/kg/day with a corresponding NOAEL of 7 mg/kg/day has been noted in dogs over the course of a 6-month feeding study (Barna-Lloyd et al. 1982). The U.S. EPA had used this study in an earlier RfD. Dogs, however, are generally considered a poor animal model for toxicity to the kidney associated with weak acids because of a decreased ability to secrete weak acids via the kidney. Thus, this study is not used in the human health risk assessment. Nonetheless, for the ecological risk assessment, 7 mg/kg/day is the most sensitive NOAEL and the use of the 7 mg/kg/day NOAEL from the study in dogs is considered further in the dose-response assessment (Section 4.3).

In addition to these laboratory bioassays, field studies are available in which the impact of picloram applications were assessed on mammalian wildlife communities. Brooks et al. (1995) examined the impact of a mixture of picloram and triclopyr as well as imazapyr and hexazinone, all used in site preparation, on small mammal and avian communities. The study area was located in Georgia and consisted of a 157-ha tract of residual hardwoods. Picloram was applied in combination with 2,4-D (Tordon 101) at a rate of 2.7 kg a.e./ha (approximately 2.4 lbs a.e./acre). After herbicide treatment and a prescribed burn, loblolly pine were planted. Data on small mammals was collected by trapping and data on birds involved visual surveys. Observations were made at pre-treatment and three-times per year at 1, 2, and 3 years after treatment. No substantial differences were noted among the different herbicides. With all herbicides, the number of small animals trapped after treatment was diminished compared to pre-treatment levels. Because no non-herbicide treated sites (i.e., control sites) were used in this study, observed changes in populations of small mammals or birds cannot be clearly associated with herbicide treatment.

Nolte and Fulbright (1997) have conducted a field study assessing the effects of a combination of picloram and triclopyr on community structure. Each herbicide was applied by helicopter at a rate of 1.9 liters/ha, but neither the rate in units of lb/acre nor the specifics of the commercial formulation are given in the publication. This paper does indicate that the application is that "commonly used on mesquite in southern Texas". No effects were seen on mammalian or avian diversity. In addition, no statistically significant effects were noted on vegetation species richness and evenness or the number of rare plant species.

4.1.2.2. Birds – As summarized by U.S. EPA (1995b), the acute toxicity of the potassium salt of picloram to birds by gavage administration appears to be similar to that in mammals with acute oral LD_{50} values of >2000 mg/kg in quail and mallard ducks. In mallard ducks, Beavers (1983)

reported an oral LD_{50} of more than 2510 mg/kg for technical grade picloram with no deaths at the highest dose tested.

In addition, 14-day dietary LC_{50} values in these species are >10,000 ppm and supplemental reproductive studies on chickens and pheasants indicated NOAELs, expressed as application rates, of 2.8 kg/ha and 11.2 kg/ha, respectively (U.S. EPA 1995b). Assuming that birds consume about 15% of their body weight during a standard toxicity study (similar to the values used in other risk assessments for which food consumption data are reported), the dietary concentration of 10,000 ppm corresponds to a 14-day NOAEL of about 1500 mg/kg body weight.

An 8-day dietary LC_{50} value of 385,260 ppm (about 58,000 mg/kg body weight) in mallard ducklings has been reported by Stevenson (1965) for Tordon but the specific formulation and % a.e. in the formulation is not specified in the study.

4.1.2.3. Terrestrial Invertebrates – Acute toxicity studies using bees are required by the U.S. EPA in the registration of pesticides—using both dietary and direct contact exposures. For picloram (K salt), the acute contact LD_{50} is >0.1 mg/bee and the dietary LC_{50} is >1000 ppm. Taking an estimated body weight for the honey bee of 0.093 g (USDA/APHIS 1993), the contact toxicity LD_{50} value of >0.1 mg/bee corresponds to a dose of >1 mg/g or 1,000 mg/kg. The RED for picloram (U.S. EPA 1995b) reported that the LD_{50} study found no significant mortality at the highest exposure level tested. There is relatively little additional data on terrestrial invertebrates. At dietary concentrations of about 5000 mg/kg over a 14-day period, picloram (acid) did not increase mortality in the brown garden snail, *Helix aspersa* (Schuytema et al. 1994). Based on these albeit limited data, there is no basis for asserting that picloram is likely to be more toxic to terrestrial invertebrates than it is to terrestrial mammals or birds.

4.1.2.4. Terrestrial Plants (Macrophytes) – Picloram is a pyridine herbicide that acts as a plant growth regulator. This is to say that picloram mimics naturally occurring plant auxins or hormones in a manner that leads to uncontrolled and abnormal growth that can lead to gross signs of toxicity or death (Grossmann et al. 2001; Hansen and Grossmann 2000; Webb and Hall 1995). In general, picloram is more toxic to broad leaf plants than to grasses or grains (Cox 1998; ExToxNet 1996b; USDA 1995; U.S. EPA 1995a,b). The yellow starthistle, *Centaurea solstitialis*, has developed resistance to picloram with resistant plants being more tolerant by factors ranging from 3 to 35 fold compared to non-resistant plants (Fuerst et al. 1996). Based on growth inhibition in sunflower seedlings, picloram was more toxic than metabolites of picloram by factors of about 300 to 3000 (Grover et al. 1975).

In assessing the potential effects of herbicides on nontarget plant species, the U.S. EPA has developed a standardized set of plant bioassays for seed germination, seed emergence, and post-emergence applications.

As summarized in the RED for picloram, the lowest reported adverse effect for the potassium salt of picloram is 0.014 g a.e./ha or 0.000014 kg a.e./ha, the EC_{25} for seed emergence in soybeans

(U.S. EPA 1995b, p. 55). This corresponds to an application rate of about 0.000012 lb a.e./acre. A more recent Tier II seed emergence study using Tordon K (Schwab 1995) has also been submitted to U.S. EPA. In this study, the most sensitive species was the pinto bean, with a NOEC of 0.27 g a.i./hectare and an EC_{25} of 7.4 g a.e./hectare. These values correspond to about 0.1 g a.i./acre and 3 g/acre [2.471 acres/ha] or 0.086 g a.e./acre and 2.6 g a.e./acre [conversion factor of 0.8606, Table 2-1]. The NOEC of 0.086 g a.e./acre, in turn, corresponds to an application rate of about 0.00019 lb a.e./acre [1 pound = 453.6 g]. Soybeans were much less sensitive than the pinto bean, with a NOEC of 8.75 g/Ha, corresponding to about 0.006 lb a.e./acre. In the seedling emergence phytotoxicity test by Schwab (1995), corn was found to be the most resistant of 10 plant species (barley, corn, onion, pinto bean, radish, rape, soybean, sunflower, tomato, and wheat) to the toxic effects of picloram (K salt) with a NOEC of 560 g a.i./ha or about 0.4 lb a.e./acre (Schwab 1995).

Studies on vegetative vigor indicate that the sunflower is the most sensitive of 12 plant species (alfalfa, barley, corn, cucumber, onion, pinto bean, radish, rape, soybean, sunflower, tomato, and wheat) (Schwab 1996). These Tier 2 studies identified effect levels for picloram in sunflower of 0.67 and 3.19 g a.i./ha (EC_{25} and EC_{50} , respectively) with a NOEC of 0.27 g a.i./ha (Schwab 1996). The most tolerant plant species in an assay for vegetative vigor is wheat, with a NOEC of 70 g a.e./ha (U.S. EPA 1995b, p. 55).

Several studies have been published in the open literature concerning the toxicity of picloram to non-target plant species. Harrington et al. (1998) followed the two-year development of southern pine seedlings and associated vegetation following spray-and-burn site preparation with various herbicides, including picloram. Miller et al. (1999) measured floristic diversity, stand structure, and composition 11 years after herbicide site preparation. Sparkes et al. (2002) examined the effects of various herbicides, including picloram, on *Bryophyllum pinnatum (Lam.*). Numerous studies have been published on efficacy and effects of picloram applications on various crop species. Rates as low as 25 g a.i./ha of picloram reduced tobacco yields as long as four years after application (Sheets and Harrell 1986). Another study found that application of picloram (K salt) at 0.05 pounds per acre resulted in a statistically significant reduction in cotton growth and yield when applied directly (Jacoby et al. 1990). Thus, picloram can be considered highly selective to broad leaf plants such as soybean but may be toxic to many different plant species at the typical application rate of 0.5 lb a.e./acre.

4.1.2.5. Terrestrial Microorganisms – The persistence of picloram in soil increases with increasing application rates or soil concentrations and this suggests that picloram is toxic to soil microorganisms. In soil column studies conducted over a 30 day period, Krzyszowska et al. (1994) noted that the soil halftimes of picloram is directly related to application rates. Application rates of 0.47, 0.97, and 1.85 kg/ha (about 0.4, 0.86, and 1.6 lb/acre) were associated with halftimes in soil of 13, 19, and 23 days, respectively.

Most of the data on the effects of picloram on soil microorganisms involve assays of microbial activity in soils with defined concentrations of picloram. Consistent with the study by

Krzyszowska et al. (1994), USDA/ARS (1995) notes a direct relationship between aerobic soil halftimes and concentrations of picloram in soil: 18 days at a concentration of 0.0025 ppm, 29 days at a concentration of 0.025 ppm, 150 days at a concentration of 0.25 ppm, and 300 days at a concentration of 2.5 ppm. At a level of 10 ppm in sandy loam soil, picloram — and several other herbicides—caused a transient decrease in nitrification after 2 but not 3 weeks of incubation (Tu 1994). As discussed by this investigator, the decrease in nitrification is relatively mild and does not suggest the potential for a substantial or prolonged impact on microbial activity. In the same study, picloram had no effect on ammonia formation or sulfur oxidation. Prado and Airoldi (2001) assayed the effect of picloram on mixed microbial activity using microcalorimetry – assays microbial activity by measuring changes in heat production from soil treated with glucose (microbial food source) and various concentrations of picloram. Time to peak heat production was attenuated and the magnitude of peak heat production was reduced by picloram concentrations as low as 1 ppm.

Welp and Bruemmer (1999) described the pH dependence of toxicity measurements of picloram (acid) in soil as determined by Fe(III) reduction test. The results showed that EC_{50} ranged from 1.93 mmol/kg [about 465 ppm] soil to more than 16.6 mmol/kg [about 4000 ppm] soil over a pH range of 3.5–7.8 (Welp and Bruemmer 1999).

Unlike the case in macrophytes, the metabolism of picloram may result in increased rather than decreased toxicity in some microorganisms. In three species of fungi, EC_{50} values for growth inhibition by picloram acid were >1600 ppm (the highest concentration tested). Corresponding values for the decarboxylated metabolite, 4A-TCP, were 50 to 80 ppm. In two species of bacteria, *Arthrobacter globiformis* and *Pseudomonas pictorum*, differences in toxicity were not substantial and ranged between 60 and 380 ppm for picloram acid and 4A-TCP (Baarschers et al. 1988). Using an assay based on the reduction of Fe(III) in soil, Welp and Bruemmer (1999) reported EC_{50} values of 1.93 to >16.6 mMoles/kg soil, corresponding to about 466 mg/kg soil to somewhat of over 4,000 mg/kg soil [MW=241.48].

4.1.3. Aquatic Organisms.

4.1.3.1. Fish

4.1.3.1.1. Acute Toxicity – As with terrestrial species, the acute lethal potency of picloram and picloram formulations has been relatively well-defined. These values are typically expressed as time-specific LC_x values where *x* is the estimate of the proportion of fish that die – e.g., 96 hour LC_{50}. A large number of acute LC_{50} values have been determined in various species of fish. Studies submitted to U.S. EPA for the registration and reregistration of picloram are summarized in U.S. EPA (1995b) and a large number of additional studies have been reviewed by Mayes and Oliver (1985). Additional studies in trout have been published by Woodward (1976, 1979, 1982).

Based on studies considered by U.S. EPA (1995b), salmonids appear to be marginally more sensitive to picloram (acid) than other fish species with a reported LC_{50} value of 5.5 mg/L in rainbow trout (confidence limits not reported) compared to LC_{50} values of 14.5 to 19.4 mg/L for

bluegill sunfish (a species of warm water fish commonly used in toxicity bioassays). These species differences are not apparent in the toxicity data summarized by U.S. EPA (1995b) on the potassium salt of picloram used in the formulations covered by this risk assessment. For the potassium salt, LC_{50} values of 13 mg/L and 26 mg/L are reported for rainbow trout and a corresponding value of 24 mg/L is reported for bluegills (U.S. EPA 1995b). Based on these data, the U.S. EPA (1995b) classified picloram acid as moderately toxic to freshwater fish based on the LC_{50} of 5.5 mg/l in trout and also classified the potassium salt of picloram as moderately toxic to freshwater fish based on the LC_{50} of 13 mg/L in trout.

The review of additional studies by Mayes and Oliver (1985) suggests differences in sensitivity between salmonids and other species of fish are more substantial (Table 4-1). For technical grade picloram (acid), the LC_{50} values for salmonids are reported as 4.8 (3.8-6.2) mg/L in cutthroat trout to LC_{50} values ranging from 5.5 to 19.3 mg/L in rainbow trout. For bluegill sunfish, the reported LC_{50} values range from 14.5 to 44.5 mg/L and an LC_{50} value of 55.3 (47.2 to 69.6) mg/L is reported for fathead minnow. As summarized in Table 4-1, the potassium salt of picloram appears to have similar toxicity to the acid form in cutthroat trout, rainbow trout, bluegill sunfish, and fathead minnow. Thus, while there is variability among multiple bioassays in the same species, the general tendency is for the LC_{50} values to be lower in salmonids than in other fish species. The quantitative consideration of higher sensitivity of salmonids relative to other fish species is discussed further in the dose-response assessment (Section 4.3.3.1). In their review, Mayes and Oliver (1985) do not clearly specify whether or not solvents were used in the various bioassays. In some cases, solvents do appear to have been used. For example, Mayes and Oliver (1985) cite a 96-hour LC_{50} value of 13 mg/L for the potassium salt of picloram. This appears to have been taken from the unpublished study by Alexander and Batchelder (1965), which was submitted to the U.S. EPA in the support of the registration of picloram.

Woodward (1976) also conducted static acute toxicity tests of technical grade picloram (acid form) with cutthroat trout and lake trout. Woodward (1976) reports LC_{50} values for cutthroat trout of 3.5 (3.4-4.0 mg/L) mg/L and for lake trout of 1.6 (1.2 - 2.0) mg/L. A later publication by Woodward (1982) reported a 96-hour LC_{50} of 3.9 (3.2 - 4.8) mg/L for fingerling cutthroat trout. As discussed in the following subsection on chronic toxicity in fish, Woodward (1976) used acetone as a vehicle whereas vehicles were not used in the studies summarized by Mayes and Oliver (1986). Unlike differences observed in the longer-term studies (Section 4.1.3.1.2), the acute toxicity data reported by Woodward (1976, 1982) is reasonably consistent with the data summarized by Mayes and Oliver (1985).

A toxicity test in a saltwater species, the sheepshead minnow, has been submitted to U.S. EPA since the publication of the RED (Boeri et al. 1995b). No mortality was observed in this species at the highest concentration tested: 131 mg/L expressed as Tordon 22 K or 27.2 mg a.e./L (Boeri et al. 1995b).

4.1.3.1.2. Subchronic Effects – For assessing the longer-term effects of picloram on fish, the U.S. EPA (1995b) used the egg and fry study in rainbow trout (*Salmo gairdneri*) by Mayes et al.

(1984), which was subsequently published in the open literature (Mayes et al. 1987). In this study, rainbow trout embryos (10 days pre-hatch) were exposed to technical grade picloram at average measured concentrations of 0 (control), 0.23, 0.38, 0.55, 0.88, 1.34, and 2.02 mg/L for 60-days post-hatch. Stock solutions were prepared by mixing technical grade picloram (acid) in deionized water and adjusting the pH to 8 with potassium hydroxide. Thus, the U.S. EPA (1995b) appropriately considered this assay as directly applicable to the potassium salt of picloram. Concentrations were maintained during the bioassay using a standard proportional diluter. No statistically significant or dose-related effects were noted on embryo hatching. Larval survival, however, was significantly reduced at (72.5% of controls) at 2.02 mg/L. In addition, concentration-related reductions were noted in both body weight and body length of fry at concentrations of 0.88 mg/L with an apparent NOEC of 0.55 mg/L.

Woodward (1976) conducted a similar bioassay using lake trout (*Salvelinus namaycush*) in which embryos were exposed to nominal concentrations 0, 0.035, 0.075, 0.240, 0.5, or 1 mg/L over 60 days. As in the study by Mayes et al. (1984), Woodward (1976) used a standard proportional diluter to adjust the concentrations among the different exposure groups. Unlike the study by Mayes et al. (1984), Woodward (1976) prepared stock solutions in acetone rather than water and concentration of picloram in the test solution was measured only in the highest test concentration. Woodward (1976) reports only a single control group and it is unclear if this represents an untreated or acetone control. Statistically significant reductions in lake trout fry survival and growth (yolk sac absorption rate, length, and weight) were noted at all concentrations and the effects are clearly concentration related for survival in fry prior to yolk sac absorption, as well as 60-day post-hatching survival, body weight, and length.

In another study of cutthroat trout (*Salmo clarki*) in which runoff exposure to picloram (acid) was simulated, Woodward (1979) reported that fluctuating concentrations of picloram (with 48 hour pulses of picloram acid on days 1, 8, 15, and 22 over total time of 24 days) resulted in a statistically significant reduction in cutthroat trout fry survival (LOEC = 1.3 mg/L) and growth (LOEC = 0.61 mg/L). The maximum concentration of picloram that did not affect survival and growth of cutthroat trout was 0.29 mg/L (NOEC) (Woodward 1979).

The discrepancies between the results of Mayes et al. (1984) and those of Woodward (1976, 1979) cannot be clearly resolved. The 1995 RED for picloram did not cite Woodward (1976). The 1995 RED for picloram considered the chronic toxicity data from field runoff studies by Woodward (1979) supplemental to the risk assessment because the studies were not required for registration but does not explicitly discuss the intermittent LOEC of 0.61 mg/L which is below the NOEC of 0.55 mg/L from the study by Mayes et al. (1984). Mayes and Oliver (1985) cite the study by Woodward (1979) without comment on the LOEC and do not cite the study by Woodward (1976), which is very similar in design to the study by Mayes et al. (1984).

The most obvious difference between the studies by Mayes et al. (1984) and those of Woodward (1976) involves the species tested, rainbow trout in the former and lake trout in the latter. Based on the acute toxicity data, lake trout have an acute LC_{50} of 1.6 (1.2 - 2.0) mg/L (Woodward

1976). Rainbow trout, on the other hand, have reported LC_{50} values in the range of 5.5 to 19.3 mg/L (Mayes and Oliver 1986). Thus, there is some basis for asserting that lake trout may be more sensitive to picloram than rainbow trout.

Other differences, however, involve the nature of the form of picloram (acid vs potassium salt), the failure of Woodward (1976) to monitor concentrations in all test solutions, and the use of acetone as a vehicle by Woodward (1976). The first two factors are not likely to be important. As reviewed by Mayes and Oliver (1985), differences in the toxicity of the various forms of picloram are not substantial. The failure of Woodward (1976) to monitor concentrations in the test solutions does increase uncertainty in the interpretation of the study but, assuming that the proportional diluters were properly calibrated, the failure to monitor concentrations would not in itself reduce substantially the credibility of the study.

The failure of Woodward (1976) to specify or possibly use an acetone control, however, is potentially serious. The current U.S. EPA/OPPTS. (2003) test guidelines for fish-early life stage toxicity studies require the use of a solvent-only control. This requirement is reasonable because solvent can impact the test organism directly and/or can impact the uptake of the test compound by the organism. Because the concentration of acetone in the test water is not reported by Woodward (1976), the potential significance of the use of acetone cannot be assessed directly. Under current standards, the study by Woodward (1976) would not be classified as acceptable using the U.S. EPA/OPPTS (2003) test criteria. While no studies have been encountered on the impact of acetone on the toxicity of picloram or other herbicides in longer-term (egg and fry) studies on trout, Mac and Steelye (1981) did note that low concentrations of acetone (10 µL/L) did increase the uptake of PCBs by lake trout over the course of a 52-day egg and fry study. The differences, however, were only statistically significant at Day 52 and no differences were noted in morality between the various experimental groups: untreated controls, trout exposed to PCBs alone, acetone alone, or PCBs with acetone.

No early life-stage or lifetime studies have been conducted with the Tordon formulations or the potassium salt of picloram in other more tolerant species of fish. Weinberg et al. (1996) have conducted an early life-stage study on fathead minnows using the triisopropanolamine salt of picloram. While the study is reported in detail, the precise method for preparing the high concentration solution is not specified. Methanol was used as a vehicle in the preparation of analytical standards. The study protocol (p. 11 of 39) does specifically state that the delivery system (a standard proportional diluter) would include a solvent control "if necessary". No results for a solvent control are reported. Thus, methanol does not appear to have been used as a vehicle in preparing the test solutions to which the fish were exposed. Statistically significant effects on growth and survival were seen at 20.1 mg/L but not at any lower concentrations (1.6 to 12 mg/L). These results appear to be expressed as the gross weight of the test material. In this study, the test material is reported to contain 10.6% a.i. and 5.9% a.e. Thus, the NOEC of 12 mg/L would correspond to about 0.71 mg a.e./L and the LOEC of 20.1 mg/L would correspond to a concentration of about 1.2 mg a.e./L. This NOEC is only modestly higher than the NOEC of 0.55 mg a.e./L reported in trout by Mayes et al. (1987).

The discrepancy between the LOEC of 0.035 mg/L in lake trout reported by Woodward (1976) and the NOEC values of 0.55 mg/L in rainbow trout (Mayes et al. 1984) and 0.71 mg/L in fathead minnow (Weinberg et al. 1996) has a major impact on this risk assessment and the use of these data in the risk assessment is detailed further in Section 4.3.3.1.

4.1.3.1.3. Field Observations – Keys (1992) reports a fish-kill incident that occurred in Montana after the application of picloram. In this incident, Tordon 22K was applied on July 12 and July 20, 1989 at a distance of 0.25 miles upstream from a fish hatchery. The amount applied and the distance of the application from the stream are not specified. The day following the second treatment, rain occurred (amount not specified) and a number of trout (characterized only as 8,880 pounds) died. Given the lack of detail in this report, it is difficult to assess whether or not the fish-kill incident was related to the applications of picloram. The plausibility of this type of event occurring after the application of picloram in Forest Service programs is discussed further in Section 4.4 (Risk Characterization).

4.1.3.2. Amphibians – Neither the published literature nor the RED for picloram (U.S. EPA 1995b) includes data regarding the toxicity of picloram to amphibian species.

4.1.3.3. Aquatic Invertebrates – In *Daphnia magna*, an acute (48-hour) LC_{50} value of 68.3 (63–75) mg/L and a chronic NOAEL of 11.8 mg/L of picloram (technical picloram)—based on mean total young per adult, total number of broods per adult, and mean brood size per adult—has been reported in the open literature (Gersich et al. 1985). At concentrations of 18.1 mg/L and higher, all of the indices for reproductive performance were decreased (Gersich et al. 1985). This information is identical to that summarized in the RED for picloram (U.S. EPA 1995b).

Information about the toxicity of picloram in mollusks is limited. No studies are available on the toxicity of picloram acid. The 1995 RED for picloram (U.S. EPA 1995b) cites the study Heitmuller (1975) for a 48-hour LC_{50} value of 18–32 mg/L for a 24.9% formulation of the potassium salt of picloram in an embryo/larvae assay in oysters. This corresponds to an LC_{50} value of about 4.5-8.0 mg a.i./L or 3.8-6.9 mg a.e./L. It is worth noting that this study did involve the testing of Tordon 22K, one of the formulations used by the Forest Service. In addition, the study by Heitmuller (1975) also involved bioassays of pink shrimp (*Penaeus duorarum*) and fiddler crabs (*Uca pubilator*), in addition to the eastern oyster (*Crassostrea virginica*). The 96 hour LC_{50} value in shrimp was 125 (114-138) mg/L expressed as the formulation, corresponding to about 31 mg a.i./L and 26.8 mg a.e./L. Fiddler crabs were not affected at concentrations of up to 1,000 mg/L of the formulation (249 mg a.i./L or 214 mg a.e./L).

No field studies are available on the toxicity of picloram to aquatic invertebrates. An unusually high number of gonadal neoplasms was identified in softshell clams from three Maine estuaries contaminated with herbicides, including picloram, 2,4-D, and 2,4,5-T (Gardner et al. 1991; Van Beneden 1993). However, the latter reports do not implicate picloram (or any specific herbicide directly) and the cause of tumors is unknown.

4.1.3.4. Aquatic Plants – The toxicity of picloram has been examined in both algae and aquatic macrophytes . The RED for picloram reports a NOEC of 13.1 mg/L and an EC_{25} for growth inhibition of 52.6 mg/L for a formulation of the potassium salt of picloram (35.2% a.i. or 30.2% a.e.) in *Selenastrum capricornutum* (U.S. EPA 1995b) for a formulation . This LC_{50} value for the formulation corresponds to an LC_{50} of 15.9 mg a.e./L. This is the only information summarized in U.S. EPA (1995b) on toxicity to aquatic plants.

Since the publication of the RED for picloram (U.S. EPA 1995b) additional studies have been submitted to the U.S. EPA on the toxicity of picloram to algae. In a Tier 2 acute toxicity test of Tordon K (24.1% picloram a.e.) using *Anabaena flos-aquae*, a freshwater blue-green alga, Boeri et al. (1994b) reports a 120-hour EC_{50} of 550 mg Tordon/L (95% CI 470-740) and 120-hour EC_{25} of 430 mg Tordon/L (95% CI 290-640). The associated NOEC at 120 hours was 390 mg Tordon/L. These Tordon K effect levels are equivalent to 132.5, 103.6, and 94.0 mg a.e./L for EC_{50}, EC_{25}, and NOEC, respectively. Acute toxicity testing of Tordon K (24.1% picloram acid) using *Navicula pelliculosa*, a freshwater diatom, suggests that this species is more sensitive to the acute toxic effects of picloram than *Anabaena flos-aquae* (Boeri et al. 1994c). Boeri et al. (1994c) reports a 120-hour EC_{50} of 3.9 mg Tordon/L (95% CI 2.0-7.8) and 120-hour EC_{25} of 1.3 mg Tordon/L (95% CI 0.42-3.7). The associated NOEC at 120 hours was 0.97 mg Tordon/L (the lowest concentration tested). These Tordon K effect levels are equivalent to 0.94, 0.31, and 0.23 mg a.e./L for EC_{50}, EC_{25}, and NOEC, respectively.

Additional studies on the toxicity of picloram to algae are available in the open literature. In a study designed primarily to assess the consistency between two different types of algal bioassays (the standard flask assay and a microplate assay), EC_{50} values for picloram (form not specified) in *Selenastrum capricornutum* were 21.7 (18.4–25.1) mg/L in the flask assay and 22.7 (18.5–27.0) mg/L in the microplate assay (St-Laurent et al. 1992). This study does not report NOEC values but, based on the reported LC_{50} value in the flask assay, the toxicity of picloram as assayed in this study is comparable to that in the assay summarized by U.S. EPA (1995b), in which the EC_{25} for growth inhibition in this algal species was reported as 52.6 mg/L or about 15.9 mg a.e./L. Peterson et al. (1994) reported that picloram (form not specified) caused slight growth inhibition (2 to 12%) in some algae species as well as substantial growth inhibition in a cyanobacteria, *Microcystis aeruginosa*., at a concentration of 1.76 mg/L. No inhibition was noted at this concentration in several other cyanobacteria species (Peterson et al. 1994). As with terrestrial microorganisms (Section 4.1.2.5), decarboxylation of picloram appears to increase toxicity to two species of *Chlorella* (algae), *C. vulgaris* and *C. pyrenoidosa*, with LC_{50} values of greater than 160 mg a.e./L for the picloram and 8 ppm and 49 ppm for 4A-TCP, the decarboxylated metabolite of picloram, in *C. pyrenoidosa* and *C. vulgaris*, respectively (Baarschers et al. 1988).

Also since the preparation of the RED, an additional study has been submitted to U.S. EPA on the toxicity of Tordon K to *Lemna gibba*, an aquatic macrophyte (Kirk et al. 1994). This bioassay was required by U.S. EPA (1994b) because of the sensitivity of terrestrial macrophytes to picloram. The NOEC in this assay was 50.5 mg a.i./L corresponding to 43.5 mg a.e./L. The

EC_{50} in this assay was 192.2 mg a.i./L (95% CI, 43.2 to 349), corresponding to 165.4 mg a.e./L (95% CI, 37.2 to 300). This is consistent with the report by Peterson et al. (1994) indicating that no statistically significant growth inhibition was observed in *Lemna gibba* at a concentration of 1.76 mg/L. Forsyth et al. (1997) assayed the effects of picloram on two other species of aquatic macrophytes: *Potamogeton pectinatus* (fennel pondweed) and *Myriophyllum sibiricum* (common water milfoil) at concentrations of 0.01 and 0.1 mg a.e/L. Picloram had no effect on growth in either species but inhibited flowering in *Myriophyllum sibiricum* at 0.1 mg/L 30-days post-treatment. This inhibition, however, was not statistically significant after 60 days post-treatment. No effects on flowering were observed in *Potamogeton pectinatus*.

As noted in Section 3.1.14, Oakes and Pollak (1999) noted that a commercial preparation of 2,4-D and picloram that contained Polyglycol 26-2 as well as Polyglycol 26-2 both inhibited oxidative function in submitochondrial particles derived from a marine algae. This information is difficult to assess quantitatively compared to the standard toxicity data on picloram or picloram formulations.

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 indirect 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 85 mg/kg under typical exposure conditions and up to about 859 mg/kg under more extreme conditions. Substantially lower doses are anticipated from the consumption of contaminated vegetation: up to about 6 to 9 mg/kg under typical conditions with an upper range of 17 to 27 mg/kg. 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 vertebrate from the consumption of contaminated vegetation are in the range of 0.00006 to 3 mg/kg/day. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, 0.000005 mg/kg/day to 0.0002 mg/kg/day. Based on general relationships of body size to body volume, larger vertebrates will be exposed to lower doses and smaller animals, such as insects, to much higher doses than small vertebrates under comparable exposure conditions. Because of the apparently low toxicity of picloram 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 rates considered in this risk assessment, 0.35 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 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 picloram 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 picloram is 0.05 (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 picloram is 0.001 (0.0001 to 0.004) 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 indirect 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 F14). 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 limited 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). Exposure scenarios for birds involve the consumption of contaminated insects by a small bird (Worksheet F14), the consumption of contaminated fish by a predatory bird (Worksheets F08 and F09), 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 3.1.12). 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 picloram.

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 (Moore 1964). 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, like bees and other terrestrial insects, might be exposed to much greater amounts of picloram 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). Because there is no information regarding the dermal absorption rate of picloram by bees or other invertebrates, this exposure scenario, detailed in worksheet F02b, also assumes complete absorption over the first day of exposure.

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 a steady-state 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. The bioconcentration data on picloram (Section 3.2.3.5) as well as the estimated rates of dermal absorption in humans (Section 3.1.12) suggest that picloram 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 picloram 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).

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, 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 that100% 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. No monitoring data have been encountered on the concentrations of picloram in insects after applications of picloram. The empirical relationships recommended by Fletcher et al. (1994) are used as surrogates as detailed in Worksheet F14. 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.

In addition to the consumption of contaminated vegetation and insects, picloram 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.

4.2.2.4. Ingestion of Contaminated Water – Estimated concentrations of picloram 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 non-target 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 non-target 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, picloram 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 μ droplet to fall 3 feet (91.4 cm) is approximately 3.2 seconds,

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

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

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

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 these particles 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 – Picloram 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 non-target 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 picloram 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. As discussed

further in Section 4.4.2.2, Bovey and Scifres (1971) have discussed the potential effects on irrigation water contaminated with picloram on alfalfa and effects on non-target vegetation have been observed irrigation water contaminated with other herbicides (e.g., Bhandary et al. 1997; Gomez de Barreda et al. 1993).

The levels of exposure associated with this scenario will depend on the concentration of picloram in the ambient water used for irrigation and the amount of irrigation water that is applied. As detailed in Section 3.2.3.4, picloram is relatively mobile and contamination of ambient water may be anticipated and can be quantified (i.e., 0.05 [0.01 to 0.2] mg a.e./L at an application rate of 1 lb a.e./acre [Worksheet B07]).

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 picloram in ambient water and an irrigation rate of 1 inch per day, the estimated functional application rate of picloram to the irrigated area is 8×10^{-6} (8×10^{-7}–3×10^{-5}) lb a.e./acre (see Worksheet F15 for details of these calculations). As discussed in the risk characterization, this level of exposure is inconsequential relative to off-site drift and runoff.

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 picloram, 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 picloram 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 picloram that might be transported by wind erosion depends on several factors, including the application, 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 picloram would be neither substantial or nor significant. For this risk assessment, it will be assumed that picloram 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 picloram in runoff, the deposition of the picloram 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. Aquatic Organisms. The potential for effects on aquatic species are based on estimated concentrations of picloram 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 picloram is 0.05 (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 picloram is 0.001 (0.0001 to 0.004) 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., 0.35 lb a.e./acre.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview. For terrestrial mammals, the dose-response assessment for chronic exposure is based on a NOAEL of 7 mg/kg/day from a 6-month dog feeding study. For acute exposures, a NOAEL of 34 mg/kg/day is used based on a teratogenicity study in rabbits. For birds, short term feeding studies are used to estimate an acute NOAEL of 1,500 mg/kg body weight. No adequate data are available on chronic toxicity in birds and the chronic NOAEL of 7 mg/kg/day derived for mammals is used to characterize risk. Relatively little data is available on terrestrial invertebrates and a standard LD_{50} value of >1000 mg/kg in bees is used to characterize risk in terrestrial invertebrates.

For assessing the potential consequences of exposures to nontarget plants via runoff, a NOEC of 0.000012 lb a.e./acre is used for sensitive species and a NOEC of 0.4 lb a.e./acre is used for tolerant species. For assessing the impact of drift, bioassays on vegetative vigor are used with a NOEC of 0.00021 lb a.e./acre for sensitive species and a NOEC of 0.062 lb a.e./acre for tolerant species.

Soil microorganisms may display detectable responses to picloram at relatively low concentrations and true NOEC values for effects on microorganisms are not available. For this risk assessment, a soil concentration of 1 ppm is used as benchmark dose and the potential consequences of soil contamination by picloram is considered further in the risk characterization.

The general dose-response assessment for aquatic species is characterized by substantial variability within different groups (fish, invertebrates, and plants) but few substantial difference among the different groups. In general, sensitive species have NOECs or LC_{50} values in the 0.2 to 4 mg/L range and tolerant species have NOECs or LC_{50} values in the 10 to over 100 mg/L range. Trout appear to be the most sensitive animal species, with acute LC_{50} values as low as 0.8 mg/L. The dose response assessment for aquatic species is complicated by a very low reported LOEC, 0.035 mg/L in lake trout. This is an older study that was not designed to meet current standards. Nonetheless, this study is well documented and is not discounted. A relatively low LOEC of 0.1 mg/L has also been reported in on species of macrophyte. The observed effect was a transient delay in flowering with no inhibition of growth.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals – As summarized in Section 4.1.2.1, data are available on experimental mammals that permit the derivation of both acute and chronic NOAEL values that can be used for risk characterization. Most acute exposure scenarios developed in this risk assessment involve an exposure period of one day. The U.S. EPA (1995b) used an acute LD_{50} value to characterize effects in mammalian wildlife. In the current risk assessment, an attempt is made to avoid the use of LD_{50} and LC_{50} values for risk characterization and rely instead on NOAEL values. The available teratology studies on picloram (Section 3.1.9) all involve gavage exposures conducted over a period of about 10 days. The NOAEL for either material toxicity or toxicity to offspring is 34 mg a.e./kg/day in rabbits (John et al. 1984) and 150 mg a.e./kg/day in rats (Schroeder 1990). The lower NOAEL of 34 mg a.e./kg/day in rabbits from the study by John et al. (1984) is used to characterize risks of acute exposure.

For chronic exposures, NOAEL values are available in rats and dogs. As discussed in Section 4.1.2, a dietary NOAEL of 20 mg/kg/day and a corresponding LOAEL of 60 mg/kg/day were observed in a two-year feeding study in male and female Fischer rats using picloram acid (Landry et al. 1986). In dogs, a corresponding NOAEL of 7 mg/kg/day with a corresponding LOAEL of 35 mg/kg/day was noted in a 6-month feeding study (Barna-Lloyd et al. 1982). For this risk assessment, the NOAEL of 7 mg/kg/day is used to characterize risks from chronic exposures.

The selections of the acute and chronic NOAEL values is intended to be protective and it could be argued that the selections are overly protective. For example, the difference between the acute NOAEL is rats and rabbits is about a factor of 5. Since both rats and rabbits are wildlife species of concern, the application of separate NOAEL values for these and related species could be considered. In some cases, systematic and substantial differences across species can be well documented and related to body size (e.g., Boxenbaum and D'Souza 1990). For picloram, the larger species – i.e., rabbits and dogs – do appear to be somewhat more sensitive than the smaller species, the rats, in both acute and chronic exposures. Nonetheless, given the large number of species that may need to be considered in various site-specific assessments, it seems prudent to use the more protective approach of selecting the most sensitive species for both acute and chronic exposures. As noted in Section 4.4.2, this protective approach has no impact on the characterization of risk in this risk assessment. Thus, unlike the approach taken with fish and plants, sub-groupings based on apparently sensitive and tolerant species is not used in this risk assessment.

4.3.2.2. Birds – As noted in Section 4.1.2.2, the acute and subchronic dietary toxicity studies in birds are not substantially different from the studies in mammals and there are no chronic toxicity studies in birds that would support the development of a separate chronic NOAEL for avian species. Consequently, for longer-term exposures, the NOAEL of 7 mg/kg/day will be used and this value is included in Worksheet G02 for the risk characterization of birds for longer term exposure scenarios.

For short-term exposures, the use of the 20 mg/kg/day NOAEL would be grossly conservative and tend to distort rather than clarify risk. In acute LD_{50} studies involving gavage applications – i.e., the administration of the compound directly into the stomach using a tube – doses of up to 2500 mg/kg body weight have not killed half of the animals – i.e., $LD_{50} > 2500$ mg/kg body weight. In 14-day feeding studies, the reported NOAEL is about 1500 mg/kg body weight (Section 4.1.2.2). These short term feeding studies are more closely analogous to environmental exposures than gavage studies and thus are more relevant to the risk assessment. Consequently, for risk characterization, the short-term NOAEL of 1,500 mg/kg body weight is used, as indicated in Worksheet G02.

4.3.2.3. Terrestrial Invertebrates – As discussed in Section 4.1.2.3, there is little information on the toxicity of picloram to terrestrial invertebrates compared to the more extensive studies available in mammals. The estimated acute contact LD_{50} value of greater than 1,000 mg/kg in bees is consistent with the available LD_{50} values on mammals and birds. Similarly, the 14-day dietary NOEL of 5000 mg/kg for the snail is similar to dietary NOAELs in rodents and birds. Thus, although the information is limited compared to the very large number of potential nontarget terrestrial invertebrates, there is no basis for suggesting that picloram is likely to be toxic to terrestrial invertebrates. For the purpose of characterizing risks, the reported LD_{50} of >1000 mg/kg/day will be used for risk characterization and is included in Worksheet G02.

4.3.2.4. Terrestrial Plants (Macrophytes) – As discussed in Section 4.1.2.4, picloram is more toxic to broadleaf plants than to grasses or grains. For assessing the potential consequences of exposures to nontarget plants via runoff, the EC_{25} for seed emergence in soybeans of 0.000014 kg a.e./ha is used (equivalent to 0.000012 lb a.e./acre from U.S. EPA 1995b, p. 55). As discussed in Section 4.1.2.4, a more recent seedling emergence assay noted a much higher NOEC of 0.00027 kg a.i./hectare – the pinto bean from the study by Schwab (1995). The reason for the substantially lesser sensitivity of soybeans in the assay by Schwab (1995) relative to the earlier assay cited by U.S. EPA (1995b) – i.e., a factor of over 500 based on the EC_{25} values – is not apparent. For this risk assessment, the NOEC of 0.000012 lb a.e./acre used by U.S. EPA (1995b) is maintained for assessing the impact of runoff and this value is used in Worksheet G04. The most tolerant plant species in seedling emergence assays appears to be corn, with an NOEC of 0.4 lb a.e./acre (Schwab 1995). This value is used in Worksheet G04 to characterize risks associated with runoff in tolerant plant species.

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. In this type of assay, the most sensitive species appears to be the sunflower, with a NOEC of 0.27 g a.i./ha (Schwab 1996), which corresponds to an application rate of about 0.00021 lb a.e./acre [0.27 g a.i./ha ÷ 1000 g/kg × 0.892 lb/acre per kg/ha × 0.86 a.e./a.i.]. 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 vegetative vigor assay is 70 g a.e./ha for wheat (U.S. EPA 1995b, p. 55), which corresponds to an application rate of about 0.062 lb a.e./acre, and this value is used in Worksheets G05a and G05b for characterizing risks to tolerant plant species associated with drift.

As also indicated in Section 4.1.2.4, some plant species may develop resistence to picloram. While this may impact an assessment of the efficacy of picloram in some types of applications, the potential for resistence to picloram in nontarget plant species has not been documented and is not used to modify the risk characterization (Section 4.4.2.2).

4.3.2.5. Terrestrial Microorganisms – Picloram appears to be toxic to soil microorganisms under conditions of exposure that are analogous to applications used in Forest Service programs. 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.

As summarized in Section 4.1.2.5, most of the data on the effects of picloram on soil microorganisms involve the latter type of studies and these studies will lead to a more conservative, and probably more realistic, assessment of risk. There does not appear to be a clear or defined threshold for the toxicity picloram to soil microorganisms. Concentrations of picloram in soil as low as 0.025 ppm appear to result in an increase in the persistence of picloram (USDA/ARD 1995) and this may be attributable to effects on microbial populations. It is less clear that this will result in remarkable changes in normal microbial functions in soil. Based on the study by Tu (1994), a concentration of 10 ppm results in only a transient change in only a transient decrease in nitrification – i.e., at 2 but not 3 weeks after incubation. Similarly, the study by Prado and Airoldi (2001) suggests that concentrations of 1 ppm in soil will only modestly inhibit microbial activity. There are not studies indicating that picloram will adversely effect mycorrhizal organisms resulting in secondary damage to plants. As noted in Section 4.1.2.4, the primary mechanism of action of picloram on terrestrial plants involves auxin activity leading to uncontrolled and abnormal growth.

For this risk assessment, a soil concentration of 1 ppm will be used as a benchmark to suggest concentrations that may result in a detectable effect on microbial populations in soil. While the toxicity of the metabolites of picloram may contribute to the effect of picloram on soil microorganisms (4.1.2.5), the effect of the metabolites should be encompassed by the available toxicity data on picloram in soil – i.e., metabolites are presumably formed in the available studies and it is the metabolites that may contribute most to the observed effects expressed in terms of initial concentrations of picloram.

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 – As summarized in Table 4-1 and detailed further in the review by Mayes and Oliver (1985), acute toxicity bioassays of picloram in fish are highly variable. Notwithstanding this variability, trout do generally appear to be more sensitive to picloram than other species. Thus, risk is characterized for both sensitive and tolerant fish species. For this risk assessment, the lower range of the lowest LC_{50} value for trout is used for the risk characterization – i.e., 0.8

mg/L in cutthroat trout reported in Mayes and Oliver (1985). Risk to more tolerant fish species is characterized using the highest reported LC_{50} value, 55.3 mg/L in fathead minnow (Mayes and Oliver 1985).

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 picloram, the sublethal effects associated with acute exposures must be assessed based on LC_{50} values 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.

Toxicity values for chronic toxicity may be based on the available egg-and-fry/early life stage studies. While these do not involve full life cycle testing, they encompass an exposure period of about 60-days during a sensitive period of development. This type of assay is used commonly by U.S. EPA (e.g., U.S. EPA 1995b) to characterize chronic toxicity in fish.

A major difficultly in the assessment of chronic effects in fish concerns the distinction between sensitive and tolerant species, particularly in the interpretation of the studies by Woodward (1976, 1979, 1982). The U.S. EPA (1995b) used the study by Mayes et al. (1984), with a NOEC of 0.55 mg/L in rainbow trout, to characterize chronic risks associated with exposure to the potassium salt of picloram. This is very similar to the chronic NOEC of 0.77 mg/L for the TIPA salt of picloram in fathead minnow. Taking this approach, no "sensitive" species would be identified for chronic effects in fish – i.e., the two NOEC values are virtually identical.

In the study by Woodward (1976), however, a different species of trout was tested, lake trout, and the reported LOEC is 0.035 mg/L, a factor of about 16 below the NOEC reported in rainbow trout by Mayes et al. (1984). As detailed in Section 4.1.3.1.2, the Woodward (1976) study may be criticized for not using a solvent control and not measuring the actual concentrations of picloram in the water. The failure to include a solvent control may be the most important criticism because a study is available on the toxicity and uptake of PCBs trout indicating that low concentrations of acetone may enhance absorption in trout during early life stages (Mac and Seelye (1981) . Although the U.S. EPA (1995b) did not discuss the Woodward (1976) study, this study clearly does not meet current guidelines for fish toxicity bioassays.

Notwithstanding these reservations, the Woodward (1976) study cannot be discounted. The study appears to have been well conducted and is from a credible source – i.e., U.S. Fish and Wildlife Service. While flawed, one reasonable interpretation of the Woodward (1976) study is

that lake trout may be more sensitive than rainbow trout. In the absence of additional experimental data – i.e., a new matched bioassay in lake trout and rainbow trout – this interpretation cannot be discounted.

For the current risk assessment, both the study in rainbow trout Mayes et al. (1984) as well as the study in lake trout (Woodward 1976) are used to characterize the potential longer risks to salmonids.

4.3.3.2. Invertebrates – As with the acute toxicity data in fish, there appears to be substantial variation in the sensitivity of different invertebrate species to picloram. As detailed in Section 4.1.3.3, the lowest LC_{50} value is 26.8 mg a.e./L for pink shrimp (Heitmuller 1975). The highest LC_{50} value is 214 mg a.e./L for the fiddler crab (Heitmuller 1975). The LC_{50} value for *Daphnia magna*, a freshwater invertebrate often used in risk assessment, is 68.3 mg/L. For this risk assessment, the LC_{50} values for pink shrimp and fiddler crab are used to bracket a plausible range of sensitivities for invertebrates after acute exposures to picloram.

For chronic exposures, only two studies appear useful for assessing risk. The NOEC of 11.8 mg/L from standard life-cycle study in *Daphnia magna* by Gersich et al. (1985) was used by U.S. EPA (1995b) and will be adopted in this risk assessment for tolerant species. Heitmuller (1975) reports a 48 hour LC_{50} value in the range of 3.8-6.9 mg a.e./L for an embryo/larvae assay in oysters. While this is not a full life-cycle assay, the LC_{50} is below the NOEC for the life-cycle study in daphnids and suggests that oyster embryo/larvae may be more sensitive to picloram than daphnids. In the absence of any further information, the lower range of this LC_{50}, 3.8 mg a.e./L is used for assessing the effects of longer term exposures in sensitive invertebrates.

4.3.3.3. Aquatic Plants – As with both fish and invertebrates, there appear to be remarkable differences in the toxicity of picloram to various species of aquatic plants. Nonetheless, there appears to be relatively little difference in the toxicity of picloram to common test species of algae (microscopic plants) and macrophytes. For algae, the lowest NOEC is for a diatom, 0.23 mg a.e./L reported in *Anabaena flos-aquae* (Boeri et al. 1994c). The most tolerant algae appears to be a freshwater blue-green alga, *Anabaena flos-aquae*, with a NOEC of 94 mg a.e./L (Boeri et al. 1994b). These two NOEC values will be used in assessing potential effects in tolerant and sensitive species of algae. The highest reported NOEC in a macrophyte is 43.5 mg a.e./L reported in duckweed (U.S. EPA 1995b). The lowest reported effect level for any macrophyte is 0.1 mg/L for common water milfoil (Forsyth et al. 1997). This is classified as a LOEC because of a transient inhibition or delay in flowering but the exposure was not associated with any decrease in growth.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. Picloram is an herbicide and the most likely damage to nontarget species will involve terrestrial plants. As is the case with any herbicide, the likelihood of damage to nontarget plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential nontarget species. Sensitive plant species could be adversely affected by the off-site transport of picloram under a variety of different scenarios depending on local site-specific conditions that cannot be generically modeled. If picloram is applied in the proximity of sensitive crops or other desirable sensitive plant species, site-specific conditions and anticipated weather patterns will need to considered if unintended damage is to be avoided. More tolerant plant species are not likely to be affected unless they are directly sprayed or subject to substantial drift. A detectable inhibition of the activity of soil microorganisms is also likely at application rates used in Forest Service programs. These changes could lead to an increase in the persistence of picloram in soil and/or a more general decrease in microbial activity. That this inhibition would be associated with detectable changes in soil productivity or other undesirable gross effects is much less certain. The potential for adverse effects on other terrestrial nontarget animal species appears to be remote. The weight of evidence suggests that no adverse effects in terrestrial animals are plausible using typical or even very conservative worst case exposure assumptions.

There is substantial variability in the toxicity of picloram to aquatic species. While this variability adds uncertainty to the dose-response assessment, it has no substantial impact on the risk characterization. None of the hazard indices for fish, aquatic invertebrates, or aquatic plants exceed a level of concern.

The risk characterization for both terrestrial and aquatic species is limited by the relatively few animal and plant species on which data are available compared to the large number of species that could potentially be exposed. This limitation and consequent uncertainty is common to most if not all ecological risk assessments.

4.4.2. Terrestrial Organisms.

4.4.2.1. Terrestrial Animals – The quantitative risk characterization for terrestrial animals is summarized in Worksheet G02. The toxicity values used for each group of animals – mammals, birds, and insects – is summarized at the bottom of Worksheet G02 and refer to values derived in the dose-response assessment (Section 4.3).

As specified in Worksheet G02, both the central estimates as well as the upper range of the hazard quotients associated with the acute and longer-term exposure scenarios are below unity by at least a factor of 5, indicating that toxic effects attributable to picloram are not likely to occur. The highest hazard quotient is 0.2 – i.e., for the large bird consuming contaminated vegetation on-site. This scenario, as well as the similar exposure scenario for the large mammal consuming vegetation on-site, is essentially used in these risk assessments as a very conservative/extreme screening scenario. The scenarios assume that the vegetation is treated at the nominal application rate of 0.35 lb/acre and that the animal stays in the treated area consuming nothing but the

contaminated vegetation. Given that most forms of vegetation treated at the nominal application rate of 0.35 lb/acre would likely die or at least be substantially damaged (Section 4.4.2), this exposure scenario is implausible. It is, however, routinely used in Forest Service risk assessments as a very conservative upper estimate of potential exposures. Other more plausible exposure scenarios are below the level of concern by factors of about 16 (HQ=0.06) to 100,000 (HQ=1e-05 or 1×10^{-5}).

The simple verbal interpretation of this quantitative risk characterization is similar to that of the human health risk assessment: the weight of evidence suggests that no adverse effects in mammals are plausible using typical or even very conservative worst case exposure assumptions.

As with most ecological risk assessments, this characterization of risk must be qualified. Picloram has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging nontarget animals. Notwithstanding this limitation, the available data are sufficient to assert that adverse effects in terrestrial animals from the use of this compound in Forest Service programs do not appear to be likely. Although based on somewhat different assessment methods and a much higher application rate (2.16 lb/acre), the conclusion reached in the current risk assessment is essentially identical to that presented by U.S. EPA (1995b) in the RED for picloram.

4.4.2.2. 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.

Picloram is an effective herbicide, at least for a number of different broadleaf weeds, and adverse effects on some nontarget plant species due to drift are likely under certain application conditions and circumstances. As indicated in Worksheets G05a and G05b, off-site drift of picloram associated with ground and aerial applications may cause damage to sensitive plant species at distances of nearly 1000 feet from the application site. The closer that the non-target 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 picloram would depend on a several site-specific conditions, including wind speed and foliar interception. In other words, in some right-of-way applications conducted at low wind speeds and under conditions in which vegetation immediately adjacent to the application site would limit off-site drift, damage due to drift would probably be limited to the area immediately adjacent to the application site. Tolerant plant species would probably not be impacted by the drift of picloram and might show relatively little damage unless they were directly sprayed.

As summarized in Worksheet G04, runoff may present a significant risk to sensitive non-target plant species under conditions in which runoff is favored – i.e., clay soil over a very wide range

of rainfall rates. At sites in which runoff is less plausible – i.e., loam or sandy soils – effects on sensitive species are not likely.

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.

Bovey and Scifres (1971) suggest that concentrations of picloram in water in the range of 0.001 to 0.004 mg/L are not likely to be associated with adverse effects but that multiple watering at concentrations of 0.004 mg/L could reduce growth and 0.01 mg/L could severely impact growth. This risk assessment supports this assertion. As indicated in Worksheet F15, peak concentrations of picloram in water are estimated at 0.0035 to 0.07 mg/L and functional application rates in the use of this water in irrigation would be in the range of 0.00008 to 0.002 lb/acre. Based on the NOEC values for seedling emergence in sensitive plants (0.000019 lb/acre) and tolerant plants (0.4 lb/acre), an inhibition of seedling emergence could be anticipated in some sensitive plant species. Based on the NOEC values for vegetative vigor in sensitive plants (0.00021 lb/acre) and tolerant plants (0.062 lb/acre), damage to growing plants could occur in sensitive but not tolerant plant species. The likelihood of observing these effects, however, may be remote. The highest concentrations of picloram in ambient water that might be used for irrigation are associated with high rainfall rates. In regions with high rainfall rates, the use of irrigation water would likely be 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. As summarized in Worksheet G04, this is substantially less than off-site losses associated with runoff from clay but similar to off-site losses associated with drift in the range of about 200 feet to 900 feet. As with the drift scenarios, wind erosion could lead to adverse effects in sensitive plant species. Wind erosion of soil contaminated with picloram 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 transport of picloram under a variety of different scenarios depending on local site-specific conditions that cannot be generically modeled. If picloram is applied in the proximity of sensitive crops or other desirable sensitive plant species, site-specific conditions and anticipated weather patterns will need to considered if unintended damage is to be avoided. More tolerant plant species are not likely to be affected unless they are directly sprayed or subject to substantial drift.

4.4.2.3. Terrestrial Microorganisms – Changes in soil microorganisms may be evident at very low concentrations in soil and 1 ppm is adopted in this risk assessment as a benchmark

associated with a modest inhibition of microbial activity, assayed as an apparent decrease and delay in glucose utilization. As summarized in Table 4-2, peak concentrations of picloram in soil at application rates used in Forest Service programs are likely to exceed this concentration. Longer term concentrations of picloram in soil will be much lower except in very arid climates – i.e., in the range of about 0.01 ppm in areas with substantial runoff or erosion. Even these lower concentrations, however, are associated with an increase in the persistence of picloram in soil, suggesting an inhibition of microbial metabolism and the persistence of picloram in soil has been shown to increase at application rates similar to those used in Forest Service programs – i.e., about 0.4 to 1.6 lbs per acre (Krzyszowska et al. 1994).

That such changes are likely to occur seems reasonably certain. The consequences of such effects, however, are far less certain. As noted in Section 4.1.3.1, field studies (Brooks et al. 1995; Nolte and Fulbright 1997) have not noted substantial adverse effects associated with the normal application of picloram that might be expected if soil microbial activity were substantially damaged. In addition, picloram has been used as an herbicide since 1964 (U.S. EPA 1995b). It does not seem plausible to assert that changes that might be anticipated in microbial populations after the application of picloram would have an adverse impact on soil productivity or other secondary changes that would lead to grossly detectable and significant effects in the environment.

4.4.3. Aquatic Organisms. There is substantial variability in the toxicity of picloram – i.e., within fish, aquatic invertebrates, and aquatic plants – that in some cases spans over an order of magnitude. An added complication in the risk assessment of picloram to aquatic species is the nature of the data on salmonids. As discussed at some length in Section 4.1.3.1, two sets of studies on the toxicity of picloram to trout are inconsistent and the study reporting the most sensitive response after longer term exposures, an LOEC of 0.035 mg/L (Woodward 1976), is a factor of about 16 below a NOEC reported in another species of trout (Mayes et al. 1984).

While this variability adds uncertainty to the dose-response assessment, it has no substantial impact on the risk characterization. As detailed in Worksheet G03, none of the hazard indices for fish or aquatic invertebrates exceed a hazard quotient of 0.09 at the upper range of plausible exposures and most hazard quotients are below the level of concern by factors of 100 to over 1000. For aquatic plants, the highest hazard quotient is 0.01 for longer-term exposures and 0.7 for short-term exposures. While there are always additional uncertainties associated with the use of general exposure assessments and while many different site specific conditions could impact exposure, the exposures assessments for aquatic species are based modeling data that are well-supported by monitoring data. While the fish-kill incident reported by Keys (1992) raises concern for the potential effects of a picloram on trout (Section 4.1.3.1.3), the very low hazard quotients for sensitive fish species (Worksheet G03) suggests that fish-kills associated with the normal application of picloram in Forest Service programs are implausible.

Thus, similar to the risk assessment of terrestrial animals, there seems no plausible basis for asserting that the use of picloram in Forest Service programs is likely to lead to adverse effects in

aquatic species. As with the risk characterization for terrestrial species, this risk characterization is limited by the relatively few animal and plant species on which data are available compared to the large number of species that could potentially be exposed. This limitation and consequent uncertainty is common to most if not all ecological risk assessments.

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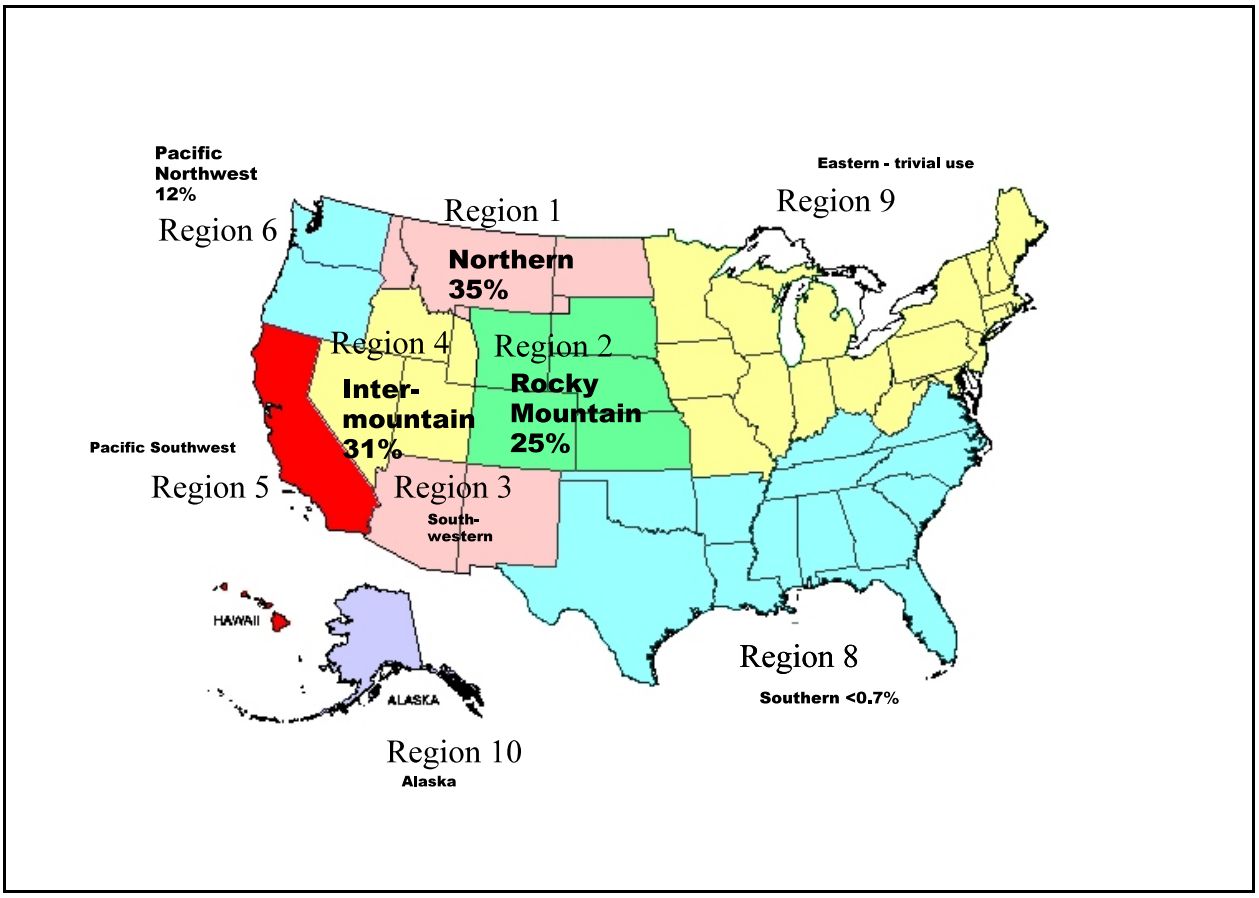

Figure 2-1. Use of picloram by the USDA Forest Service in various regions of the United States.

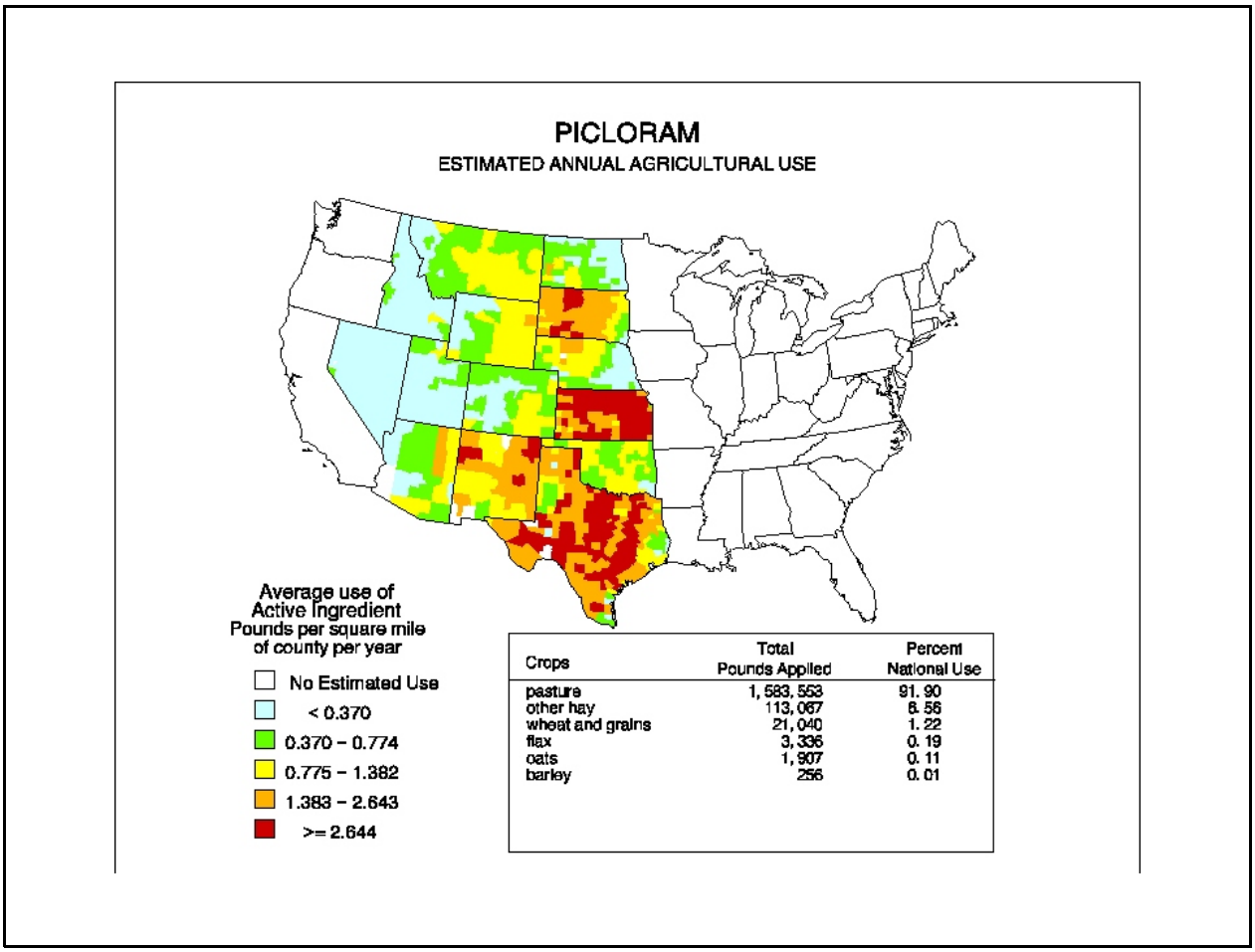

Figure 2-2. Agricultural use of picloram in the United States for 1992 (USGS 1998).

Table 2-1. Identification and Physical/Chemical Properties of Picloram and the Potassium Salt of Picloram.

Property	Value	Reference
Synonyms	Formulations: Tordon 22K, Tordon K	C&P Press 1998
CAS Number	1918-02-1 (acid) 081510-83-0 (salt)	Budavari et al. 1989 C&P Press 1998
U.S. EPA Registration Number	62719-6	C&P Press 1998
MW $C_6H_3Cl_3N_2O_2$	241.48 ($acid^+$) 280.6 (potassium salt)	Budavari et al. 1989 U.S. EPA (1995b)
a.i. (K-salt) to a.e. conversion	0.8606	241.48÷280.6
Henry's Law Constant (atm m^3/mole)	3.3×10^{-10}	Mabury and Crosby 1996
pK_a	3.6 2.3 (22°C) 1.9	Budavari et al. 1989 Baker 1989c USDA/ARS 1995
Vapor pressure	6.16×10^{-7} mm Hg (35°C) 6.0×10^{-10} mm Hg (25°C)	Budavari et al. 1989 Baker 1989c
Water solubility	430 mg/L (acid, pH 2.5) ∞ (salt) 2×10^5 mg/L (salt) 4.3×10^5 mg/L (K salt) 7.2 mg/L (technical in distilled water)	USDA/ARS 1995 C&P Press 1998 Knisel et al. 1992 Neary et al. 1993 Washburn 2002
$K_{o/w}$ (acid)	22.9 84 79 [log $K_{o/w}$ = 1.9] 1.8 0.89 [pH 5-9] {log Ko/w = -0.05}	SRC 1998 Baker 1989c Washburn 2002 Bidlack (1980) USDA/ARS 1995
$K_{o/c}$ (acid, ml/g)	16 16 (2.2 to 92.9) 29 (7-48) 23(14-33) [Silt Loam, 2.9% OM] 47(22-71) [Sandy Loam, 3.3% OM] 29.9(23.7-36.1) [Sandy Loam, 3.3% OM] 45.3(9-82) [Silt Loam, 2.9% OM]	Knisel et al. 1992 Havens et al. 2001 USDA/ARS 1995 Close et al. 1998 Close et al. 1998 Close et al. 1999 Close et al. 1999
Foliar $t_{1/2}$ (field dissipation)	8 days	Knisel and Davis 2000
Water $t_{1/2}$ (field dissipation)	15 days [0.046 day^{-1}] 14 [0.048 day^{-1}]	USDA 1989c,d Scifres et al. 1977
Water $t_{1/2}$ (surface water with degradation via photolysis.)	2.6 days	Woodburn et al. 1989
Soil, aerobic $t_{1/2}$ in days	90 (24 to 272) 18 to 300	Havens et al. 2001 USDA/ARS 1995
Soil $t_{1/2}$ (field dissipation)	90 days 131 days 108 (31 to 206) 203 (160-246) [Silt Loam] 244 (181-299) [Sandy Loam]	Knisel et al. 1992 Micheal and Neary 1993 USDA/ARS 1995 Close et al. 1998 Close et al. 1998

Table2-2: Use of picloram by USDA Forest Service in 2001 by Type of Use (USDA/FS 2002)

Use Classification	Total Pounds	Total Acres	Pounds per acre average	Proportion of Use by Pounds	Proportion of Use by Acres
Noxious Weed Control	12,865.90	62,897.12	0.20	0.9989	0.9992
Recreation Improvement	3.50	7.00	0.50	0.0003	0.0001
Rights-of-Way	11.10	44.80	0.25	0.0009	0.0007
Grand Total	12,880.50	62,948.92	0.20	1	1

Table 2-3: Use of picloram by USDA Forest Service in 2001 by Region (USDA/FS 2002)

Region	Pounds	Acres	lbs/acre	Proportion of Total Pounds	Proportion of Total Acres
Northern (R1)	4450.06	22147.83	0.20	0.345	0.35
Rocky Mountain (R2)	2759.65	15422.42	0.18	0.214	0.25
Southwestern (R3)	5.00	30.00	0.17	0.000	0.00
Intermountain (R4)	4015.10	14776.19	0.27	0.312	0.23
Pacific Southwest (R5)	0.00	0.00	N/A	0.000	0.00
Pacific Northwest (R6)	1565.69	10402.18	0.15	0.122	0.17
Southern (R8)	85.00	170.00	0.50	0.007	0.003
Eastern (R9)	0.0004	0.30	0.001	3e-08	5e-06
Total	**12880.50**	**62948.92**	**0.20**	1	1

Table 3-1: Concentrations of picloram in streams after the application of known amounts

Application Method	Application Rate (kg/ha)[a]	Concentration in water (ppb)[a]	Application Rate (lb/acre)[b]	Water Contamination Rate (ppb per lb/acre applied)[c]
Aerial	5.6	241	5.00	48.25
Ground broadcast	5.6	77	5.00	15.41
Injection	5	10	4.46	2.24
Injection	0.3	6	0.27	22.42
Injection	1.3	21	1.16	18.11
Injection	0.3	10	0.27	37.37
Injection	0.6	4	0.54	7.47

[a] Taken from data from Michael and Neary 1993, Table 3, p. 407.
[b] 1 kg/ha = 0.892 lb/acre
[c] Concentration in ppb divided by application rate in lb/acre.

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

Chemical Specific Parameters

Parameter	Clay	Loam	Sand	Comment/ Reference
Halftimes (days)				
Aquatic Sediment	2000	2000	2000	Note 1
Foliar	8	8	8	Knisel and Davis 2000
Soil	150 days at 0-1", 200 days at 1" to 1', 320 days at 1' to 2', and 2000 days at 2' to 5' layer.			Note 2
Water	14	14	14	Scifres et al. (1977)
Ko/c	48	29	7	Note 3
K_d	1.44	0.43	0.021	Note 4
Water Solubility, mg/L	200000	200000	200000	Knisel and Davis 2000
Foliar wash-off fraction	0.6	0.6	0.6	Knisel and Davis 2000

Note 1 Aquatic sediment halftimes not encountered. Value of 2000 days based on halftimes for deep soil layers (Close et al. 1999, Table 5, p. 70).

Note 2 Soil halftimes for picloram are complex and depend on application rate and soil depth. Aerobic soil halftimes vary with soil concentration: 18 days at 0.0025 ppm ,29 days at 0.025 ppm , 150 at 0.25 ppm, and 300 days at 2.5 ppm (ARS 1995). The effect of soil depth has been demonstrated by Close et al. (1998, 1999), with soil halftimes over a range of 160 to 324 days in the upper soil layer (about 1 foot) and 318 to 2146 days at depths of 1 foot to about 5 feet (Close et al. 1998, Table 4, p. 57). An application rate of 1 lb/acre is equivalent to 11.21 $\mu g/cm^2$. Assuming a soil incorporation depth of 1 cm and a density of 1 g/cm^3, the initial soil concentration would be about 11.2 ppm in the top 1 cm and 0.37 ppm in the top one foot of soil. For the GLEAMS modeling, a soil halftime of 150 days is used for the upper one inch layer, 200 days for the 1" to 1 foot layer and 320 days for the 1' to 2' layer, and 2000 days for the 2' to 5' layer.

Note 3 Central value and range taken from USDA/ARS (1995) assuming highest value in clay, followed by loam and then sand. Value for loam supported by values from Close et al. (1998, 1999).

Note 4 Based on $K_{o/c}$ and estimates of proportion (*P*)of organic carbon in clay (0.03), loam (0.015), and sand (0.003), where $K_d = K_{o/c} * P$.

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 picloram 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	0.00	0.00	0.00	0.00	0.00	0.00
10	0.00	0.00	0.00	0.00	0.00	0.00
15	0.10	10.21	0.00	0.00	0.62	19.36
20	0.18	22.28	0.06	2.47	1.18	16.55
25	0.24	35.66	0.26	6.81	1.37	26.33
50	0.44	98.00	0.87	11.57	1.59	48.24
100	0.57	184.02	0.93	16.45	1.29	67.98
150	0.57	187.13	0.85	17.86	1.05	74.53
200	0.54	178.01	0.75	17.64	0.89	72.87
250	0.51	166.37	0.67	16.92	0.77	75.56

Table 3-4: Summary of modeled concentrations of picloram 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	0.00	0.00	0.00	0.00	0.00	0.00
10	0.00	0.00	0.00	0.00	0.00	0.00
15	0.69	6.98	1.0e-05	1.5e-04	3.25	9.43
20	0.84	14.32	0.15	0.61	4.09	9.96
25	0.96	21.73	0.45	1.39	3.95	16.97
50	1.31	59.10	1.01	2.42	3.16	32.04
100	1.57	125.79	0.90	5.19	2.37	48.15
150	1.56	139.78	0.75	5.19	1.99	54.74
200	1.49	141.84	0.64	5.19	1.75	58.48
250	1.41	139.22	0.56	5.08	1.58	61.62

Table 3-5: Chemical and site parameters used in GLEAMS Modeling for hexachlorobenzene.

Chemical Specific Parameters

Parameter	Clay	Loam	Sand	Comment/ Reference
Halftimes (days)				
Aquatic Sediment	2190	2190	2190	Note 1
Foliar	1	1	1	Note 2
Soil, upper 1 cm	7.1	7.1	7.1	Note 3
Soil, lower layers	1640	1640	1640	Note 3
Water	1533	1533	1533	Note 4
Ko/c (mL/g)	50000	50000	50000	Note 5
K_d (mL/g)	1500	750	150	Note 6
Water Solubility, mg/L	0.006	0.006	0.006	ATSDR 2002
Foliar washoff fraction	0.1	0.1	0.1	Note 2

Note 1 ATSDR (2002) gives reported halftimes for hexachlorobenzene in soil ranging from 3 to 6 years. For aquatic sediment, the upper range is used – i.e., 3 years × 365days/year = 2190 days

Note 2 Volatilization will rapidly remove hexachlorobenzene from plant surfaces. For the GLEAMS modeling, all hexachlorobenzene is assumed to be deposited on soil. Thus, the values for foliar half-time and washoff do not impact the results of the modeling.

Note 3 For the top 1 cm, the halftime is based on the study by Beall (1976), as discussed in the text. ATSDR (2002) gives reported halftimes for hexachlorobenzene in soil ranging from 3 to 6 years. For lower soil layers, the mid-point, 4.5 years is used – 4.5 years×365 = 1642.5 ≈ 1640 days.

Note 4 ATSDR (2002) gives reported halftimes for hexachlorobenzene in surface water ranging from 2.7 to 5.7 years. The average, 4.2 years or about 1533 days, is used.

Note 5 Knisel and Davis (2000) give a $K_{o/c}$ of 50,000. ARS (1995) reports a Ko/c of 30,649 based on a Kd of 462.8 in a soil with 2.6% OM.

Note 6 Calculated as $K_d = K_{o/c} \times OC$. The $K_{o/c}$ is taken as 50,000 from Knisel and Davis (2000) and the proportion of OC in sand, loam, and clay is estimated as 0.003 for sand, 0.015 for loam, and 0.030 for clay.

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 12 inches.
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 12 inches.

Table 3-6: Summary of modeled concentrations of hexachlorobenzene in soil (all units are mg/kg or ppm per lb/acre)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.027	0.665	0.023	0.588	0.023	0.588
10	0.030	0.665	0.026	0.588	0.026	0.588
15	0.030	0.665	0.026	0.588	0.026	0.588
20	0.030	0.665	0.026	0.588	0.027	0.588
25	0.030	0.665	0.026	0.588	0.027	0.588
50	0.028	0.665	0.026	0.588	0.027	0.588
100	0.023	0.665	0.026	0.588	0.028	0.588
150	0.019	0.665	0.024	0.588	0.030	0.588
200	0.012	0.665	0.021	0.588	0.031	0.588
250	0.007	0.665	0.017	0.588	0.031	0.588

Table 3-7: Summary of modeled concentrations of hexachlorobenzene 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	0	0	0	0	0
10	0	0	0	0	0	0
15	0.0036	0.58	0	0	0	0
20	0.0140	2.29	0	0	0	0
25	0.0294	4.83	0	0	0	0
50	0.162	27.4	0	0	0	0
100	0.470	88.9	0.05	8.77	0	0
150	0.794	165	0.15	26.8	0	2.0e-05
200	0.905	221	0.27	52.0	0	4.0e-05
250	0.943	268	0.38	80.5	1.1e-03	0.18

Table 3-8: Summary of modeled concentrations of hexachlorobenzene in a pond (all units are µg/L or ppb per lb/acre)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0	0	0	0	0	0
10	0	0	0	0	0	0
15	0.09	0.15	0	0	0	0
20	0.32	0.50	0	0	0	0
25	0.62	0.94	0	0	0	0
50	2.77	3.62	0	0	0	0
100	6.82	8.52	1.02	1.58	0	0
150	10.9	15.9	2.69	5.38	1.0e-05	2.0e-05
200	12.2	21.8	4.59	11.18	3.0e-05	4.0e-05
250	12.6	27.2	6.26	17.81	2.1e-02	1.0e-01

Table 4-1: Summary of key studies on the toxicity of picloram to fish.

Species	Endpoint	Value (mg a.e./L)	Form/Vehicle	Reference
		Acute		
Bluegill Sunfish	Acute LC_{50}'s	14.5 to 45	Acid	Mayes and Oliver 1986
Fathead minnow	Acute LC_{50}	55.3 (47.2 - 69.6)	Acid	Mayes and Oliver 1986
Cutthroat trout	Acute LC_{50}	4.8 (3.8-6.2)	Acid	Mayes and Oliver 1986
		3.5 (3.4-4.0)	Acid/Acetone	Woodward 1976
		3.9 (3.2-4.8)	Acid/Acetone	Woodward 1982
Rainbow trout	Acute LC_{50}'s	5.5 to 19.3	Acid	Mayes and Oliver 1986
Lake trout	Acute LC_{50}	1.6 (1.2 - 2.0)	Acid/Acetone	Woodward 1976
Bluegill Sunfish	Acute LC_{50}'s	24 to 137	K-salt	Mayes and Oliver 1986
Cutthroat trout	Acute LC_{50}	1.5 (0.8-3.0)	K-salt	Mayes and Oliver 1986
Rainbow trout	Acute LC_{50}'s	13 to 48	K-salt	Mayes and Oliver 1986
		Chronic		
Rainbow trout	Chronic NOEC	0.55	K-salt/None	Mayes et al. 1987
	Chronic LOEC	0.88	K-salt/None	Mayes et al. 1987
Fathead minnow	Chronic NOEC	0.71	TIPA salt/None	Weinberg et al. 1996
	Chronic LOEC	1.2	TIPA salt/None	Weinberg et al. 1996
Lake trout	Chronic LOEC	0.035	acid/Acetone	Woodward 1976
Cutthroat trout	Peak NOEC [TWA[1]]	0.29 [0.04]	acid/Acetone	Woodward 1979
	Peak LOEC [TWA[1]]	0.61 [0.098]	acid/Acetone	Woodward 1979

[1] TWA calculated as the sum of exposure concentrations on various days reported in Table 1 of Woodward (1979) divided by the observation period of 25 days.

Table 4-2: Summary of modeled concentrations of picloram in soil (all units are mg/kg or ppm per lb/acre)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	1.390	5.46	1.112	4.43	0.909	4.15
10	0.715	4.61	0.441	3.64	0.426	3.79
15	0.435	4.08	0.192	3.54	0.089	3.53
20	0.307	4.00	0.114	3.53	0.048	3.53
25	0.237	3.99	0.077	3.53	0.034	3.53
50	0.102	3.99	0.026	3.53	0.018	3.53
100	0.015	3.99	0.015	3.53	0.014	3.53
150	0.013	3.99	0.014	3.53	0.013	3.53
200	0.013	3.99	0.013	3.53	0.012	3.53
250	0.013	3.99	0.013	3.53	0.012	3.53