SELECTED COMMERCIAL FORMULATIONS OF TRICLOPYR - GARLON 3A and GARLON 4 Risk Assessment Final Report

Submitted to:

FOREST SERVICE

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

2,4-D	dichlorophenoxyacetic acid
2,4,5-T	2,4,5-trichlorophenoxyacetic acid
a.e.	acid equivalents
a.i.	active ingredient
AEL	adverse-effect level
ACGIH	American Conference of Governmental Industrial Hygienists
AChE	acetylcholinesterase
AMPA	aminomethylphosphonate
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
BEE	butoxyethyl ester
bw	body weight
ChE	cholinesterase
cm	centimeter
CNS	central nervous system
DAA	days after application
d.f.	degrees of freedom
EC_{50}	concentration causing 50% inhibition of a process
EC_{100}	concentration causing complete inhibition of a process
F	female
F_1	first filial generation
g	gram
HQ	hazard quotient
IARC	International Agency for Research on Cancer
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
K_{ow}	octanol-water partition coefficient
Kp	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
m	meter
M	male
MCS	multiple chemical sensitivity
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
MW	molecular weight
MOS	margin of safety
MSDS	material safety data sheet
NCI	National Cancer Institute

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NRC	National Research Council
OPPTS	Office of Pesticide Planning and Toxic Substances
ppm	parts per million
PSP	phenolsulfonphthalein
RBC	red blood cells
RfD	reference dose
TBEE	triclopyr butoxyethyl ester
TCDD	2,3,7,8-tetrachlorodibenzo(*p*)dioxin
UF	uncertainty factor
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
>	greater than
≥	greater than or equal to
<	less than
≤	less than or equal to
=	equal to
≃	approximately equal to

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 mercurey	760
centigrade	Fahrenheit	1.8C°+32
centimeters	inches	0.3937
cubic meters (m^3)	liters (L)	1,000
Fahrenheit	centigrade	0.556F°-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 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

BACKGROUND

Two commercial formulations of triclopyr, Garlon 3A and Garlon 4, are used by the USDA in vegetation management programs. In 1989, the Southern Region of the Forest Service prepared a series of environmental impact statements accompanied by risk assessments covering the use of these products. The present document provides updated risk assessments for human health and ecological effects to support a reassessment of the environmental consequences of using these products in future Forest Service programs.

Triclopyr is the pyridine analogue of 2,4,5-T, and, like 2,4,5-T, acts by mimicking the activity of auxin, a natural plant growth hormone. Both of the commercial formulation contain inerts. Garlon 3A contains the triethylamine salt of triclopyr (44.4%) as well as emulsifiers, surfactants, and ethanol. Garlon 4 contains the butoxyethyl ester (BEE) of triclopyr (61.6%) as well as inerts (38.4%) that include deodorized kerosene.

Although aerial applications may be used in some instances, backpack (selective) foliar, hack and squirt, basal stem, and boom spray or roadside hydraulic spraying are the most common methods for applying triclopyr Forest Service programs. The typical application rate used by the Forest Service is 1 lb a.i./acre and few applications will exceed 2.5 lbs a.i./acre. In some instances, areas treated with triclopyr may be subject to brown-and-burn operations. In previous Forest Service vegetation management programs, triclopyr has been applied in relatively small amounts, compared with the application of other herbicides. In the late 1980s, triclopyr amine was applied to 9,900 acres/year and the ester was applied to 13,100 acres. More recently, the use of triclopyr has increased, with about 16,000 acres being treated with the acid amine and 15,000 acres being treated with the ester in 1995.

HUMAN HEALTH RISK ASSESSMENT

Triclopyr has a low order of acute lethal potency with oral LD_{50} values generally ranging from about 300-1,000 mg/kg. The structural similarities between triclopyr and 2,4,5-T might suggest qualitative similarities between these two compounds in terms of potential human health effects. Many of the potential health effects associated with exposure to 2,4,5-T, however, are related to the occurrence of 2,3,7,8-tetrachlorodibenzo(*p*)dioxin (TCDD) in 2,4,5-T, and TCDD is not likely to occur in triclopyr.

The signs and symptoms associated with exposure to triclopyr acid, triclopyr BEE, or the Garlon formulations are similar for each agent and include lethargy, impaired coordination, weakness, labored respiration, and tremors. The liver and kidney appear to be the primary target organs for acute and chronic exposure. Based on a review of the toxicology and pharmacokinetics of triclopyr acid and triclopyr BEE, the U.S. EPA has determined that the two forms are toxicologically equivalent, which seems to be a reasonable assessment. An assessment of the toxic inerts in the Garlon formulations, ethanol and deodorized kerosene, suggests that the inerts are not toxicologically significant, relative to the amount of triclopyr in these formulations.

Workers involved in broadcast applications, either aerial or boom spray, are exposed to similar levels of triclopyr from the application of either Garlon 3A or Garlon 4. Because triclopyr BEE is likely to be absorbed more rapidly than triclopyr acid, the levels of triclopyr exposure associated with the application of Garlon 4 are somewhat higher than those associated with the application of Garlon 3A. Immediately after application, some members of the general public could be exposed to triclopyr levels comparable to those for workers. Over prolonged periods, however, the levels of exposure for the general public will tend to be much lower than those for workers.

The current RfD for triclopyr is 0.005 mg/kg/day. The lack of consistent species differences in sensitivity, discussed below, suggests that U.S. EPA's use of an uncertainty factor of 10 for species-to-species extrapolation may be conservative. Conversely, the dose-duration relationships for triclopyr suggest that the RfD may be under-protective for chronic exposure. These concerns cannot be addressed further without additional experimental data. Nonetheless, the RfD of 0.005 mg/kg/day is accepted as the basis for the risk characterization.

For workers, no exposures approach levels that are likely to produce frank signs of toxicity. Nonetheless, there is a reasonable concern that workers applying the compound over a prolonged period of time in the course of a single season and/or over several seasons could be at risk of impaired kidney function. For the general public, the potential for adverse effects from most exposure scenarios involving triclopyr is of relatively little concern. On the other hand, application rates >1 lb a.i./acre would result in an estimated daily intake from contaminated vegetation that approaches exposure levels at which effects on kidney function might be detectable. No frank effects of toxicity are likely to occur at any of the projected levels of exposure.

ECOLOGICAL RISK ASSESSMENT

The toxicity studies on terrestrial animals are generally consistent with those on experimental mammals. The data on birds suggest that triclopyr and the commercial formulations of triclopyr have a low order of acute oral toxicity, with LC_{50} values ranging from 1,000 to >10,000 ppm. Birds appear to be no more sensitive than mammals to triclopyr. In addition to the laboratory bioassays, there are several field studies that have assessed the effects of triclopyr on birds and mammals. These studies suggest that at application rates equal to or greater than those contemplated by the Forest Service effects on animal populations will be secondary to changes in vegetation and food supply and that these changes will either have no effect or will be beneficial to birds and mammals.

Triclopyr and other pyridinecarboxylic acid herbicides such as picloram mimic indole auxin plant growth hormones and cause uncontrolled growth in plants. These herbicides behave similarly to the chlorophenoxy acid herbicides, such as 2,4-D and 2,4,5-T. At sufficiently high levels of exposure, the abnormal growth is so severe that vital functions cannot be maintained and the plant dies.

The toxicity of triclopyr to fish and aquatic invertebrates is relatively well characterized. Some aquatic macrophytes may be more sensitive than aquatic animals to triclopyr, but the available data, albeit sparse, do not suggest that algae are particularly sensitive to triclopyr. There is a major difference in the potential hazards posed by Garlon 3A and Garlon 4 to aquatic species that can be attributed almost completely to differences in the inherent toxic potency of triclopyr acid and triclopyr BEE as well as an apparent antagonism of the toxicity of triclopyr by components in Garlon 3A.

For terrestrial animals, there is little information to suggest that dermal exposure or exposure from the consumption of contaminated water will to lead to levels that approach those of concern. The consumption of contaminated vegetation is the only scenario in which the hazard quotient is exceeded. Immediately after triclopyr is applied, small mammals that consume contaminated vegetation exclusively are likely to intake levels of triclopyr that result in a hazard quotient greater than unity. Although signs of frank effects are not likely to occur at these levels of exposure, kidney function could be impaired.

For terrestrial plants, direct deposition, either through unintentional direct spraying or spray drift presents a plausible hazard. If plants are accidentally sprayed at the application rates used by the Forest Service, the plants, with the possible exception of grasses, are likely to be damaged, particularly in scenarios involving the upper ranges of anticipated application rates. This scenario may be regarded as accidental, and is relatively easy to control with proper management and application. Spray drift could cause detectable damage to nontarget plants within about 30 m downwind of a spray zone. At distances >30 m, detectable damage is unlikely. Based on conservative exposure assumptions, it is reasonable to assume that the maximum levels of triclopyr in soil associated with treatments contemplated by the Forest Service will be far below those associated with damage to nontarget plants. This characterization, however, is somewhat tempered by a field study indicating that application rates of Garlon 4 at approximately 3-10 lbs/acre can lead to decreased germination and plant growth for periods of approximately 8-80 days after application.

At plausible levels of acute exposure in standing water and streams, 0.07-0.5 mg/L, Garlon 3A is not likely to have any effect on fish, aquatic invertebrates, and most algae. Some sensitive macrophytes might be affected. At an application rate of 1 lb/acre, Garlon 4 could cause transient behavioral changes in some aquatic species at the upper range of estimated exposure levels at an application rate of 1 lb/acre. At application rates $\geq$2 lbs/acre, the upper range of exposure could be lethal to fish and perhaps some sensitive invertebrates.

1. INTRODUCTION

Two commercial formulations of triclopyr, Garlon 3A and Garlon 4, are used by the USDA in vegetation management programs. In 1989, the Southern Region of the Forest Service prepared a series of environmental impact statements accompanied by risk assessments covering the use of these products (USDA 1989a,b,c). The present document provides updated risk assessments for both human and health and ecological effects to support a reassessment of the environmental consequences of using these products in future Forest Service programs.

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 the commercial formulations of triclopyr, an assessment of potential exposure to these products, 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.

Although this is a technical support document and addresses some highly specialized technical areas, an effort has been made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts and terms common to all parts of the risk assessment are described in as plain a language as possible in a separate document: *The Preparation of Environmental Documentation and Risk Assessments for the Forest Service* (SERA 1995a). In addition, these terms are defined in the glossary to this risk assessment. Moreover, some of the specialized terms and concepts are defined, as necessary, in the text.

The risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. Much of the early literature is summarized in the previous chemical background statement on triclopyr (Sassaman et al. 1984), previous risk assessments and environmental impact statements covering this compound (USDA 1989a,b,c), as well as unpublished reviews prepared for the U.S. EPA (Ghassemi et al. 1981) and the Department of Natural Resources of the State of Washington (Shipp et al. 1986). A review of the potential human health and ecological effects of triclopyr is available on-line from EXTOXNET (1992). A review of triclopyr has also been published by Swadener (1993).

As part of the pesticide registration process, manufacturers are required to conduct various studies regarding the toxicity and environmental fate of pesticides. These studies are classified as confidential business information (CBI), and, although these studies are submitted to the U.S. EPA, they are not generally released for public review. Summaries of the studies used in the original registration process are contained in the various reviews cited above. The U.S. EPA is in the process of reviewing studies on triclopyr and triclopyr formulations, including more recent CBI studies, as part of the reregistration process (Smith 1996). Summaries of these studies are

provided by U.S. EPA (1995a,b) and additional details have been obtained from EPA personnel involved in the reregistration review (Smith 1996).

Because the existing reviews provide adequate summaries of most of the available information on triclopyr and in the interest of economy, an updated chemical background statement has not been prepared with the current risk assessment. Much of the information that would be included in such an update is presented in the above cited reviews. In addition, information relevant to this risk assessment, taken from previous reviews as well as more recent publications and other sources, is summarized in the appendices that accompany this document.

2. PROGRAM DESCRIPTION

2.1. OVERVIEW

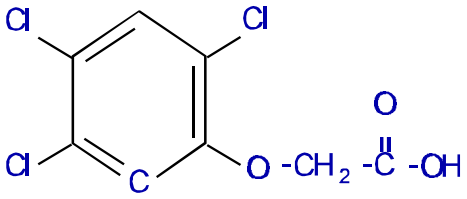
Triclopyr is the active ingredient in two herbicides used by the Forest Service, Garlon 3A and Garlon 4. Triclopyr is the pyridine analogue of 2,4,5-T, and, like 2,4,5-T, acts by mimicking the activity of auxin, a natural plant growth hormone. Both of the commercial formulations contain inerts. Garlon 3A contains the triethylamine salt of triclopyr (44.4%) as well as emulsifiers, surfactants, and ethanol. Garlon 4 contains the butoxyethyl ester (BEE) of triclopyr (61.6%) as well as inerts (38.4%) that include deodorized kerosene.

Although aerial applications may be used in some instances, backpack (selective) foliar, hack and squirt, basal stem, and boom spray or roadside hydraulic spraying are the most common methods for applying triclopyr in Forest Service programs. The typical application rate used by the Forest Service is 1 lb a.i./acre, and few applications will exceed 2.5 lbs a.i./acre. Sometimes, areas treated with triclopyr may be subject to brown-and-burn operations. In previous Forest Service vegetation management programs, triclopyr has been applied in relatively small amounts, compared with the application of other herbicides. In the late 1980s, triclopyr amine was applied to 9,900 acres per year and the ester was applied to 13,100 acres. More recently, the use of triclopyr has increased, with approximately 16,000 acres being treated with the acid amine and 15,000 acres being treated with the ester in 1995.

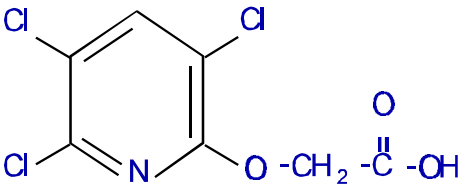
2.2. TRICLOPYR AND COMMERCIAL FORMULATIONS

Triclopyr is the pyridine analogue of 2,4,5-T (2,4,5-trichlorophenoxyacetic acid) and differs from 2,4,5-T only by the presence of a nitrogen (N) atom in the ring structure (Figure 2-1). Like 2,4,5-T, triclopyr mimics auxin, a plant growth hormone, thus disrupting the normal growth and viability of plants.

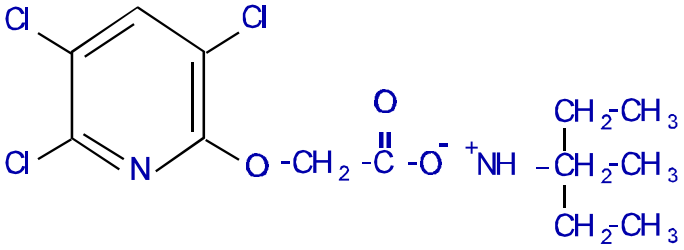
Some basic chemical and physical properties of triclopyr and triclopyr BEE are summarized in Table 2-1 and Table 2-2, respectively. At ambient temperatures, triclopyr is a fluffy solid (Budavari et al. 1989) and is readily soluble in water (Table 2-1). In aqueous solutions, the hydrogen atom of the carboxylic acid group (**COOH**) may be associated (e.g., **-COOH**) or dissociated (e.g., $\mathbf{-COO^-} + \mathbf{H^+}$) depending on the pH of the solution. The dissociation constant, or pK_a, for the carboxylic acid group is approximately 3. Thus, at a pH of 3, 50% of the acid is associated and 50% is disassociated. As the acidity of the solution decreases (i.e., the pH of the solution increases) the proportion of triclopyr that is ionized or dissociated increases. The pH of most biological fluids ranges from approximately 5 to 9. Thus, within this range of pH, most of the triclopyr acid has a net negative charge ($\mathbf{-COO^-}$).



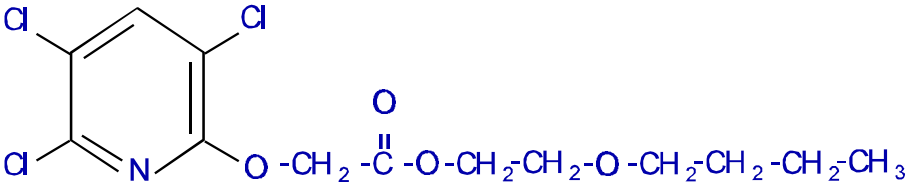
2,4,5-T



Triclopyr acid



Triclopyr, triethylamine salt



Triclopyr, Butoxyethyl ester (TBEE)

Figure 2-1: Structure of the Various Forms of Triclopyr and 2,4,5-T.

Table 2-1. Physical, chemical, and biochemical properties of triclopyr.

CAS Number:	55335-06-3
Molecular Weight:	256.5
Melting point (◦C):	150.5 (Tomlin 1994
Density (g/cm^3):	1.85 at 21◦C (Tomlin 1994)
Vapor Pressure (mm Hg):	1.50×10^{-6} mm Hg (25◦C) (Tomlin 1994)
	1.26×10^{-6} mm Hg (25◦C) (WSSA 1989)
	5.30×10^{-6} mm Hg (40◦C) (WSSA 1989)
Water Solubility:	0.408 g/L (purified) (20◦C) (Tomlin 1994)
	7690 g/L at pH 5 (20◦C) (Tomlin 1994)
	8100 g/L at pH 7 (20◦C) (Tomlin 1994)
	8220 g/L at pH 9 (20◦C) (Tomlin 1994)
	430 mg/L (25◦C) (Neary et al. 1993, WSSA 1989))
Henry's law constant:	9.89×10^{-10} atm-m^3/mole (25◦C)(calculated from vapor pressure and water solubility)
pKa:	3.97 (Tomlin 1994)
	2.7 (McCall and Gavit 1986)
	2.93 (Woodburn et al. 1993a)
	2.68 (Weber 1994)
Log K_{ow}:	0.42 (pH 5) (Tomlin 1994)
	-0.45 (pH 7) (Tomlin 1994)
	-0.96 (pH 9) (Tomlin 1994)
	2.53 (non-ionized; estimated)(Meylan and Howard 1995)
Dermal Permeability Coefficient:	0.00324 cm/hour (log K_{ow}=2.53) (estimated; U.S.EPA 1992b)
	0.00002 cm/hour (log K_{ow}=-0.45) (estimated; U.S.EPA 1992b)
Soil Adsorption K_{oc}:	59 (Tomlin 1994)
	27 (McCall and Gavit 1986, Kenaga 1980)
	20 (Weber 1994)
Evaporation Rate:	low (Neary et al. 1993)
Foliar Halftime (days):	3-10 (DT50 in plants) (Tomlin 1994)
	4 (metabolism by aquatic plants) (Woodburn et al. 1993b).
	average 42% decline over 6 days of triclopyr applied to various forest vegetation in northern Idaho (Whisenant and McArthur 1989).
Soil Halftime (days):	46 (average) (Tomlin 1994, WSSA 1989, Weber 1994)
	45 (average) (Neary et al. 1993)
	40 (average) (McCall and Gavit 1986)
	14 (in selected Canadian forest soils) (Stephenson et al. 1990)
Water Halftime:	10 hours (photodegradation in sunlit water) (WSSA 1989)
	2.8-14.1 hours (photodegradation in sunlit water; 0-1 m deep) (McCall and Gavit 1986)
	0.71-1.86 days (photodegradation in natural river water) (Woodburn et al. 1993a).
	0.5-3.6 days (field study in Lake Seminole, GA under midsummer conditions) (Woodburn et al. 1993b).
	3.8-4.3 days (field test in northern Ontario) (Solomon et al. 1988).
Air Halftime (days):	3.3 (estimated; Meylan and Howard 1993)

Table 2-2. Physical, chemical, and biochemical properties of triclopyr butoxyethyl ester.

CAS Number:	64470-88-8
Molecular Weight:	356.64
Melting Point (◦C):	-----
Density (g/cm^3):	-----
Vapor Pressure (mm Hg):	-----
Water Solubility:	2.1 mg/L at 25◦C (estimated; Meylan and Howard 1994)
Henry's law constant:	5.98×10^{-8} atm-m^3/mole (25◦C) (estimated; Meylan and Howard 1991)
Log K_{ow}:	4.01 (estimated; Meylan and Howard 1995)
Dermal Permeability Coefficient:	0.00899 cm/hour (estimated; U.S. EPA 1992b; log K_{ow} = 4.01)
Soil Adsorption K_{oc}:	560 (estimated; Meylan and Howard 1992)
Evaporation Rate:	-----
Foliar Halftime (days):	average 42% decline over 6 days of triclopyr, butoxyethyl ester applied to various forest vegetation in northern Idaho (Whisenant and McArthur 1989). initial halftime of approximately 10-15 days after aerial application to litter in bush fields of southwest Oregon (Newton et al. 1990).
Soil Halftime (days):	40 (average) (McCall and Gavit 1986) 14 (in selected Canadian forest soils) (Stephenson et al. 1990)
Water Halftime:	12.5-83.4 hours (photodegradation in sunlit water; depth of 0-1 m) (McCall and Gavit 1986) 0.30 days (hydrolysis at 25◦C and pH 9; McCall et al. 1988). 8.7 days (hydrolysis at 25◦C and pH 7; McCall et al. 1988). 84.0 days (hydrolysis at 25◦C and pH 5; McCall et al. 1988). 3.8 - 4.3 days (field test in northern Ontario) (Solomon et al. 1988).
Air Halftime (days):	0.63 (estimated for gas-phase triclopyr butoxyethyl ester) (method of Meylan and Howard 1993)

Table 2-3. Summary of commercial formulations containing triclopyr covered in this risk assessment[a].

Formulation	Ingredient	Pounds (a.e.)/gal	Grams (a.e.)/L
Garlon 3A (DowElanco)	triclopyr: triethlyamine salt (44.4%)	3	360
Specific gravity = 1.135	inerts (55.6%)		
	water		
	emulsifiers and surfactants		
	ethanol (1%)		≃10
	others not specified		
Garlon 4 (DowElanco)	triclopyr: butoxyethyl ester (61.6 %)	4	480
Specific gravity = 1.08	inerts (38.4%)		
	kerosene[b] (>1%, ≤6%[c])		>10≤60
	others not specified		

[a]Data taken from DowElanco (1992, 1993a), unless otherwise specified.

[b]Density of kerosene = 0.8 (Budavari et al. 1989).

[c]Betso (1987)

a.e. = acid equivalents

As summarized in Table 2-3, two commercial formulations of tryclopyr are covered in this risk assessment—Garlon 3A and Garlon 4. Both of these formulations are produced by DowElanco (DowElanco 1992, 1993a,b, 1994). Garlon 3A contains the triethylamine salt of triclopyr (44.4%) as well as emulsifiers, surfactants, and ethanol. Garlon 4 contains the butoxyethyl ester (BEE) of triclopyr (61.6%) as well as inerts (38.4%) that include deodorized kerosene.

The two different forms of triclopyr, triethylamine salt and butoxyethyl ester, are illustrated in Figure 2-1. In comparing information on the acid, salt, and ester of triclopyr, it is often useful to express exposure or dose as units of acid equivalents (a.e.). Both the triethylamine salt and butoxyethyl ester have similar molecular weights (357.7 for the triethylamine salt and 356.6 for the butoxyethyl ester). Thus, compared with the acid form of triclopyr (MW=256.5), both of triclopyr compounds contain approximately 72% triclopyr (256.5÷357.7 = 0.717; 256.5÷356.6 = 0.719). Application rates are commonly expressed in units of active ingredient (a.i.), while most monitoring studies and toxicity studies express doses (e.g., mg agent/kg body weight) or concentrations (mg agent/L of water or mg agent/kg of soil) in units of acid equivalents (a.e.). Unless otherwise specified, application rates given in this report are expressed as active ingredient and doses or concentrations are expressed as acid equivalents.

Garlon 3A contains approximately 1% ethanol. Information on the amount of kerosene in Garlon 4 is not available for this risk assessment. The formulation must contain at least 1% of the inert to require that the inert be identified on the label. This may be taken as the lower limit of the concentration of kerosene in Garlon 4. In a letter to the Forest Service concerning the 1989 risk assessments involving triclopyr (USDA 1989a,b,c), DowElanco indicated that no individual inert is present at greater than 6% in Garlon 3A or Garlon 4 (Betso 1987). This letter, however, does not specifically identify kerosene as one of the inerts covered by this statement.

2.3. APPLICATION METHODS

Proposed application methods and vegetation management uses for triclopyr are summarized in Table 2-4. Detailed descriptions of the silvicultural uses of herbicides and the various methods of herbicide applications are available in the general literature (e.g., Cantrell and Hyland 1985, Cantrell et al. 1985) and earlier environmental impact statements conducted by the Forest Service (USDA 1989a,b,c). The following summary focuses on those aspects of application that are most germane to the exposure assessments (sections 3.2 and 4.2).

The most commonly used application method is backpack (selective) foliar applications. 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 exposures, application crews are directed not to walk through treated vegetation. Usually, a worker treats approximately 0.5 acres/hour with a plausible range of 0.25-1.0 acres/hour.

Hack and squirt applications are a form of cut surface treatment in which the bark of a standing tree is cut with a hatchet and the herbicide is applied with a squirt bottle. This treatment method

Table 2-4. Proposed and potential uses and application methods for triclopyr formulations

Use	Application Method				
	Broadcast		Selective		
	Aerial	Boom Spray	Backpack	Cut Surface	Basal Stem
Oak regeneration			3A, 4	*3A*	4
Conifer release			3A, 4	*3A*	4
General weeds			3A, 4		
Hardwood release			3A, 4	*3A*	4
Hardwood sprout control					4
Noxious weeds			3A, 4		4
Rights-of-way	*3A*	*3A*, 4	3A, 4	*3A*	
Site preparation	*3A*	*3A*, 4	3A, 4	*3A*	
Thinning			3A, 4	*3A*	
Vegetation, NOS			3A, 4	*3A*	
Wildlife habitat improvement	*3A*		3A, 4	*3A*	4

3A = Garlon 3A; **4** = Garlon 4; NOS = not otherwise specified;
Normal font = planned use; *Italic* font = potential use

is used to eliminate large trees during site preparation, conifer release operations, or rights-of-way maintenance. As with selective foliar applications, a worker usually treats about 0.5 acres/hour with a plausible range of 0.25-1.0 acres/hour.

In streamline applications, the herbicide is sprayed directly onto the bark of the lower 2–3 feet of the stem in a horizontal band to one side of the tree. The surfactant in the herbicide formulation allows the active ingredient to spread around the stem. This treatment method is generally used on relatively small trees (e.g., maximum diameters of approximately 4 inches). In these applications, the herbicide sprayer or container is carried by backpack. The nozzle on the wand or gunjet of the backpack sprayer should not be positioned higher than the handlers' waist,

reducing the likelihood that the chemical will come into direct contact with the arms, hands, or face of the worker.

Boom spray or roadside hydraulic spraying 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) with approximately 200 gallons of the herbicide mixture (270 gallons/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 1989b, p 2-9 to 2-10).

Aerial applications are restricted to the use of helicopters (i.e., fixed wing aircraft may not be used). Liquid formulations of triclopyr are 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.

In some instances, areas treated with triclopyr may be subject to brown-and-burn operations. As discussed in USDA (1989b), these operations involve burning a treated area 45–180 days after treatment with the herbicide.

2.4. MIXING AND APPLICATION RATES

Garlon 3A and Garlon 4 are used for the control of a number of woody plant species as well as annual and perennial broadleaf weeds and are labeled for similar uses such as the maintenance of rights-of-way and wildlife openings.

For the control of woody plants, Garlon 3A is mixed at a rate of 2-3 gallons per 20-100 gallons of spray solution per acre [6-9 lbs a.e./acre using a 0.06-0.45 lbs a.e./gallon (7,188-53,910 mg/L) solution]. The same application rate is recommended for site preparation, except that lower spray volumes/higher concentrations are used (10-30 gallons of total spray per acre). For broadleaf weed control, much lower concentrations and application rates are recommended: 0.33-1.5 gallons of formulation in 20-100 gallons of spray solution per acre [1-4.5 lbs a.e./acre using a 0.01-0.225 lbs a.e./gallon (1,998-26,955 mg/L) solution]. Similar rates of application can be used for conifer release in the northeast (0.5-1 gallon of Garlon 3A per acre) or in the Pacific northwest and California [0.33 to 0.5 gallons per acre]. Very concentrated solutions may be used for some selective applications such as cut surface (50% dilution of formulation) or hack and squirt (100% formulation). In certain control programs, aerial applications using a helicopter are permitted. In many broadcast applications, the use of non-ionic agricultural surfactants are recommended (DowElanco 1993a).

The recommended application rates for Garlon 4 are somewhat less than those of Garlon 3A. For the control of woody plants, Garlon 4 is mixed at the rate of 1-2 gallons per 20-100 gallons of

Table 2-5. Use of triclopyr by the Forest Service in 1995

Use	Acres Treated	Average Application Rate (lbs a.e./acre)
GARLON 3A (TRICLOPYR TRIETHYLAMINE)		
Conifer release	5,285	0.8
Hardwood release	507	0.5
Noxious weeds	36	3
Rights-of-way	85.4	0.8
Site preparation	7,730	0.5
Thinning	757	0.7
Wildlife habitat	1,667.5	0.7
TOTAL	16,067.9	0.6
GARLON 4 (TRICLOPYR BUTOXYETHYL ESTER)		
Conifer release	5,559.5	0.7
General weeds	20	2.4
Hardwood release	743	1.4
Noxious weeds	74.5	0.7
Rights-of-way	244	2.0
Site preparation	6,399.5	0.9
Thinning	572	1.5
Wildlife habitat	679	1.4
Release - unspecified	380	0.4
Release - general	47	1.7
Pre-harvest site preparation	20	1.2
TOTAL	14,738.5	0.9

Source: USDA/FS 1995

spray solution per acre [4-8 lbs a.e./acre using a 0.04-0.4 lbs a.e./gallon (4,792-47,920 mg/L) solution]. For broadleaf weed control, much lower concentrations and application rates are recommended: 0.25-1 gallon of formulation in 20-100 gallons of spray solution per acre [1-4 lbs

a.e./acre using a 0.01-0.2 lbs a.e./gallon (1,998-23,960 mg/L) solution]. As with Garlon 3A, comparable or somewhat lower application rates are used for site preparation. For streamline applications, relatively concentrated (20-30% dilutions of the formulation) may be used.

The Forest Service does not plan to use triclopyr at the highest labelled application rates. As summarized in Table 2-5, the typical rate used by the Forest Service in 1995 for triclopyr was approximately 0.6 lbs a.i./acre for the acid amine and 0.9 lbs a.i./acre for the ester. All but one application (3.0 lbs a.i./acre) was less than 2.5 lbs a.i./acre (USDA/FS 1995).

In previously conducted Forest Service vegetation management programs (USDA 1989a,b,c), triclopyr was applied in relatively small amounts, compared with the application of other herbicides. For example, in Forest Service Region 8 (comprised of Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North California, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and part of West Virginia), there are approximately 12,000,000 acres of National Forests and Grassland, of which up to 600,000 acres were treated with various herbicides each year. In the late 1980s, triclopyr amine was applied to 9,900 acres/year and the ester was applied to 13,100 acres (USDA 1989b, p.2-4). More recently, the Forest Service use of herbicides in Region 8 has been reduced to treatment of fewer than 100,000 acres/year. Nonetheless, the use of triclopyr has increased, with approximately 16,000 acres being treated with the acid amine and 15,000 acres being treated with the ester in 1995 (USDA/FS 1995).

3. HUMAN HEALTH RISK ASSESSMENT

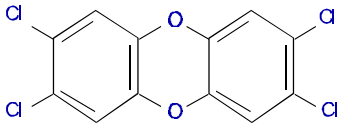
3.1. HAZARD IDENTIFICATION

3.1.1. Overview. Like any chemical, triclopyr at sufficiently high doses can be lethal. Nonetheless, triclopyr has a low order of acute lethal potency with oral LD_{50} values generally ranging from approximately 300-1,000 mg/kg. The structural similarities between triclopyr and 2,4,5-T might suggest qualitative similarities between these two compounds in terms of potential human health effects. However, many of the potential health effects of 2,4,5-T are related to the occurrence of 2,3,7,8-tetrachlorodibenzo(*p*)dioxin (TCDD) in 2,4,5-T. This contaminant is not likely to occur in triclopyr.

The symptoms associated with triclopyr acid, triclopyr BEE, and the Garlon formulations appear to be similar and include lethargy, impaired coordination, weakness, labored respiration, and tremors. The liver and kidney appear to be the primary target organs affected by acute or chronic exposure to triclopyr. Based on a review of the toxicology and pharmacokinetics of triclopyr acid and triclopyr BEE, the U.S. EPA has judged that these two forms are toxicologically equivalent. Although there are inconsistencies in the available data, which suggest some differences in apparent potencies, the differences may be related to absorption rates, which are taken into consideration in this risk assessment. Overall, however, the assessment of toxicological equivalence seems reasonable. Triclopyr acids are probably less readily absorbed than triclopyr BEE, because, in general, ionized compounds are less readily absorbed than less polar and more hydrophobic compounds such as esters. Once absorbed, endogenous esterases probably break the ester linkage in triclopyr BEE, with the consequent formation of triclopyr acid, which would account for the similar toxic effects and potencies of the two Garlon formulations. This hypothesis is consistent with available studies regarding the metabolism and kinetics of triclopyr.

A quantitative assessment of toxic inerts in the Garlon formulations, ethanol and deodorized kerosene, suggests that these inerts are not toxicologically significant, relative to the amount of triclopyr in these formulations.

3.1.2. Acute Toxicity and Mechanisms of Action. Information regarding the acute toxicity of triclopyr and its formulations is summarized in Appendix 1. Although the toxicity of triclopyr is relatively well characterized, the mechanisms of action in mammals is unclear and there are no clinical or epidemiology studies regarding toxic effects in humans. As noted in section 2, triclopyr is the pyridene analogue of 2,4,5-T. Like 2,4,5-T, the toxicity of triclopyr to plants appears to involve the mimicking of auxin growth hormones (section 4). The toxicity of 2,4,5-T in humans has been investigated extensively, and, detailed clinical and epidemiology studies are available (Goetz et al. 1994, Sharp et al. 1986). The structural similarity between triclopyr and 2,4,5-T has only limited relevance to the assessment of human health effects. The mammalian toxicity of 2,4,5-T, particularly the induction of reproductive effects, and the toxic effects of 2,4,5-T in humans are largely attributable to the contamination of 2,4,5-T with TCDD:



which is formed as an impurity in the synthesis of 2,4,5-T from the chlorination of phenols. Because triclopyr is based on a pyridene ring rather than an aromatic ring, the occurrence of TCDD in triclopyr is not plausible (EXTOXNET 1992).

Like any chemical, triclopyr at sufficiently high exposure levels can cause toxic effects, including death. Nonetheless, triclopyr has a low order of acute lethal potency. In other words, it can be lethal but only at very high doses. Oral doses required to kill 50% of exposed animals (LD_{50} values) range from 300 to 1,000 mg/kg. As discussed in section 3.1.8, triclopyr is poorly absorbed by the skin, and very high doses (>1,000 mg/kg) applied to the skin have not caused death or other signs of toxicity.

The signs and symptoms of acute oral intoxication generally include lethargy, impaired coordination, weakness, labored respiration, and tremors. Anorexia and diarrhea have also been observed in rodents and domestic animals. Similar signs and symptoms are associated with triclopyr acid, triclopyr BEE, and the Garlon formulations (Appendix 1). The few available studies regarding histopathology and clinical chemistry data on triclopyr suggest that the liver and kidney are the primary target organs in acute intoxication (Rowe et al. 1980). Furthermore, similar effects are noted in longer-term studies involving exposure to triclopyr (section 3.1.4).

3.1.3. Role of Inerts. As discussed in section 2, the Garlon formulations contain two toxic inerts, ethanol (Garlon 3A) and kerosene (Garlon 4).

The toxicity of ethanol is extremely well characterized in humans, and the hazards of exposure include intoxication from acute exposure as well as liver cirrhosis and fetal alcohol syndrome (WHO 1988). For chronic exposure, the alcohol contained in Garlon 3A will not be of toxicological significance because of the rapid breakdown of alcohol in the environment and the relatively high levels of alcohol associated with chronic alcohol poisoning. Similarly, alcohol is not likely to pose an acute toxic hazard. Approximately 15 mL of alcohol is contained in 1 oz of an alcoholic beverage containing 50% alcohol (100 proof) [0.5 · 1 oz · 29.6 mL/oz ≃ 14.8 mL]. This level may cause mild intoxication in sensitive individuals. Each mL of Garlon 3A contains 0.01 mL of ethanol. Therefore, 1,480 mL, or approximately 1.5 L, of Garlon 3A must be consumed to equal the amount of alcohol contained in 1 oz of an alcoholic beverage. The same amount of Garlon 3A contains 540,000 mg a.e. of triclopyr [1.5 L · 360,000 mg a.e./L]. For a 70 kg man, this dose would equal approximately 770 mg a.e./kg, which is similar to the LD_{50} for rats. As discussed in the dose-response section (section 3.3), this estimate may be a reasonable approximation of a lethal dose for triclopyr in humans. Thus, compared with the active

ingredient, which is triclopyr, the amount of ethanol in Garlon 3A is not toxicologically significant in terms of potential toxicity.

Moreover, the acute toxicity of Garlon 3A is substantially less than the acute toxicity of triclopyr. As summarized in Appendix 1, the acute oral LD_{50} of triclopyr to rats is approximately 713 mg/kg (Olson 1967). The corresponding values for Garlon 3A range from approximately 2,140 to 2,830 mg/kg (Keeler et al. 1974) or from approximately 1,540 to 2,040 mg a.e./kg. In other words, when measured either as gross weight or as acid equivalents of triclopyr, Garlon 3A appears to be less toxic than triclopyr. This notion suggests that components in Garlon 3A antagonize the acute toxicity of triclopyr. A similar pattern is apparent in the responses of cattle to triclopyr and Garlon 3A (Appendix 1) [(Rowe et al. 1980) compared with (Dow Chemical Co. 1987)].

The importance of kerosene in assessing the potential toxicity of Garlon 4 is more difficult to assess. As summarized in section 4, there is evidence that Garlon 4, compared with Garlon 3A or triclopyr, is substantially more toxic to aquatic species; however, this potency can be attributed to differences between the acid and ester forms of triclopyr and not the presence of kerosene. Like Garlon 3A, Garlon 4 causes substantially less acute toxicity in mammals than does triclopyr [oral LD_{50} values in rats = 2,140-2,460 mg/kg (1,540-1,770 mg a.e./kg)] (Lichy et al. 1975). Furthermore, in studies involving repeated dosing of cattle, Garlon 3A, Garlon 4 and triclopyr cause similar effects (Appendix 1) [(Rowe et al. 1980) compared with (Dow Chemical Co. 1987)].

Deodorized kerosene is classified by U.S. EPA (1995c) as a List 3 Inert. As indicated in SERA (1994), this list contains pesticide inerts that the U.S. EPA considers lacking in toxicological data. The toxicity of kerosene was reviewed recently by ATSDR (1995). At sufficiently high doses, kerosene can cause many gastrointestinal, central nervous system (CNS), and renal effects. Although some of the effects observed are consistent with the effects (e.g., diarrhea, lethargy, tremors, etc.) observed in mammals given large oral doses of Garlon 4, the same effects are observed in animals given triclopyr alone or Garlon 3A.

The acute lethal dose of kerosene for humans ranges from approximately 2,000 to 12,000 mg/kg; the acute oral LD_{50} values in experimental mammals range from approximately 16,000 to 23,000 mg/kg. As discussed in section 3.3, there is no information regarding the acute lethal potency of triclopyr to humans. In experimental mammals, acute oral LD_{50} values for triclopyr range from approximately 300 to 500 mg/kg (Appendix 1). Thus, the acute lethal potency of kerosene is approximately 50 times less than the acute lethal potency of triclopyr [16,000 ÷ 300 = 53 or 23,000 ÷ 500 = 46]. Given the relative potency of kerosene and given that the amount of kerosene in Garlon 4 is at least 2 times less than the amount in triclopyr (see section 2), the acute effects associated with exposure to Garlon 4 are probably attributable to triclopyr and not to kerosene.

In contrast, the material safety data sheet (MSDS) for Garlon 4 (DowElanco 1994) specifies that inhalation exposure to Garlon 4 vapors may cause CNS depression attributable to kerosene. As discussed in ATSDR (1995), CNS depression is consistent with inhalation exposure to kerosene.

No monitoring data are available regarding kerosene levels during the application of Garlon 4. Middendorf et al. (1992) monitored triclopyr in air at levels ranging from approximately 5 to 15 $\mu g/m^3$, based on the personal breathing zone air of workers involved in backpack sprays. If kerosene is present at a concentration of $\leq$20% in Garlon 4, the corresponding concentration of kerosene in the air would range from approximately 1 to 3 $\mu g/m^3$. The NOAEL for neurological effects in experimental mammals after exposure to kerosene, which ranged from 14 days to 1 year, is approximately 100 mg/m^3; the NIOSH TLV for petroleum distillates is 350 mg/m^3 (ATSDR 1995). Thus, plausible levels of exposure to kerosene during applications of Garlon 4 are approximately 30,000-100,000 below the NOEL for kerosene in experimental mammals and a factor of 120,000-350,000 below the TLV for petroleum distillates.

Although some components of kerosene are known to be carcinogenic to humans (e.g., benzene) kerosene is not classified as a carcinogen, and quantitative risk assessments have not been conducted on kerosene (ATSDR 1995).

As discussed in section 3.4, exposure to Garlon 4 may present a hazard, based on the toxicity of triclopyr. Relative to those concerns, the presence of kerosene in Garlon 4 is not toxicologically significant.

3.1.4. Subchronic or Chronic Systemic Toxic Effects. Studies regarding the chronic and subchronic toxicity of triclopyr are summarized in Appendix 2. For the most part, the information presented in Appendix 2 is taken from reviews, cited in section 1, and study descriptions provided by U.S. EPA (Smith 1996). Some of these summaries [e.g., the monkey study by Molello et al. (1976)] are not very detailed. Nonetheless, summaries of the studies that have a direct impact on the risk assessment are adequate. No recent studies regarding the toxicity of triclopyr to mammals have been published since the last Forest Service risk assessment.

The kidney appears to be the most sensitive target organ for triclopyr, and the dog appears to be the most sensitive species. The lowest effect level for triclopyr is 2.5 mg/kg/day in the dog (Quast et al. 1977, 1988). In the 1977 study, this dose was associated with decreased phenolsulfonphthalein (PSP) urinary excretion as well as reduced absolute and relative kidney weights. As discussed by Nolan (1985 with attachments), the inhibition of PSP excretion in the dog could be attributed to competition between triclopyr and PSP for elimination via anion transport. In the absence of other toxic effects, the 2.5 mg/kg/day dose in the 1977 dog study was classified as a NOEL by U.S. EPA. This determination formed the basis of U.S. EPA's provisional acceptable daily intake of 0.025 mg/kg/day (U.S. EPA 1985) (section 3.3).

In a follow-up study (Quast et al. 1988), the dose of 2.5 mg/kg/day was associated with a statistically significant increase in serum urea nitrogen and creatinine in male dogs. These effects

were also evident but more pronounced at 5 mg/kg/day. The NOEL for this effect was 0.5 mg/kg/day. Creatinine and urea, which are normal metabolites formed by mammals, are eliminated almost exclusively in the urine. Increases in the levels of these compounds can be caused by impaired kidney function (i.e., decreased glomerular filtration). Although these effects are the most sensitive endpoints available for exposure to triclopyr, they are not particularly sensitive indicators of kidney damage. Usually, before increases in blood urea nitrogen (BUN) or serum creatinine are evident, glomerular filtration must be depressed by 50-70% (Goldstein and Schnellmann 1996).

One of the considerations in designating the 2.5 mg/kg/day dose as a NOEL in the earlier study (Quast et al. 1977) was that BUN levels were unaffected. In the later study (Quast et al. 1988), a statistically significant increase in BUN levels were noted in male dogs at 2.5 mg/kg/day (57% increase over pre-exposure levels) and 5.0 mg/kg/day (108% increase over pre-exposure levels). This caused the U.S. EPA to classify the dose of 2.5 mg/kg/day from Quast et al. (1988) as an adverse effect level. At the lowest dose, 0.5 mg/kg/day, BUN levels were elevated by 38% over pre-exposure levels, but this increase was not statistically significant. As discussed in section 3.3., this resulted in the lowering of the provisional U.S. EPA Office of Pesticides RfD to 0.005 mg/kg/day using the 0.5 mg/kg/day dose group as the NOEL for effects on kidney function.

In rodents, kidney effects-hematological and histopathological changes and increased kidney weight—have been observed after subchronic exposure to triclopyr doses as low as 7 mg/kg/day for 90 days (Barna-Lloyd et al. 1992). Damage was characterized as degeneration of the proximal tubules of the kidneys ($\geq$20 mg/kg/day $\cdot$ 90 days) (Landry et al. 1984) and increases in kidney weight (Eisenbrandt et al. 1987, Landry et al. 1984). The highest NOEL below the 7 mg/kg/day AEL for kidney effects in rodents is 5 mg/kg/day for 90 days (Landry et al. 1984). This result is supported by additional NOAELs of 3 mg/kg/day for exposure periods ranging from 90 days (Humiston et al. 1975) to 2 years (Dunn et al. 1980, Eisenbrandt et al. 1987). All of these NOAELs are based on the lack of tissue pathology in the kidney rather than tests of kidney function.

As discussed in section 3.1.12, the available data on the pharmacokinetics of triclopyr in dogs and rodents are not adequate to determine whether these differences account for the differences in the apparent NOAELs for kidney toxicity between these species. As indicated in the dose-response assessment (section 3.3.2), the apparent difference in sensitivity may be attributed to the differences in the endpoints on which the NOAELs are based, functional changes in dogs and histopathologic changes in rodents.

The other general systemic toxic effects of triclopyr are un-remarkable. At high doses, signs of liver damage may be apparent as well as decreases in food consumption, growth rate, and gross body weight (Barna-Lloyd et al. 1992, Humiston et al. 1975, Landry et al. 1984).

3.1.5. Reproductive and Teratogenic Effects. As summarized in Appendix 2, triclopyr has been subject to six teratogenicity studies, four in rabbits (Bryson 1994a,b, Hanley et

al. 1984 Smith et al. 1977) and two in rats (Bryson 1994c, Hanley et al. 1984). In addition, a 3-generation reproduction study was conducted in rats (Hanley et al. 1976, 1984). At gavage doses associated with maternal toxicity, approximately 100 mg/kg, fetal effects include decreased ossification as well as fetal loss (Bryson 1994a,b,c). At lower doses ($\leq$30 mg/kg/day), no effects are apparent after gavage or dietary administration.

Consistent with the acute toxicity studies (section 3.1.1), the comparative studies conducted by Bryson (Bryson 1994a,b) suggest that the triethlyamine and butoxyethyl forms of triclopyr have comparable levels of biological activity when doses are expressed as acid equivalents. Based on maternal toxicity, however, triclopyr BBE may be somewhat more toxic than the triethylamine salt.

3.1.6. Carcinogenicity and Mutagenicity. As summarized in Appendix 2, no increases in the incidence of malignant neoplasms have been noted in chronic bioassays in mice (Molello et al. 1979) and rats (Dunn et al. 1980, Eisenbrandt et al. 1987). In addition, various *in vitro* assays using triclopyr have failed to detect any mutagenic activity (Appendix 3). The chronic mouse bioassay did note a significant increase in the incidence of benign alveolar adenomas in CDF_1/Cox male mice, compared with matched controls. This effect was not observed in female mice. In an early review of these data by U.S. EPA (Kasza 1983), it was concluded that these data were not sufficient to support a quantitative risk assessment for triclopyr because of the high incidence of benign neoplasms in this strain of mice and the lack of a significant increase in tumors between exposed animals and historical controls.

Data regarding the carcinogenicity of triclopyr are currently under review by the U.S. EPA Office of Pesticides as part of the re-registration process for triclopyr (U.S. EPA, 1995b). There is no apparent reason for altering the earlier interpretation (Kasza 1983) of the significance of the assay in mice. The adequacy of the bioassays in rats is less certain. The U.S. EPA (1995b) seems to suggest that the doses used in the rat bioassays may not be adequate [i.e., the highest dose tested, 36 mg/kg/day (Eisenbrandt et al. 1987) may not have been sufficiently close to the maximum tolerated dose]. This dose, however, was associated with increased kidney weights, which appears to be the most sensitive effect for triclopyr.

Nonetheless, while the data may be regarded as adequate or inadequate for a qualitative assessment, none of the cancer studies are adequate to support a quantitative risk assessment for carcinogenicity.

3.1.7. Irritation and Sensitization. As summarized in Appendix 1, exposure to triclopyr formulations may cause irritation to the skin and eyes. The irritant potencies for eyes and skin appear to be different for the different formulations. In dermal exposures, triclopyr itself does not cause irritation (Olson 1967). Exposure to undiluted Garlon 3A causes slight erythema (Keeler et al. 1974); whereas, exposure to undiluted Garlon 4 causes more severe effects including moderate erythema, slight edema, and slight to moderate necrosis (Lichy et al. 1975). Thus, the irritant potential for dermal exposures appears to be: triclopyr < Garlon 3A < Garlon 4.

Ocular exposure appears to follow a different pattern, with Garlon 4 causing no irritation (Lichy et al. 1975), Garlon 3A causing severe irritation and corneal damage (Keeler et al. 1974), and triclopyr itself causing only mild irritation (Olson 1987).

3.1.8. Systemic Toxic Effects from Dermal Exposures. As discussed in section 3.2., many of the most plausible exposure scenarios for workers and the general public involve dermal exposure. As summarized in Appendix 1, animal studies involving dermal exposure to triclopyr, Garlon 3A, or Garlon 4 at doses greater than the oral LD_{50} (>2,000 mg/kg) have failed to demonstrate mortality in experimental mammals. This result suggests that triclopyr, like many herbicides, is less readily absorbed after dermal exposure than after oral exposure.

Consistent with this relationship between oral and dermal LD_{50} values, the available experimental studies in both experimental mammals and humans indicate that triclopyr is well absorbed after oral administration and poorly absorbed after dermal application.

After oral administration of 3 or 60 mg/kg of ^{14}C-triclopyr acid to rats, approximately 89-95% of the dose was recovered in the urine as unmetabolized triclopyr, indicating that at least this proportion of the administered dose was absorbed. Very little residue was recovered in the feces or carcass (Timchalk et al. 1990). The excretion rates after oral (halftime = 3.5 hours) and intravenous exposures (halftime = 1-2 hours) to rats suggest that the absorption is the rate limiting step in urinary excretion. These investigators also noted that urinary excretion was saturated at the oral dose of 60 mg/kg.

The rapid urinary elimination of triclopyr has also been noted in cattle after oral exposure to triclopyr, with 86.4% of the administered dose eliminated unchanged in the urine and no residues detected in the milk or feces. In this study, almost all of the administered dose was eliminated in the urine after 24 hours (Eckerlin et al. 1987).

The dermal absorption of triclopyr BEE has been measured *in vitro* using flow-through diffusion cells with skin from rats and humans. After 72 hours, the extent of absorption for un-occluded preparations was 3.7% and 0.7% for rat and human preparations, respectively. Using occluded preparations, the corresponding values increased to 8.6% and 3.3% for rat and human preparations, respectively (Hotchkiss et al. 1992).

These results in experimental mammals and with *in vitro* human skin preparations are consistent with an *in vivo* pharmacokinetics study using volunteers and oral and dermal exposure to triclopyr (Carmichael et al. 1989). After single oral doses of ^{14}C-labelled triclopyr acid at 0.1 and 0.5 mg/kg, more than 80% of the dose was recovered unmetabolized in the urine within 48 hours. For these oral exposures, the estimated absorption coefficients (k_a) were 0.851 hours^{-1} at 0.1 mg/kg and 0.291 hours^{-1} at 0.5 mg/kg. The corresponding absorption rates after oral exposure were 0.851 hours^{-1} and 1.39 hours^{-1}, respectively, at the same dose levels.

Dermal exposures consisted of placing 0.65-1.1 mL of Garlon 4 on the forearm so that the applied dose was 5 mg triclopyr/kg body weight. This solution was left on the skin surface for 8 hours and then removed by *"rubbing the dosed area with a paper towel"* (Carmichael et al. 1989, p. 432). Kinetic parameters were determined by measuring triclopyr levels in blood over 12 hours and urine over 84 hours. The average dermal absorption of triclopyr in five volunteers was 1.37% of the applied dose. Based on the pharmacokinetics analysis, the best estimate of the absorption fraction was 1.65%. Presumably, the measured and estimated proportions refer to the total amount of triclopyr recovered in the urine over the 84-hour collection period.

The average absorption halftime for triclopyr, relative to the total amount absorbed, was 16.8 hours [range 11-23 hours in five volunteers]. A dermal absorption coefficient (k_a) of 16.3 $hours^{-1}$ is given in Table 2 of Carmichael et al. (1989). This appears to be an error. The dermal absorption coefficient corresponding to an average absorption halftime of 16.8 hours is 0.041 $hours^{-1}$:

$$t_{\frac{1}{2}} = \frac{\ln(2)}{k}$$

which is very close to the k_a of 0.0448 given in another publication by the same senior author (Carmichael 1989). This is also very close to the average dermal absorption rate of 0.046 $hour^{-1}$ (range of 0.0163-0.0873 $hour^{-1}$ in 14 individuals) reported by Middendorf (1992). The Middendorf study, which involved applications of Garlon 4 by backpack sprayers, is used in developing the worker exposure assessment and is described in more detail in section 3.2.2.1.

As indicated in the risk characterization (section 3.4), the consequences of dermal exposure to triclopyr and triclopyr BEE are assessed by comparing estimates of absorbed dermal doses to values derived from oral toxicity studies in which dose is expressed as mg/kg/day. Based on the study by Carmichael et al. (1989), the oral absorption of triclopyr is more rapid than dermal absorption by a factor of approximately 20-35 [0.851-1.39 ÷ ≈0.04], with almost all of the orally administered dose being absorbed on the day of exposure. For the dermal exposure, only slightly more than 1% of the administered dose was absorbed over a nominal period of exposure of 8 hours. The term *nominal* is used because the method employed by the investigators to terminate the exposure, wiping with a paper towel, may not have removed all of the triclopyr from the surface of the skin. As discussed by Webster and Maibach (1992), the skin can serve as a reservoir for chemicals not yet absorbed into the systemic circulation. Thus, the functional period of exposure may have been longer than 8 hours.

In terms of comparing equivalent toxic insults to the animal after oral and dermal exposure, the most reasonable measure may be the amount absorbed during a 1-day period (Durkin et al. 1995). Based on the modelled absorption faction of 0.0165 (1.65%) and the absorption rate of 0.041 $hour^{-1}$ relative to the absorption fraction, derived from the reported absorption halftime of 16.8 hours (Carmichael et al. 1989), the estimated absorption rate relative to the total applied dose is 0.00068 $hour^{-1}$ [0.0165·0.041 $hour^{-1}$] or approximately 0.016 day^{-1}.

Because the urinary excretion rate is much more rapid than the dermal penetration rate, the observed rate of urinary excretion can be used as a surrogate for the dermal absorption rate, assuming that the compound is eliminated only in the urine or correcting for other routes of excretion (e.g., Feldmann and Maibach 1974). As discussed in Durkin et al. (1995), the maximum rate of urinary excretion in a 24-hour period may be the best estimate for comparing absorbed dermal doses with oral doses in terms of toxicological insult.

Data regarding the amount triclopyr excreted in the urine are not provided by Carmichael et al. (1989). In a separate publication (Carmichael 1989), this information is provided for dermal exposure to 3.7 mg/kg of triclopyr from Garlon 4 exposure. The maximum urinary excretion, about 3 mg (Carmichael 1989, Figure 1, p. S26), occurred during the first 24 hours. Assuming an average body weight of 73 kg, from Carmichael et al. (1989), the total applied dose was approximately 270 mg [73 kg · 3.7 mg/kg]. Thus, the proportion of the absorbed dose during the first 24 hours was 0.011 [3 mg ÷ 270 mg].

Based on an analysis of dermal absorption by humans of 47 diverse organic compounds, Durkin et al. (1995) proposed the following relationship between the average daily absorption rate (AR in % applied dose per day) and molecular weight (MW):

$$\log AR_{Ave} = -0.004\ MW + 1.5.$$

For triclopyr BEE (MW=356.64), the estimated rate is 1.18% or 0.0118 day^{-1}, very close to the proportion of 0.0116 calculated above from the data in Carmichael (1989).

For this risk assessment, the value of 0.016 day^{-1} (0.00067 $hour^{-1}$) from the study by Carmichael et al. (1989) will be used. An upper limit for dermal absorption will be taken as a factor of 2 higher, 0.032 day^{-1}, than this typical rate to encompass the ratio of highest k_a to mean k_a reported by Middendorf (1992, Table C-10), (0.0873 ÷ 0.046 = 1.9) and the ratio of the highest to mean absorbed doses reported in Carmichael et al. (1989, Table 2, p. 435) (3.1 ÷ 1.65 = 1.87).

The dermal absorption rates for triclopyr acid and triethylamine salt of triclopyr (Garlon 3A) have not be experimentally determined. The above equation for estimating fractional dermal absorption cannot be applied because, as discussed by Durkin et al. (1995), this equation may grossly overestimate absorption for compounds with a log K_{ow} <1.85. As indicated in Table 2-1, log K_{ow} for triclopyr acid at a neutral pH is -0.45.

In general, ionized compounds are absorbed much less readily than compounds that are not ionized. This factor is implicit in the U.S. EPA (1992) method for estimating dermal penetration rates (K_p):

$$\log K_p = -2.7 + 0.71 \log K_{o/w} - 0.0061\ MW$$

where $\mathbf{K_{ow}}$ is the octanol water partition coefficient and **MW** is the molecular weight. For aqueous solutions of relatively weak acids such as triclopyr ($pK_a \simeq 3$, Table 2-1), the ratio of ionized to non-ionized forms of the acid is very high at a neutral pH. The general relationships may be expressed as:

$$HA + H_2O \rightleftharpoons H_3O^+ + A^-$$

$$K_a = \frac{[H_3O^+] \cdot [A^-]}{HA}$$

where HA is the non-ionized form of the acid and A^- is the ionized form of the acid. Thus, for an acid such as triclopyr with a pK_a of about 3, the ratio of ionized to non-ionized forms is approximately 10,000:1 at a pH of 7 [0.001÷0.0000001].

As summarized in Table 2-1, the octanol:water partition coefficient (K_{ow}) for triclopyr acid is much less at pH 7 (log K_{ow}=-0.45) than the corresponding value for non-ionized triclopyr (K_{ow}=2.53). Consequently, the estimated dermal penetration rate (K_p) for triclopyr at pH 7, 0.00002 cm/hour, is approximately 160 times less than the K_p for the non-ionized acid (0.00324 cm/hour). For exposure to aqueous solutions of Garlon 3A, such as those described in section 3.2, the lower penetration rate seems most appropriate.

As discussed in Section 3.2, some exposure scenarios require the use of absorption coefficients. No measured absorption coefficients are available for triclopyr from Garlon 3A or triclopyr acid at neutral pH. By analogy to dermal penetration rates, it seems reasonable to argue that the absorption coefficient for an aqueous solution of triclopyr acid will be less than that of triclopyr BEE because, as illustrated above, most of the acid will be ionized and relatively lipophobic.

As noted by Durkin et al. (1995), there is no statistically significant correlation between dermal absorption per unit time, as a proportion of applied dose, and dermal penetration rates (K_p). Thus, while it seems plausible that the dermal absorption fraction for triclopyr acid is likely to be less than that of triclopyr BEE, an analytical determination of the magnitude of the difference is not possible. For this risk assessment, it will be assumed that the daily dermal absorption fraction for triclopyr acid is a factor of approximately 3 less than that of triclopyr BEE. This factor is selected because it leads to absorption estimates that are in the mid-range of the rates for compounds with a low K_{ow} from Durkin et al. (1995). Thus, a fractional absorption rate of 0.005 day^{-1} will be used as the central estimate with an upper range of 0.01 day^{-1}.

This approach for triclopyr acid can be viewed as anti-conservative, in that it lowers the exposure estimates for triclopyr from Garlon 3A. A very conservative approach would be to consider that triclopyr acid is absorbed as rapidly as triclopyr BEE. This position is discussed further in the risk characterization. Taking the position that triclopyr acid is absorbed at only a 3-fold lower rate than triclopyr BEE can also be viewed as too conservative, because the estimated dermal penetration rate of triclopyr acid is less than that of triclopyr BEE by a factor of almost 450

[0.009 cm/hour ÷ 0.00002 cm/hour]. In the absence of additional experimental data, however, a greater downward adjustment for the dermal absorption fraction of triclopyr acid does not seem warranted.

3.1.9. Inhalation Exposures [including Brown and Burn]. There is very little information regarding the toxicity of triclopyr or triclopyr formulations after inhalation exposure (Appendix 1) (Keeler et al. 1974, Yakel and Johnson 1980). As noted in section 3.1.3, Garlon 4 contains kerosene in sufficient quantities to warrant a cautionary statement on the product label; however, the plausible levels of exposure are far below those of concern.

Although inhalation of the herbicides of concern is not a typical route of exposure, it is possible in brown-and-burn operations. As indicated in section 2.3, brown-and-burn operations are conducted 45–180 days after treatment with the herbicide. The potential for inhalation exposure to tryclopyr from brown-and-burn operations has been assayed directly by McMahon and Bush (1992). For brown-and-burn operations conducted 32-97 days after application, at which time mean triclopyr residues ranged from 9.9 to 21 mg/kg, no triclopyr was detected in the air based on 140 breathing zone samples (detection limit = 0.1-4 $\mu g/m^3$).

No information is available on the combustion products of triclopyr. One potential concern in the combustion of any chlorine containing organic matter is the generation of chlorinated dioxins (Marty 1993). It is not clear whether triclopyr would contribute to the formation of such compounds. As discussed in section 3.1.2., the direct formation of TCDD is implausible. Given the relatively brief foliar halftimes for triclopyr (see Table 2-1), it also seems implausible that triclopyr, either as a parent compound or as combustion products, would contribute substantially to the hazards associated with exposure to wood combustion products.

3.1.10. Impurities and Metabolites. There is no information regarding the impurities that may be present in triclopyr formulations. As noted above, triclopyr is not extensively metabolized in humans or experimental mammals, and there are no specific data regarding the toxicity of the metabolites. The toxicity studies on which the dose-response assessment is based involve *in vivo* exposures that should encompass the toxicity of the metabolites of triclopyr. The lack of information on the toxicity of the metabolites adds relatively little uncertainty to the risk assessment. The significance of impurities is less certain. Nonetheless, based on the comparison of the acute toxicity of triclopyr and triclopyr formulations (see section 3.1.1), there is no basis for arguing that highly toxic impurities exist.

3.1.11. Toxicological Equivalence of Acid and Ester Forms. A central issue in the risk assessments for Garlon 3A and Garlon 4 involves the toxic equivalence of the different active ingredients, triclopyr triethylamine (Garlon 3A) and triclopyr BEE (Garlon 4). As noted in section 3.1, the acute oral LD_{50} values and signs associated with acutely toxic exposures are almost the same for the two formulations. Similarly, on repeated dosing, triclopyr triethylamine and BEE elicit similar responses in teratology studies (Bryson 1994a,b), although more severe effects were seen in dams in the high dose group of triclopyr BEE. As briefly summarized by

Veenstra et al. (1983), Dow Chemical company has conducted comparative pharmacokinetics studies that suggest that these two compounds are likely to be similar in their biological action. These studies have not been published and were not available for the preparation of this risk assessment. Nonetheless, this assertion is consistent with the published studies on the elimination kinetics of triclopyr acid and triclopyr BEE that suggest that these two compounds are eliminated at similar rates (Carmichael et al. 1989, Timchalk et al. 1990) and that triclopyr BEE is rapidly hydrolyzed to triclopyr acid in mammals (Kastl et al. 1986).

The following generalizations, while somewhat speculative, seem plausible. Triclopyr acids are probably less readily absorbed than triclopyr BEE because, in general, ionized compounds are less readily absorbed than less polar and more hydrophobic compounds such as esters. Once absorbed, endogenous esterases probably break the ester linkage in triclopyr BEE, with the consequent formation of triclopyr acid. This generalization would account for the similar toxic effects and potencies of the two Garlon formulations and is consistent with the available metabolism and kinetic studies.

For this risk assessment, Garlon 3A and Garlon 4 will be treated as toxicologically equivalent for systemic toxic effects attributable to triclopyr. This is the position taken by U.S. EPA (1995b) based on a review of the toxicology and pharmacokinetics of these two compounds. As noted above (section 3.1.8), however, there is relatively good information on the dermal absorption of triclopyr BEE from Garlon 4 but no information on dermal absorption of triclopyr acid or triclopyr acid from Garlon 3. Based on the structure-activity relationships discussed in section 3.1.8, the estimated dermal absorption of triclopyr acid is likely to be less than that of triclopyr BEE. Thus, while the dose-response assessment is based on the assumption of toxicological equivalence between triclopyr acid and triclopyr BEE, the exposure assessments involving dermal absorption for these two forms of triclopyr differ and this difference has somewhat of an impact on the risk characterization (section 3.4).

3.1.12. Pharmacokinetic Differences Among Species. As summarized in section 3.1.3, the highest NOELs below any AELs for dogs and rodents differ by a factor of about 10 [5 mg/kg/day in rodents ÷ 0.5 mg/kg/day in dogs]. Nolan (1985) suggests that this apparent difference in species sensitivity may have a pharmacokinetics basis. As summarized in Nolan (1985), the halftime of triclopyr in dogs (96 hours, $k_e = 0.007\ h^{-1}$) is substantially longer than halftimes in rabbits (0.7 hours, $k_e = 0.99\ h^{-1}$), rats (1.5 hours, $k_e = 0.46\ h^{-1}$), or monkeys (3.1 hours, $k_e = 0.22\ h^{-1}$), and this difference may be related to the limited capacity for anion transport in the dog kidney (i.e., Knoefel and Huang 1969).

The discussion by Nolan (1985) does not provide detailed information on the kinetic studies supporting the reported halftimes; however, the reported halftime for rats, 1.5 hours, is like the 3.5-hour terminal elimination halftime ($k_e = 0.192\ h^{-1}$) after oral exposure noted in the kinetic study by Timchalk et al. (1990). Since the elimination rate is a reciprocal function of the elimination halftime, this suggests that triclopyr is eliminated approximately 27-64 times more rapidly by the rat than by the dog [96 ÷ (3.5-1.5) or equivalently (0.192-0.46) ÷ 0.007]. The

difference in elimination rates is somewhat greater than but on the same order of magnitude as the difference in the highest NOELs below any AELs for dogs and rodents, which is a factor of 10 as indicated above.

The implication of these kinetic differences is that the dog may not be the most appropriate species for assessing potential human health effects from exposure to triclopyr. The lack of a published study on dogs makes this concern difficult to evaluate. Detailed information has been published on the pharmacokinetics of 2,4,5-T in rats and dogs (Piper et al. 1973) as well as humans (Gehring et al. 1973). This information, together with the available kinetic data on triclopyr, is summarized in Table 3-1.

As with triclopyr, 2,4,5-T is not metabolized extensively and is eliminated almost exclusively in the urine. Also like triclopyr, 2,4,5-T is eliminated much more slowly by the dog than by rats or humans (see Table 3-1), and the elimination rates in dogs are quite similar, 0.009 $hour^{-1}$ for 2,4,5-T and 0.007 $hour^{-1}$ for triclopyr. As reviewed by Piper et al. (1973), the differences in the kinetics of 2,4,5-T in rats and dogs may account of differences in the toxicity of this compound to these species. The acute oral LD_{50} is approximately 300 mg/kg in the rat and approximately 100 mg/kg in the dog. The relative difference in acute oral toxicity, a factor of 3, is much less than the difference in elimination rates, about a factor of 16 [0.147÷0.009]. The relative difference in acute oral toxicity is similar to the relative differences in peak plasma levels of 2,4,5-T after single oral doses of 5 mg/kg in rats (approximately 15 μg/mL) and dogs (approximately 25 μg/mL) (Figure 3, p. 346 of Piper et al. 1973).

In estimating the effects of chronic exposure, the elimination rate is the sole determinant in time to steady state based on first order elimination and first order absorption, but the plasma level at steady state is inversely proportional to the product of the elimination rate and volume of distribution (Vd):

$$C_{t_\infty} \propto \frac{1}{k_e \cdot Vd}$$

(see O'Flaherty 1981, p. 233, Eq. 5.20). As indicated in Table 3-1, this value is very similar for dogs and humans for 2,4,5-T, suggesting that if a given dose were administered repeatedly at fixed intervals, the plasma levels would be comparable and would be about 10 times higher than plasma levels in the rat. This, in turn, suggests that, at least for 2,4,5-T, the dog is a better animal model than the rat, even though the elimination rate for 2,4,5-T by the dog is much lower than that seen in rats or humans.

The possible effects of protein binding complicates this assessment. As indicated in Table 3-1, 2,4,5-T is more tightly bound to plasma protein in the human (0.987) than in the rat (0.891). While protein binding studies have not been conducted on the dog, *in vitro* studies suggest that 2,4,5-T may be very tightly bound to plasma proteins in the dog (Hook et al. 1974, 1976). If it is bound more tightly in the dog than in the human, the concentration of free 2,4,5-T will be lower

Table 3-1. Some pharmacokinetic parameters for triclopyr and 2,4,5-trichlorophenoxy acetic acid (2,4,5-T).

Species	k_a ($hours^{-1}$)	plasma k_e ($hours^{-1}$)	Vd (L/kg)	Plasma Protein Binding	$(k_eVd)^{-1}$
		2,4,5-T			
Rat[a]		0.147	14.4	0.891	0.47
Dog[a]		0.009	22.1	high	5.03
Human[b]	0.918	0.03	6.1	0.987	5.46
		Triclopyr			
Rat[c]	0.192	0.628	0.051		31.2
Dog		0.007[d]			
Human[e]	1.39	0.290	0.317		10.9

[a] Piper et al. (1973), Table 1, p. 342, single oral dose of 5 mg/kg as 2,4,5-T acid.

[b] Gehring et al. (1973), single oral dose of 5 mg/kg as 2,4,5-T acid.

[c] Timchalk et al. (1990), single oral doses of 3 and 60 mg/kg as triclopyr acid.

[d] Based on halftime of 96 hours (Nolan 1985).

[e] Carmichael et al. (1989), single oral dose of 0.5 mg/kg as triclopyr acid.

Key:

k_a, first order absorption rate.
k_e, first order elimination rate.
Vd, volume of distribution.

in the dog than in the human, perhaps making the dog less sensitive than the human under comparable conditions of exposure.

The above analysis suggests that, at least for 2,4,5-T, the available kinetic data indicate that the dog may be a more appropriate species than the rat for risk assessment, at least for chronic exposure scenarios. Rather than being too conservative, comparable chronic exposures may lead

to somewhat lower concentrations of total 2,4,5-T in the dog and perhaps much lower levels of free 2,4,5-T.

The pharmacokinetics data on triclopyr are much less extensive than those for 2,4,5-T (see Table 3-1). The elimination rates in dogs for these two compounds are almost the same, based on the halftime for triclopyr reported by Nolan (1985). Based on the triclopyr study by Tominack et al. (1990), rats eliminate triclopyr much more rapidly than they eliminate 2,4,5-T (by a factor of about 4). Similarly, the elimination rate of triclopyr by humans is about a factor of 10 higher than the rate for 2,4,5-T. At comparable chronic exposures, a consideration of both elimination rates and volumes of distribution suggest that plasma levels of triclopyr will be about a factor of 3 higher in rats, compared with plasma levels in humans. As illustrated in the above analysis on 2,4,5-T, however, the rapid elimination rate of 2,4,5-T for the dog does not necessarily suggest that the dog is an inappropriate test species. In addition, by analogy to 2,4,5-T, the consideration of protein binding may be important for triclopyr. There are no experimental data regarding the levels of protein binding in any of these species.

As discussed further in the dose-response assessment (section 3.3), the apparent discrepancies noted in dose-severity relationships between dogs and rats may be attributed to differences in the sensitivity of endpoints assessed, functional effects in dogs, and histopathological lesions in rats, rather than pharmacokinetics differences in species.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. Two general exposure assessments are presented in this section, job-specific assessments and incident assessments. Job-specific assessments estimate absorption associated with relatively complex job activities, such as mixing, loading, or applying triclopyr, in which multiple routes of exposure are likely. All of these assessments are given as a range based on the projected application rates, empirical observations of variability in exposure rates, and projected variations in herbicide usage [i.e., number of acres treated per hour]. Incident assessments are relatively easy to make. They estimate absorption from spilling a solution onto the skin or wearing contaminated clothing.

Workers involved in broadcast applications, either aerial or boom spray, are exposed to similar levels of triclopyr from the application of either Garlon 3A or Garlon 4. Because triclopyr BEE is likely to be absorbed more rapidly than triclopyr acid, the levels of triclopyr exposure associated with the application of Garlon 4 are somewhat higher than those associated with the application of Garlon 3A. Central estimates of exposure for these workers are approximately 0.01 mg/kg/day for Garlon 4 and approximately 0.004 mg/kg/day for Garlon 3A. Central estimates for ground workers are much lower: 0.006 mg/kg/day for Garlon 4 and 0.002 mg/kg/day for Garlon 3A. Upper limits of exposure estimates for all worker groups are similar, approximately 0.2 for Garlon 4 and 0.01 for Garlon 3A. Immediately after application, some members of the general public could receive exposures comparable to those for workers. Over prolonged periods, however, levels of exposure will tend to be much lower than those for workers.

3.2.2. Workers.

3.2.2.1. ***Job Categories*** **--** As outlined in the program description (see section 2), this risk assessment is concerned with both aerial applications and four types of ground applications: backpack, cut surface, basal stem, and boom spray. As discussed in SERA (1995), occupational exposure generally involves inhalation and dermal exposure, with the dermal route contributing far more to exposure than the inhalation route. Several studies have been conducted in which the absorbed dose can be estimated as a function of the amount of material handled and chemical specific exposure factors, expressed as mg agent/kg · lb a.i handled.

Much of the literature on occupational exposure rates involves exposures to 2,4-D (SERA 1994, 1995b). For ground applications of 2,4-D, plausible estimates and ranges of exposure rates are $9.6x10^{-5}$ ($4.9x10^{-6}$ to $1.9x10^{-3}$) mg/kg/lb a.i. for roadside hydraulic spraying and $1.4x10^{-3}$ ($4.4x10^{-5}$ to $4.2x10^{-2}$) mg/kg/lb a.i. for cut surface, streamline, and directed foliar applications (see Table 3-2 in SERA 1995b). All of these exposure rates are from applications in which gloves, other protective clothing, and good hygiene practices were employed.

As reviewed in SERA (1994), exposure rates for workers involved in aerial applications are much less than those for workers involved in ground applications. For 2,4-D, exposure rates of $2x10^{-5}$ to $4x10^{-5}$ mg/kg/lb a.i. are typical for pilots and mixer/loaders. The rates of exposures for flaggers are approximately 1-2% of those for pilots and mixer/loaders. There is wide variation among exposure rates for workers involved in aerial applications, with the upper and lower limits of exposure rates each spanning about an order of magnitude (SERA 1994, Table 11). Thus, for aerial workers, except flaggers, involved in the application of 2,4-D, a typical rate with plausible ranges for exposure is $3x10^{-5}$ ($3x10^{-6}$ to $3x10^{-4}$) mg/kg/lb a.i.

The dermal absorption of triclopyr seems to be less than that of 2,4-D. As noted in section 3.1.8, the dermal absorption of triclopyr, as Garlon 4, by volunteers was only about 1.65% over a 4-day period (Carmichael et al. 1989). In humans, approximately 5.8% of a dermal dose of 2,4-D was eliminated in the urine over a 5-day observation period, with most of this dose, 5.2%, eliminated within 4 days (Feldmann and Maibach 1974). Thus, based on relative rates of dermal absorption, occupational exposure to triclopyr should be lower than that associated with 2,4-D, by a factor of approximately 0.32 [1.65 ÷ 5.2].The usefulness of this estimate can be evaluated based on a worker exposure study by Middendorf (1992). A synopsis of this study was published by Middendorf et al. (1992). A summary of relevant data from the full report (Middendorf 1992) is summarized in Table 3-2. Workers applied Garlon 4 by backpack spray to various sites. Total absorption was determined by the analysis of triclopyr in the urine over a 5-day collection period. The absorption rates, in terms of mg/kg · lb a.i. handled, are summarized in Table 3-2 for three sites reported in Middendorf (1992). As with most studies of this kind, exposure rates among workers varied by a factor of approximately 100. As discussed by Middendorf (1992), a major source of variation appears to involve the use of gloves. Neither of two workers with the highest exposure rates, workers H and I at site 2, wore gloves. All of the workers at site 1, the group with the lowest exposure rate, wore gloves.

Using the 2,4-D rates for backpack workers [$1.4x10^{-3}$ ($4.4x10^{-5}$ to $4.2x10^{-2}$) mg/kg/lb a.i.] and correcting for the relative difference in dermal absorption (0.32), the expected exposures for workers applying triclopyr by backpack would be $4.5x10^{-4}$ ($1.4x10^{-5}$ to $1.3x10^{-2}$) mg/kg/lb a.i. This estimated mean rate is 10 times less than the mean rate reported by Middendorf (1992) for all three sites combined and 2 times less than the observed rate at site 1 in the Middendorf (1992) study, in which all workers wore gloves. As noted above, the discrepancy between the rates estimated for triclopyr based on 2,4-D exposure data and those from the Middendorf data for all sites combined are consistent with the use of good hygiene practices employed in the 2,4-D studies. The triclopyr rates at site 1, at which gloves were worn, are consistent with the estimates based on 2,4-D rates.

For this risk assessment, worker exposure to Garlon 4 will be based directly on the 2,4-D exposure rates summarized above and will not be adjusted for differences in dermal exposure between 2,4-D and triclopyr BEE. This approach is taken because the mean exposure rate at site 1 from Middendorf is almost the same as the mean rate for 2,4-D [0.0009 versus 0.0014] with no adjustment for differences in dermal absorption. In addition, the range of rates for 2,4-D exposures ($4.4x10^{-5}$ to $4.2x10^{-2}$) encompasses and is relatively close to the range noted in the Middendorf (1992) study for all sites combined ($3x10^{-4}$ to $1.4x10^{-2}$). Thus, for the upper limits of exposure, this approach should reflect realistic exposure estimates for applications that do not involve the use of gloves and other protective measures.

Table 3-3 summarizes worker exposure to Garlon 4 according to various job categories. The plausible levels of exposure for ground and aerial applications are estimated as the product of an application rate of 1 lb/acre, the area treated per hour (acres treated/hour by a worker), and the exposure rate (mg/kg · lb a.i.). All calculations are based on the assumption that the worker applies the product for 8 hours/day. This is a reasonably conservative estimate for workers on an extended 10-hour day; however, it overestimates exposure for workers who

Table 3-2. Estimated absorption rates for workers involved in backpack applications of triclopyr BEE as Garlon 4.

Worker	Amount Handled (lb a.i.)[a]	Body Weight (kg)[b]	Amount Absorbed (mg)[b]	Exposure Rate (mg/kg bw·lb a.i.)
		Site 1 (all wore gloves)		
A[c]	4.8	91.2	0.065	0.00015
B	4.8	83.3	0.259	0.00065
C	4.8	93.2	0.697	0.00156
D	4.8	78.3	1.902	0.00506
	Geometric mean (95% C.I.):			0.0009 (0.00008 - 0.006)
		Site 2		
G[c]	4	103	0.561	0.00136
H (no gloves)	4	71.9	4.108	0.01428
I (no gloves)	4	63.8	3.001	0.01176
J	4	85.1	0.831	0.00244
K	4	61.5	0.921	0.00374
L	4	74.2	1.152	0.00388
	Geometric mean (95% C.I.):			0.0045 (0.001 - 0.02)
		Site 3		
M[c]	5.6	93.2	1.143	0.00219
N	5.6	90.5	2.006	0.00396
O	5.6	71.9	1.039	0.00258
P	5.6	71.9	0.745	0.00185
Q	5.6	91.9	0.647	0.00126
R	5.6	105	0.207	0.00035
	Geometric mean (95% C.I.):			0.0016 (0.0004-0.006)
		All Sites Combined		
	Geometric mean (95% C.I.):			0.004 (0.0003 - 0.014)

[a] Middendorf (1992), Table 2, pp. 7-8
[b] Middendorf (1992), Table 3, p. 25
[c] Mixer
C.I. = Confidence Interval

Table 3-3. Quantitative summary of occupational exposure to triclopyr from Garlon 4, excluding accidental or incidental exposure

Treatment Method	Treatment Rate (acres/hour)	Exposure Rate (mg a.e./kg bw/lb a.e.)	Daily Dose (mg a.e./kg bw)[a]
Boom spraying	15 11-21	$9.6 \cdot 10^{-5}$ $4.9 \cdot 10^{-6}$ - $1.9 \cdot 10^{-3}$	0.01 0.0004-0.3
Backpack, streamline, and cut surface	0.5 0.25-1	$1.4 \cdot 10^{-3}$ $4.4 \cdot 10^{-5}$ - $4.2 \cdot 10^{-2}$	0.006 0.00009-0.3
Aerial applications (pilots and mixer/loaders)	60 40-100	$3 \cdot 10^{-5}$ $3 \cdot 10^{-6}$ - $3 \cdot 10^{-4}$	0.01 0.001-0.2

[a] Assuming an application rate of 1 lb/acre and an 8-hour work day.

work a standard 8-hour day. The overestimation of worker exposure is a relatively minor factor, given the remarkable variability in exposure rates among individuals.

Estimated daily doses are presented as a central value and a range. The central value is based on the approximate geometric mean of the anticipated range of treatment rates and mean exposure rate. The lower range of the daily dose is based on the lower range of the treatment rates and the lower range of the exposure rate. The upper range of the daily dose is based on the upper end of the range of treatment rates and the upper range of the exposure rate.

There is a linear relationship between exposure and the application rate. As discussed in section 2.4, the Forest Service may use lesser or greater application rates. The consequences of differing rates of application are discussed in the risk characterization (section 3.4).

No studies regarding occupational exposure to Garlon 3A were located in the literature. As discussed in section 3.1.8, it is likely that the dermal absorption rate for triclopyr acid in a neutral solution will be less than the rate for triclopyr BEE. Although the extent of the difference cannot be determined analytically, a factor of 3 is used as a plausible but not too conservative an estimate. A quantitative summary of occupational exposure to triclopyr from Garlon 3A, based on rates taken at a factor of 3 less than those for Garlon 4, is presented in Table 3-4.

Table 3-4. Quantitative summary of occupational exposure to triclopyr from Garlon 3A, excluding accidental or incidental exposure[a]

Treatment Method	Treatment Rate (acres/hour)	Exposure Rate[b] (mg a.e./kg bw/lb a.i.)	Daily Dose (mg a.e./kg bw)[a]
Boom spraying	15 11-21	$3.2 \cdot 10^{-5}$ $1.6 \cdot 10^{-6}$ - $6.3 \cdot 10^{-4}$	0.004 0.0001-0.1
Backpack, streamline, and cut surface	0.5 0.25-1	$4.6 \cdot 10^{-4}$ $1.5 \cdot 10^{-5}$ - $1.4 \cdot 10^{-2}$	0.002 0.00003-0.1
Aerial applications (pilots and mixer/loaders)	60 40-100	$1 \cdot 10^{-5}$ $1 \cdot 10^{-6}$ - $1 \cdot 10^{-4}$	0.005 0.0003-0.08

[a]Assuming an application rate of 1 lb/acre and an 8-hour work day.

[b]Rates taken as a factor of 3 less than the rates for Garlon 4. [See text for details.]

This factor will be incorporated directly into the risk assessment by lowering the exposure rates given for Garlon 4 (see Table 3-3) by a factor of 3. This approach assumes that almost all of the absorbed dose in occupational exposures is attributable to dermal absorption (Carmichael 1989). The study by Middendorf (Middendorf 1992, Middendorf et al. 1992) indicates that approximately 14% (9.1-19.8%) of the occupational exposures to triclopyr BEE may be due to inhalation exposure. This estimate is based on air monitoring data and the assumption that all of the inhaled triclopyr BEE is absorbed. This assumption probably overestimates the significance of inhalation exposure, but the extent of the overestimation cannot be quantified.

3.2.2.2. ***Immersion or Contaminated Clothing*** **--** Incidental occupational exposure may occur from improper handling or use of the herbicide, or from accidental contamination of the skin or clothing by a spill. All of these scenarios can be modelled using Fick's first law. As discussed in Durkin et al. (1995), scenarios that use Fick's first law require an estimate of the permeability coefficient, K_p, expressed in cm/hour. There are not experimentally determined K_p values for triclopyr and triclopyr BEE in the available literature. Calculated values are discussed in section 3.1.8 and summarized in Table 2-1 (K_p = 0.00002 cm/hour for triclopyr at pH 7) and Table 2-2 (K_p = 0.009 cm/hour for triclopyr BEE).

The commercial formulations of triclopyr covered by this risk assessment contain triclopyr at levels of 360 g a.e./L (Garlon 3A) and 480 g a.e./L (Garlon 4) (see Table 2-2). During the handling process, an individual may immerse a part of the body into the formulation for a short time, either through mischance or imprudent handling. An extreme scenario would involve a

worker who places both hands in the concentrated formulation of Garlon 4 (480 g a.e./L). For this risk assessment, the surface area of the hands will be estimated at 0.084 m^2 (U.S. EPA 1992). Concentrations of 480 g/L are equivalent to 480 mg/mL, which, in turn, is equivalent to 480 mg/cm^3.

For this scenario, the estimated absorbed dose of triclopyr as acid equivalents from triclopyr BEE in Garlon 4 is approximately 0.86 mg/kg

$$0.009 \text{ cm/hour} \cdot 480 \text{ mg/cm}^3 \cdot 1/60 \text{ hour} \cdot 840 \text{ cm}^2 \div 70 \text{ kg}.$$

For Garlon 3A, the corresponding exposure is much less because of the lower K_p and lower concentration:

$$0.00002 \text{ cm/hour} \cdot 360 \text{ mg/cm}^3 \cdot 1/60 \text{ hour} \cdot 840 \text{ cm}^2 \div 70 \text{ kg},$$

which is equal to approximately 0.0014 mg/kg.

3.2.2.3. ***Accidental Spills*** **--** In accidental spill scenarios, it is important to estimate the amount of liquid adhering to the surface of the skin. In one study, as much as 4 mg liquid/cm^2 of skin surface was retained on hands removed immediately from beakers containing water or ethanol (Mason and Johnson 1987). When beakers containing light paraffin oil were used, approximately twice this amount was retained. In most instances, using these values should result in a plausible upper estimate of retention because chemical loss from the skin surface due to moving or washing are not considered. Thus, the amount of chemical transferred to the skin after a spill may be calculated as:

$$D_{Skin} = RF \cdot P \cdot A \qquad \textbf{(3-5)}$$

remaining on surface of skin (µg)
ıtion factor (µg/*cm*^{2}) (*for example*, 4,000–8,
ɔrtion of agent in the liquid
area exposed (*cm*^{2})

Any person handling a concentrated formulation or located near the area where the handling takes place may be subject to an accidental spill. This is different from immersion in that most of the liquid will run off the surface of the skin immediately after the spill unless the material is kept in contact with the skin by saturated clothing. If the clothing is saturated, the scenario outlined above applies. If the material spills onto the skin and is not kept in contact with the skin, the exposure will be much less.

Consider the effects of spilling triclopyr over the lower legs. The surface area of the lower legs is taken as 2,070 cm^2 (U.S. EPA 1992). The upper limit of the amount of liquid adhering to the

surface of the skin is taken as 8 mg/cm^2 of skin (Mason and Johnson 1987). Assuming a density of 1.0 for the aqueous solution, this is equivalent to 0.008 mL/cm^2. Hence, the volume of liquid adhering to the skin is 16.56 mL [2,070 cm^2 · 0.008 mL/cm^2]. For concentrations of 360-480 mg/mL, the amount of triclopyr adhering to the skin can be estimated at approximately 6,000 mg for Garlon 3A [16.56 mL · 360 mg a.e. triclopyr/mL] and 8,000 mg for Garlon 4 [16.56 mL · 480 mg a.e. triclopyr/mL].

To estimate the absorbed dose, some estimate of absorption rate as percent of applied dose per hour is necessary. As discussed in section 3.1.8, human absorption rates for triclopyr from Garlon 4 are available from Carmichael et al. (1989) and Carmichael (1989). The central estimate is approximately 0.016 day^{-1} (0.0007 hour^{-1}) with an upper range of about 0.032 day^{-1} (0.001 hour^{-1}). Assuming that the skin is washed thoroughly after 1 hour, the absorbed dose can be estimated as 0.08 mg/kg with an upper range of 0.11 mg/kg

$$8{,}000 \text{ mg} \cdot 0.0007\text{-}0.001 \text{ h}^{-1} \cdot 1 \text{ h} \div 70 \text{ kg}.$$

As discussed in section 3.1.8, the absorption rate for triclopyr as an acid is estimated at 0.005-0.01 day^{-1} (0.0002-0.0004 hour^{-1}). Thus, for the same exposure scenario using Garlon 3A, the estimated exposure would be 0.02-0.04 mg/kg,

$$6{,}000 \text{ mg} \cdot 0.0002\text{-}0.0004 \text{ h}^{-1} \cdot 1 \text{ h} \div 70 \text{ kg}.$$

3.2.3. General Public.

3.2.3.1. ***Scenarios and Assumptions*** **--** Under normal conditions, members of the general public should not be exposed to substantial levels of triclopyr. During application, members of the general public are excluded from treatment areas. In cases of accidental spills, exclusion zones are established and members of the general public are not permitted to enter the area.

Nonetheless, any number of exposure scenarios could be constructed for the general public, based on varying assumptions concerning application rates, dispersion, canopy interception, and human activity. For this risk assessment, several very conservative scenarios are developed. As discussed below, most of these scenarios should be regarded as extreme.

Many of the exposure scenarios for the general public involve a child. This is because the relationships of surface area and consumption rates to body weight result in estimated doses for young children that are higher than those for adults (U.S. EPA 1989a). Consumption-specific values are taken from U.S. EPA (1989a,b). The chemical-specific assumptions for triclopyr are the same as those used for workers.

Dermal exposure scenarios that involve children use the same set of assumptions: the child is 2- to 3-years old, weighs 10-11 kg, and has a total body surface area of 0.6 m^2 or 6,000 cm^2 (U.S.

EPA 1992). For most scenarios, the child is assumed to be naked, maximizing the surface area of the body in contact with the chemical. In all cases, there are linear relationships among the exposed surface area of the body, the estimated absorbed dose, and the subsequent risk.

3.2.3.2. ***Direct Spray*** **--** For this exposure scenario, it will be assumed that a naked child is sprayed directly with triclopyr by a hydraulic sprayer and that the child is completely covered (i.e., 100% of the surface area of the body is exposed). The highest spray solution recommended for any broadcast application of the Garlon 3A is 15% (3 gallons Garlon 3A in 20 gallons of spray solution for woody plant control, DowElanco 1993a) which corresponds to 54 g/L or 54 mg/mL. Therefore, the dose deposited on the child would be 2,592 mg

$$0.008 \text{ mL/cm}^2 \cdot 54 \text{ mg/mL} \cdot 6{,}000 \text{ cm}^2$$

Taking the absorption rate of 0.002-0.004 hour^{-1} and assuming that the child is washed completely 1 hour after being sprayed, the absorbed dose is estimated as approximately 0.047 to 0.094 mg/kg,

$$2{,}592 \text{ mg} \cdot 0.0002 \text{ to } 0.0004 \text{ h}^{-1} \div 11 \text{ kg.}$$

For Garlon 4, the estimated doses would be higher, reflecting the more rapid dermal absorption rate for triclopyr BEE. The highest spray solution recommended for any broadcast application of Garlon 4 is 10% [8 quarts Garlon 4 in 20 gallons of spray solution for woody plant control (DowElanco 1992)], which corresponds to 48 g/L or 48 mg/mL. Thus, the dose deposited on the child would be 2,304 mg

$$0.008 \text{ mL/cm}^2 \cdot 48 \text{ mg/mL} \cdot 6{,}000 \text{ cm}^2$$

Taking the absorption rate of 0.0007-0.001 hour^{-1} and assuming that the child is washed completely 1 hour after being sprayed, the absorbed dose is estimated at approximately 0.15-0.21 mg/kg,

$$2{,}304 \text{ mg} \cdot 0.0007\text{-}0.001 \text{ hour}^{-1} \div 11 \text{ kg.}$$

A less severe accidental scenario would involve a young woman whose feet and legs [2,915 cm^2] are sprayed directly and the assumption that the spray is not removed for 1 hour. For Garlon 3A, the deposited amount would be 1,260 mg,

$$0.008 \text{ mL/cm}^2 \cdot 54 \text{ mg/mL} \cdot 2{,}915 \text{ cm}^2,$$

and the absorbed dose would be 0.004 to 0.008 mg/kg,

$$1{,}260 \text{ mg} \cdot 0.0002\text{-}0.0004 \text{ h}^{-1} \cdot 1 \text{ hour} \div 64 \text{ kg.}$$

Using the same set of assumptions as above for Garlon 4, the absorbed dose would be 0.012-0.017 mg/kg,

$$0.008 \text{ mL/cm}^2 \cdot 48 \text{ mg/mL} \cdot 2{,}915 \text{ cm}^2 \cdot 0.0007\text{-}0.001 \text{ h}^{-1} \cdot 1 \text{ hour} \div 64 \text{ kg}.$$

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. As discussed in Durkin et al. (1995), some estimate of dislodgeable residue of the herbicide must be available. This information is not available for triclopyr, either as residues from Garlon 3 or Garlon 4A.

Immediately after the spray application, levels of exposure may approximate those involving contact with direct spray, as estimated above. Generally, after the liquid carrier dries, exposure levels are expected to decrease. For example, in a study by Harris and Solomon (1992), 2,4-D was applied to turf at a nominal rate of 11 μg/cm^2. Immediately after the liquid carrier dried, the dislodgeable residue of 2,4-D was 0.92 μg/cm^2, about 10 times less than the nominal application rate.

It is not clear whether similar relationships will hold for triclopyr residues associated with the application of Garlon 3A or Garlon 4. Based on the analyses of residues from gill cups after the application of triclopyr triethlyamine salt and triclopyr BEE, initial deposits were approximately 70-80% of the nominal application rate for both compounds (Newton et al. 1990). The extent to which these residues would be dislodgeable from normal activity, however, is uncertain. As summarized in Appendix 4, washoff of triclopyr (applied as Garlon 4) from leaves is approximately 62% 1 hour after application and approximately 11-17% 2 days after application (Michael et al. 1992).

For the purpose of crudely comparing the potential hazards associated with dermal contact with contaminated vegetation, it will be assumed that dislodgeable residues for both forms of triclopyr would be approximately 10% of the nominal application rate, by analogy to 2,4-D. An application rate of 1 lb/acre corresponds to about 1.12 kg/ha or 11 μg/cm^2. Therefore, the dislodgeable residue is estimated as approximately 1 μg/cm^2. Following the methods provided by Durkin et al. (1995, equation 4, p. 68), the transfer rate would be approximately 1 μg/(cm^2·hour) [$10^{0.05}$]

$$1.09 \cdot \log(1.0) + 0.05 = 0.05.$$

The exposed dose for an individual, wearing shorts and a short-sleeved shirt, in contact with the contaminated vegetation for 1 hour would be approximately 5 mg

$$1 \ \mu\text{g/(cm}^2\cdot\text{hour)} \cdot 5{,}300 \text{ cm}^2 \cdot 1 \text{ hour}.$$

For estimating the absorbed dose, it will be assumed that the individual does not wash thoroughly for 12 hours.

Using the dermal absorption rate for Garlon 4, 0.0007-0.001 h^{-1}, and assuming a 64 kg body weight for a young woman, the absorbed dose would be 0.0007-0.0009 mg/kg,

$$5 \text{ mg} \cdot 0.0007\text{-}0.001 \text{ h}^{-1} \cdot 12 \text{ h} \div 64 \text{ kg}.$$

A similar calculation for Garlon 3A yields dose estimates of 0.0002-0.0004 mg/kg,

$$5 \text{ mg} \cdot 0.0002\text{-}0.0004 \text{ h}^{-1} \cdot 12 \text{ h} \div 64 \text{ kg}.$$

Each of the above dose estimates apply to residues immediately after application. As summarized in Appendix 4, there are a variety of field studies regarding the dissipation of triclopyr residues in plants. The two most detailed studies are those of Newton et al. (1990) and Thompson et al. (1994). The Newton study involved the aerial application of triclopyr triethylamine (2.2 and 4.4 kg/ha) or triclopyr BEE (1.65-3.3 kg/ha) to Oregon brushfields. Foliar halftimes for the triclopyr amine ranged from approximately 20 to 60 days (k_e = 0.012-0.034). For triclopyr BEE, the halftimes ranged from approximately 31 to 290 days (k_e = 0.002-0.022 $days^{-1}$). In the study by Thompson et al. (1994), a triclopyr BEE formulation, RELEASE (which appears to be identical to Garlon 4) was applied by backpack sprayers to sites predominated by sugar maple with other shrub species. The dissipation/decay coefficients for both triclopyr BEE (k_e = 0.42-0.65 $days^{-1}$) as well as the acid (k_e = 0.09-0.26 $days^{-1}$) were substantially more rapid (halftimes of 1-6 days) than those noted in the study by Newton. Halftimes of approximately 6-28 days (k_e = 0.02-0.1 $days^{-1}$) have also been noted by Whisenant and McArthur (1989) on various types of vegetation after the backpack sprayer application of triclopyr BEE.

Given this wide variability in the reported dissipation/degradation rates combined with the wide variability in estimated exposures for contact with contaminated vegetation, the effect of foliar decay on exposed dose will not be modeled quantitatively. A qualitative discussion regarding the decay of foliar residues is presented the risk characterization (section 3.4).

3.2.3.4. ***Contaminated Water*** **--** Water can be contaminated from runoff, leaching from contaminated soil, from a direct spill, or unintentional contamination from aerial applications. Two general processes, degradation and dispersion, will act to decrease concentrations of the contaminant in ambient water. For triclopyr, the major degradative process appears to be photolysis, with the nature of the degradation products varying substantially between natural waters (oxamic acid and other non-chlorinated aliphatics) and sterile buffered solutions (oxidative dechlorination). In either type of water, the halftime of triclopyr acid under conditions simulating natural sunlight is relatively short: about 0.5 days in natural water and 1.3 days in sterile water. Under conditions of darkness, the halftime in sterile water is approximately 3 months (Woodburn et al. 1993a). There are several relevant monitoring studies (Appendix 4) that are useful for estimating exposure to triclopyr in lakes or streams.

3.2.3.4.1. Lakes -- When applied to a standing body of water such as a pond or lake, the concentrations of triclopyr will depend largely on the mixing depth, because triclopyr does not concentrate extensively or rapidly in biota or sediments. For example, in a test application of Garlon 3A to a lake in Georgia, initial monitored concentrations were very close to nominal expected levels based on depth of the lake and application rate. The halftime of triclopyr in the lake water at different locations ranged from 0.5 to 3.6 days (Woodburn et al. 1993b). Triclopyr BEE may be somewhat more persistent in lake water, with field halftimes of 4-8 days, but, as with triclopyr triethylamine, the initial measured concentrations are reasonably close to those expected from nominal applied rates and the size of the water body (Kreutzweiser et al. 1995).

Although an application is being made for the registration of Garlon 3A for aquatic applications, neither Garlon 3A nor Garlon 4 are currently registered for aquatic applications, and any spraying of a standing body of water would be accidental. As noted above, the actual levels that may be expected will vary substantially with the application rate and depth of the water. For this risk assessment, the basic scenario examined by Kreutzweiser et al. (1995) will be used as a starting point: an application rate of 4.0 kg/ha (3.6 lbs/acre) over a 15 cm deep body of water which results in an initial concentration of 2.7 mg/L. This initial concentration is also close to that used in the study by Woodburn et al. (1993b).

The above scenario can be expressed as a rate: 11.25 mg· cm/(L·lbs/acre),

$$2.7 \text{ mg/L} \cdot 15 \text{ cm (water depth)} \div 3.6 \text{ lbs/acre}.$$

A standard exposure scenario involves a 10 kg child consuming 1 L of contaminated water. In terms of application rate and water depth, the intake rate or dose can be expressed as 1.125 mg·cm/(kg·lbs/acre),

$$1 \text{ L}/10 \text{ kg} \cdot 11.25 \text{ mg·cm/(L·lbs/acre)}.$$

For example, an application rate of 2 lbs/acre is typical of the use of Garlon 4 in rights-of-way management. Assuming that a body of water with an average depth of 0.1 m (10 cm) was accidentally oversprayed, the dose would be 0.25 mg/kg,

$$1.25 \text{ mg·cm/(kg·lbs/acre)} \cdot 2 \text{ lb/acre} \div 10 \text{ cm}.$$

For assessing the consequences of longer-term exposure, the dissipation rates of triclopyr must be considered. For this and similar exposure scenarios, the central estimate of dose will be taken as the geometric mean of the concentrations or doses between two time intervals:

$$Conc_{TWA} = (C_{t_1} \cdot C_{t_2})^{0.5}$$

This approach is taken because the geometric mean is the median daily dose (i.e., on half of the days doses or concentrations are above this level and on the other half they are below this level).

Using a time-weighted arithmetic average dose would tend to overemphasize the early exposure period, which is covered by the exposure assessment for time zero.

The concentration or dose at any time, t_i, can be calculated from the initial concentration or dose and the dissipation or elimination rate (k_e):

$$C_{t_i} = C_0 \cdot e^{-k_e t_i}$$

For example, as calculated above, the initial dose of triclopyr associated with an application rate of 2 lbs/acre of Garlon 4 over a body of water with an average depth of 0.1 m is 0.25 mg/kg. The field halftime for triclopyr BEE is estimated as 4-8 days (k_e = 0.09-0.17 days^{-1}). Subchronic toxicity studies in mammals are usually conducted over a 90-day period. Taking this as the duration of concern, the expected dose at 90 days would be 0.00000006-0.00008 mg/kg, with corresponding geometric means of 0.0001-0.004 mg/kg/day.

Several scenarios like the one above could be constructed by varying the application rate, mixing depth, and duration of exposure. Nonetheless, the exposure rates given provided above will be used in the risk characterization to describe the kinds of incidents that are of concern, based on the dose-response assessment for triclopyr.

3.2.3.4.2. Streams -- Like lake contamination, stream contamination will be a function of application rate and the physical characteristics of the stream (i.e., width, depth, and flow rate). Stream monitoring data are available for both triclopyr (Norris et al. 1987) and triclopyr BEE (Kreutzweiser et al. 1995, Smith and McCormack 1988, Thompson et al. 1991, 1995). Details of these studies are summarized in Appendix 4.

Peak concentrations in stream water, normalized for application rate, are very consistent among studies, ranging from approximately 0.03 to 0.1 mg/L per kg a.e./ha of application rate. The low end of this range is based on applications of triclopyr (0.1 mg/L at 3.4 kg/ha in Norris et al. 1987) and triclopyr BEE (0.056 mg/L at 1.9 kg/ha in Smith and McCormack 1988). The high end of the range is associated with the levels of 0.23-0.35 mg/L after and aerial application of 3.67 kg/ha of Garlon 4. [All of these application rates are expressed as kg a.e./ha.]

These peak rates are reasonably consistent with what might be expected from simple dilution. For example, an application rate of 1 kg/ha is equivalent to 1,000,000 mg/10,000 m^2 or 100 mg/m^2. Using a stream depth of 0.1-1 m, instantaneous mixing would result in initial maximum concentrations of 100-1,000 mg/m^3 or 0.1-1 mg/L [m^3 = 1,000 L]. Relatively modest water flows would rapidly lower stream levels to the 0.03-0.1 mg/L range noted above.

Further dilution and other degradative processes would be associated with rapid decreases in water levels. In the studies cited above, monitored concentrations dropped to levels that were below the limits of detection (approximately 0.001-0.005 mg/L) in a matter of hours.

For acute exposure, triclopyr levels in streams will be estimated as 0.03-0.1 mg/L, from the above monitoring data. Based on monitoring study by Norris et al. (1987), these estimates should encompass peak levels associated with rain events over the first couple of months after treatment.

The best study for assessing the effects of longer-term stream contamination is that of Norris et al. (1987). This study presents stream levels over a 21-day period following the aerial application of triclopyr at a rate of 3.4 kg a.e./ha. Based on a graphical summary of the monitoring data which includes peak levels associated with one rain event (Figure 2, p. 139, Norris et al. 1987), the time weighted average concentration over the first 19 days—the period during which detectable levels were found—is approximately 0.007 mg/L. Normalizing for application rate (3.4 kg a.e./ha or 3 lbs/acre), the level is 0.002 mg/L per lb a.e./acre. If extended over a 90-day period, the average value would approach the limit of detection, 0.001 mg/L per lb a.e./acre.

3.2.3.5. ***Oral Exposure from Contaminated Fish*** **--** There is no indication that triclopyr or triclopyr BEE will bioconcentrate in fish or other aquatic organisms that might be consumed by humans. In laboratory studies on blue gill sunfish exposed to triclopyr (^{14}C-labeled on the pyridine ring) at 2.5 mg/L for 96 hours, whole body residue were 2.33 mg/kg (BCF $\simeq$ 1 L/kg) and levels in edible flesh were 0.13 mg/kg (BCF=0.05 L/kg) (Lickly and Murphy 1987). In a field study, no detectable levels of triclopyr were found in fish after an initial application rate of 2.5 mg a.e./L as Garlon 3A. Modest levels of bioconcentration, however, were noted in crayfish and clams (BCF $\leq$4 L/kg) with rapid decreases in tissue levels as water levels decreased (Woodburn et al. 1993b).

Given the rapid decrease in triclopyr concentrations in water, as discussed above, and the low bioconcentration potential for this compound, oral exposure to triclopyr from contaminated fish should not substantially increase the hazards associated with the use of triclopyr. The range of dose estimates from the direct consumption of contaminated water, which can span a factor of 40 or more depending on specific exposure assumptions, is likely to outweigh contributions from the consumption of contaminated aquatic species.

3.2.3.6. ***Oral Exposure from Contaminated Vegetation*** **--** After ground or aerial applications, triclopyr will be deposited on vegetation. Although members of the general public are excluded from the area while treatments are being conducted, it is conceivable that contaminated vegetation could be consumed by individuals shortly after treatment. The most plausible scenario involves the consumption of contaminated berries.The most relevant publication for assessing exposure from such a scenario is that of Siltanen et al. (1981). These investigators monitored levels of triclopyr on cowberries and bilberries after backpack sprays of Garlon 3A at application rates of 0.25, 0.75, and 2.25 kg a.e./ha [0.22, 0.67, and 2 lbs/acre]. The residue data plotted over a 98-day post-application observation period are illustrated in Figure 3-1. In this figure, the residues are normalized (i.e., divided by) the application rate in kg a.e./ha.

Although there is substantial scatter in the data, there is no consistent deviation from the simple first order dissipation model. In Figure 3-1, the best estimate of the residue level is indicated by

the thick solid line. The thick dashed lines represent the 95% confidence interval and the thin outer lines represent the 95% prediction interval. These data fit a first order model (p=0.00032) with a dissipation rate of 0.018 $days^{-1}$, which corresponds to a halftime of approximately 38 days.

For this exposure assessment, the residues immediately after application will be estimated as approximately 1.6 mg/kg · kg a.i/ha, from Figure 3-1. This corresponds to about 1.8 mg/kg berry · lb a.i/acre. The upper 95% prediction limit of 5 mg/kg · kg a.i/ha or 5.6 mg/kg · lb a.i/acre will be used as a plausible worst case scenario.

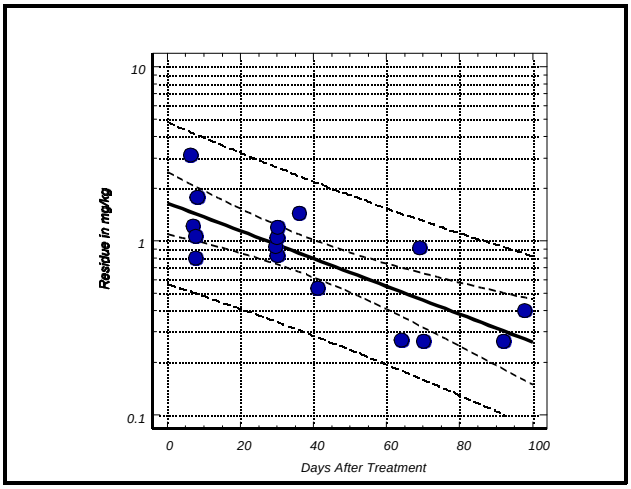


Figure 3-1: Residues of triclopyr on cowberries and bilberries normalized for application rate in kg/ha [data from Siltanen et al. 1981].

For this exposure assessment, it will be assumed that a 64 kg woman (U.S. EPA 1985) consumes 1 lb (0.454 kg) of contaminated berries. Based on these assumptions, the central estimate of the dose associated with an application rate of 1 lb a.i./acre is 0.013 mg/kg

$$1.8 \text{ mg/kg} \cdot 0.454 \text{ kg} \div 64 \text{ kg},$$

with an upper limit of 0.04 mg/kg

$$5.6 \text{ mg/kg} \cdot 0.454 \text{ kg} \div 64 \text{ kg}.$$

Longer-term exposure to contaminated vegetation will be based on the geometric mean of the residue levels between time zero and day 90 using the first order model. For the best estimate, the geometric mean of the residues at day 0 (1.8 mg/kg berry · lb a.i/acre) and day 90 (0.3 mg/kg berry · lb a.i/acre) is approximately 0.7 mg/kg berry · lb a.i/acre. The geometric mean of the upper limit of residues between day 0 (5.6 mg/kg berry · lb a.i/acre) and day 90 (≃1.0 mg/kg berry · lb a.i/acre) is 2.3 mg/kg berry · lb a.i/acre.

Thus, for longer-term exposure, the central estimate of the dose is 0.004 mg/kg,

$$0.7 \text{ mg/kg} \cdot 0.454 \text{ kg} \div 64 \text{ kg},$$

with an upper limit of 0.016 mg/kg

$$2.3 \text{ mg/kg} \cdot 0.454 \text{ kg} \div 64 \text{ kg}.$$

Although this approach is somewhat conservative, it seems justified given the scatter in the data from Siltanen et al. (1981), the wide range of halftimes that have been reported for various forms of triclopyr on different types of vegetation, and the inconsistent relationship in dissipation rates between triclopyr and triclopyr BEE.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The current RfD for triclopyr is 0.005 mg/kg/day. The RfD is based on a study in which the triclopyr triethylamine salt was administered in the diet to dogs at levels that resulted in daily doses of 0.5, 2.5, or 5.0 mg/kg/day over a 1-year period. The two higher doses were classified as adverse effect levels based on dose-related increases in serum urea nitrogen and creatinine, indicative of decreased glomerular filtration. The lowest dose was classified as a NOAEL. This dose was divided by 100, a factor of 10 to account for uncertainties in species-to-species extrapolation and another factor of 10 to encompass sensitive individuals in the population.

The lack of consistent species differences in sensitivity, discussed below, suggests that U.S. EPA's use of an uncertainty factor of 10 for species-to-species extrapolation may be conservative. This is not to suggest that the data are sufficient to propose an uncertainty factor of unity. The limitations on the quantitative analysis of the acute toxicity data, the nature of the species comparison of pharmacokinetics, the qualitative nature of the comparison of the chronic toxicity data, and the lack of any chronic toxicity data on humans suggest that the uncertainties are sufficiently high to justify the use of some factor for interspecies extrapolation.

Dog studies conducted over a period of approximately 1-year are often classified as chronic rather than subchronic. Consequently, the uncertainty factor of 10 for extrapolating from subchronic to chronic (i.e., life span) exposures is omitted by the U.S. EPA in the derivation of the RfD. While this general approach is often justified, the dose-duration relationships for triclopyr suggest that this approach may be under-protective for chronic exposures.

3.3.2. Existing Guidelines.

The U.S. EPA has not derived an agency-wide RfD for triclopyr, and the compound is not scheduled for review. The U.S. EPA's Office of Prevention, Pesticides, and Toxic Substances, which is responsible for the registration of pesticides, has derived a provisional RfD for triclopyr of 0.005 mg/kg/day (U.S. EPA 1995b). As indicated in section 3.1.11., the U.S. EPA (U.S. EPA 1995b) has concluded that the triethylamine acid and butoxyethyl ester of triclopyr are toxicologically equivalent; thus, this RfD is applicable to both forms of triclopyr.

The RfD is based on the study by Quast et al. (1988), summarized in Appendix 2, in which the triclopyr triethylamine salt was administered in the diet to dogs at levels that resulted in daily doses of 0.5, 2.5, or 5.0 mg/kg/day over a 1-year period. The two higher doses were classified as adverse effect levels based on dose-related increases in serum urea nitrogen and creatinine,

indicative of decreased glomerular filtration. The lowest dose was classified as a NOAEL. As summarized in Appendix 2, there is a dose-dependent increase in BUN in male rats at all dose levels: 38% at 0.05 mg/kg/day, 57% at 2.5 mg/kg/day, and 208% at 5 mg/kg/day. The low dose is regarded as a NOAEL because the increase, relative to pre-exposure levels was not statistically significant. This dose was divided by 100, a factor of 10 to account for uncertainties in species-to-species extrapolation and another factor of 10 to encompass sensitive individuals in the population. Thus, the resulting RfD is 0.005 mg/kg/day.

The previous Forest Service dose-response assessments of triclopyr (USDA 1989a,b,c) are based on U.S. EPA's 1985 assessment of triclopyr, which considers the dose of 2.5 mg/kg/day from the study by Quast et al. (1977) a NOAEL, based on decreased PSP urinary excretion. The differences between the two Quast studies and the different endpoints measured is discussed in section 3.1.4. Using the same uncertainty factor of 100, the provisional RfD was set at 0.025 mg/kg/day (U.S. EPA 1985), which is 5 times greater than the current RfD. No other guidelines regarding exposure to triclopyr were located in the literature.

3.3.3. Dose-Severity/Time Relationships. As summarized in section 3.2, some exposure scenarios for the general public and workers yield estimates that are above the current RfD of 0.005 mg/kg/day. These exposure estimates are based on an application rate of 1 lb a.e./acre. The Forest Service uses application rates up to 3 lbs a.i./acre. Because the relationship of exposure to application rate is assumed to be linear, exposures to workers and the general public may be even further above the RfD than suggested by the exposure scenarios in Section 3.2. Consequently, some attempt must be made to characterize the consequences of exposures above the RfD.

As noted above, the RfD is considered to be a daily dose at which no adverse effects are anticipated in a population over a lifetime exposure. As discussed in SERA (1995a), the RfD is intended to be a conservative estimate and does not explicitly incorporate information on dose-duration or dose-severity relationships. In other words, doses below the RfD, regardless of the duration of exposure, are of no substantial concern as long as the RfD is based on a sound set of data. The assumption that exposures above the RfD will result in adverse human health effects is not necessarily correct, particularly when the duration of exposure is substantially less than lifetime.

All exposure scenarios considered in this risk assessment are less than lifetime. As discussed in section 3.2, triclopyr rapidly dissipates or degrades, and high levels of exposure generally occur only over short periods. Workers may be exposed repeatedly during an application program in a particular season and may use triclopyr formulations over the course of a career but exposures at occupational levels will be intermittent and less than lifetime.
Based on the data summarized in Appendix 1 (acute toxicity) and Appendix 2 (subchronic and chronic toxicity), the dose-severity relationships for triclopyr are illustrated in Figure 3-2. In this figure, dose is plotted against the severity of the effect using the standard severity classification (NOELs/NOAELs/AELs/FELs). In addition, data regarding NOELs and NOAELs are combined.

This is done for two related reasons. First, the primary concern for this risk assessment is the delineation between regions of adverse and non-adverse effects. Thus, the distinction between a NOEL and NOAEL is not critical. Second, an examination of the studies summarized in Appendices 1 and 2 suggests that many reported NOELs may be artifacts of the level of detail at which the animals are examined. For example, just because there are not adverse effects based on gross examination of organs does not mean that effects might not be seen if all organs were examined microscopically.

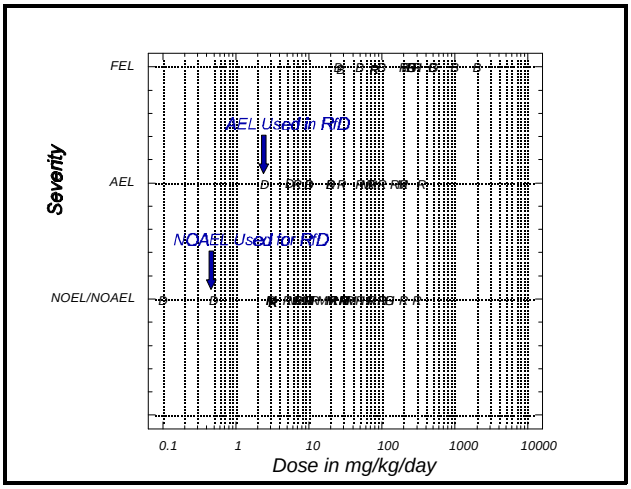


Figure 3-2: Dose/severity relationships for triclopyr for dogs (D), rats (R), rabbits (B), and mice (M). [see text for details and figures 3-3 and 3-4 for time axis]

The studies summarized in Figure 3-2 span exposure periods ranging from 1 day to more than 2 years. The temporal axis for these data are included in Figure 3-3.

As illustrated in all of these figures, there is substantial scatter in the experimental data. For the most part, the scatters seems to be attributable to differences in experimental design rather than to inconsistencies in the data. For example, all of the rabbit studies and many of the rat studies involve assays for teratogenic or reproductive effects. These studies are not directly comparable to the toxicity studies in dogs and large domestic mammals that assayed effects on kidney function.

The most important comparisons in these figures and the corresponding data in Appendices 1 and 2 involve kidney toxicity, the most sensitive effect and the effect on which the RfD is based. While a visual examination of these figures might suggest that dogs are the most sensitive species, this may be an artifact of experimental design.In subchronic exposures, all of the kidney effects noted in rats are based on histopathological changes (NOAEL of 5 mg/kg/day and LOAEL of 20 mg/kg/day for 90 days [Landry et al. 1984]) or increased kidney weight [NOAEL of 7 mg/kg/day and LOAEL of 28 mg/kg over 90 days (Barna-lloyd et al. 1992)]. The effect and no effect levels based on changes in kidney weight in rats after chronic exposure are very similar to those for subchronic exposures [NOAEL of 12 mg/kg/day and LOAEL of 36 mg/kg over 2 years (Eisenbrandt et al. 1987)]. In the dog studies, described above, the increases in serum urea nitrogen and creatinine at 2.5 mg/kg/day occurred in the absence of pathological changes in the kidney. This result is fairly consistent with the rat studies, which, according to the available summaries, did not assay changes in kidney function. Consequently, there is no compelling evidence that dogs are substantially more sensitive than other species are to triclopyr. The lower NOAEL for the dog (0.5 mg/kg/day over approximately 1 year) may be attributable to the use of

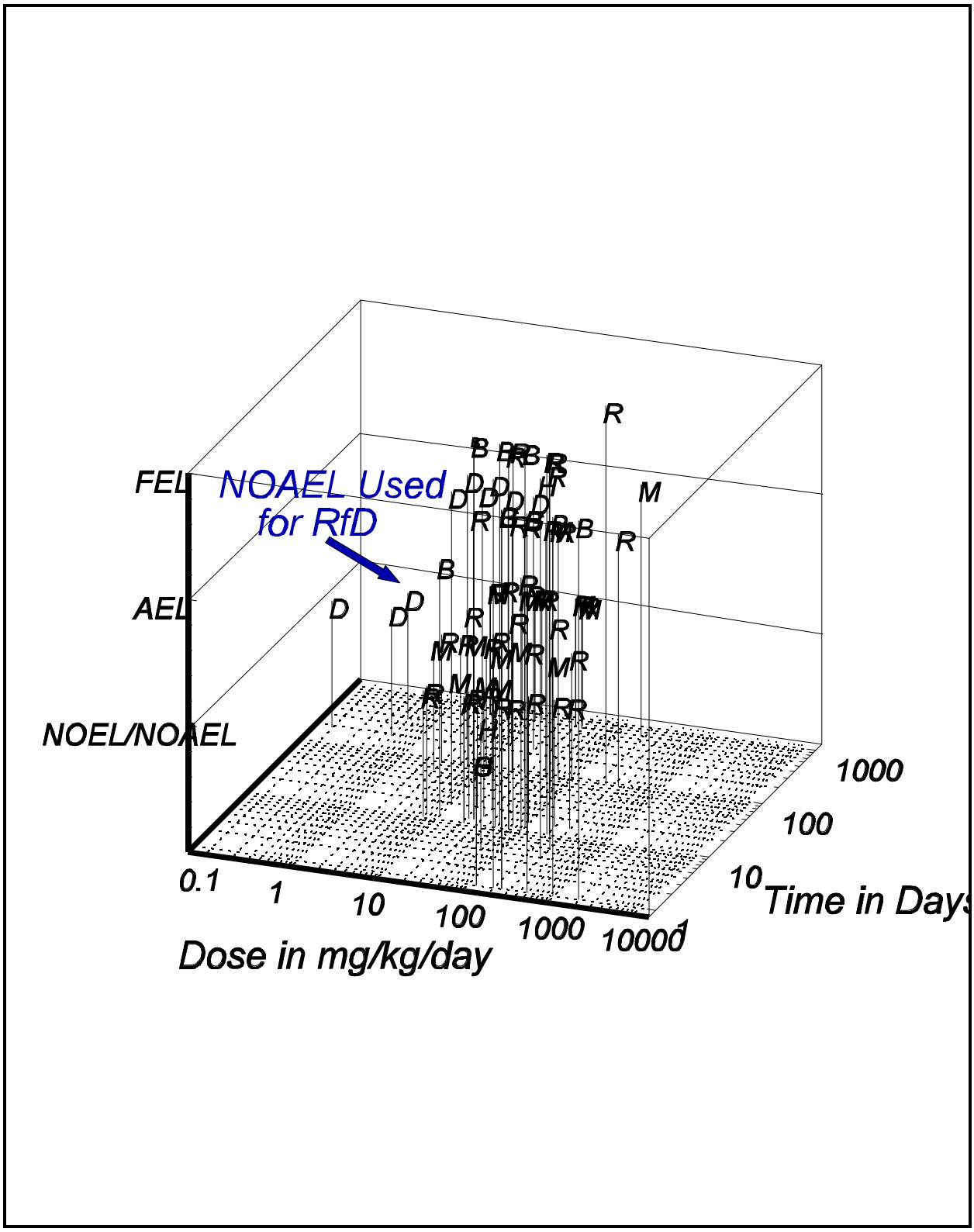


Figure 3-3: Dose/duration/severity relationships for triclopyr for dogs (D), rats (R), rabbits (B), and mice (M).

a more sensitive endpoint, a functional change, compared with an endpoint based on organ weight or pathological damage.

The issue of species sensitivity is also important in assessing the use of a 10-fold factor for species-to-species extrapolation, as used in the RfD for triclopyr. For many chemicals, differences in species sensitivity are apparent and generally indicate that small animals are less sensitive [i.e., have higher LD_{50} values] than large animals. This general pattern is the basis for the uncertainty factor of 10 used for animal-to-human extrapolation in the derivation of the RfD (Dourson and Stara 1986) and is often used to extrapolate across species [e.g., Davidson et al. 1986] based on the general allometric relationship:

$$LD_{50} = aW^{b}$$

where ***W*** is the body weight and ***a*** and ***b*** are model parameters. When small species are less sensitive than larger species, the slope parameter, ***b***, is negative.

As illustrated in Figure 3-4, triclopyr does not follow this pattern: there is no apparent relationship between body weight and toxicity measured as acute oral LD_{50} values. All of the LD_{50} values used in this figure are taken from Appendix 1. Where body weights are not specified in this appendix, they are taken from standard reference sources (e.g., U.S. EPA 1989a). The LD_{50} values for mice, rats, guinea pigs, and rabbits are based on standard tests in which the animal is given a single dose by gavage and observed for 14 days. The LD_{50} values for horses (Osweiler 1983) and cattle (Rowe et al. 1980) are not strictly comparable in that the LD_{50} values represent cumulative doses administered to the animals over 4-7 days, with observation periods of up to 17 days. Nonetheless, there is no statistically significant relationship between body weight and acute lethal potency either including or excluding these data points. While the span of body weights used in this analysis is relatively narrow if the data on horses and cattle are excluded, the results are consistent with the qualitative assessment of the subchronic and chronic studies, discussed above, suggesting that species differences in sensitivity are not remarkable.

The lack of consistent species differences in sensitivity suggests that U.S. EPA's use of an uncertainty factor of 10 for species-to-species extrapolation may be conservative. This is notto suggest that the data are sufficient to propose an uncertainty factor of unity. The limitations on the quantitative analysis of the acute toxicity data, the nature of the species comparison of pharmacokinetics, the qualitative nature of the comparison of the chronic toxicity data, and the lack of any chronic toxicity data on humans suggest that the uncertainties are sufficiently high to justify the use of some factor for interspecies extrapolation. Although the data are not adequate for the quantitative derivation of an alternative uncertainty factor, a factor of 3, the approximate geometric mid-point between 1 (no uncertainty factor) and 10 (the standard uncertainty factor) has been proposed in the derivation of some RfDs. While somewhat arbitrary, it is no more so than the standard use of uncertainty factors of 10.

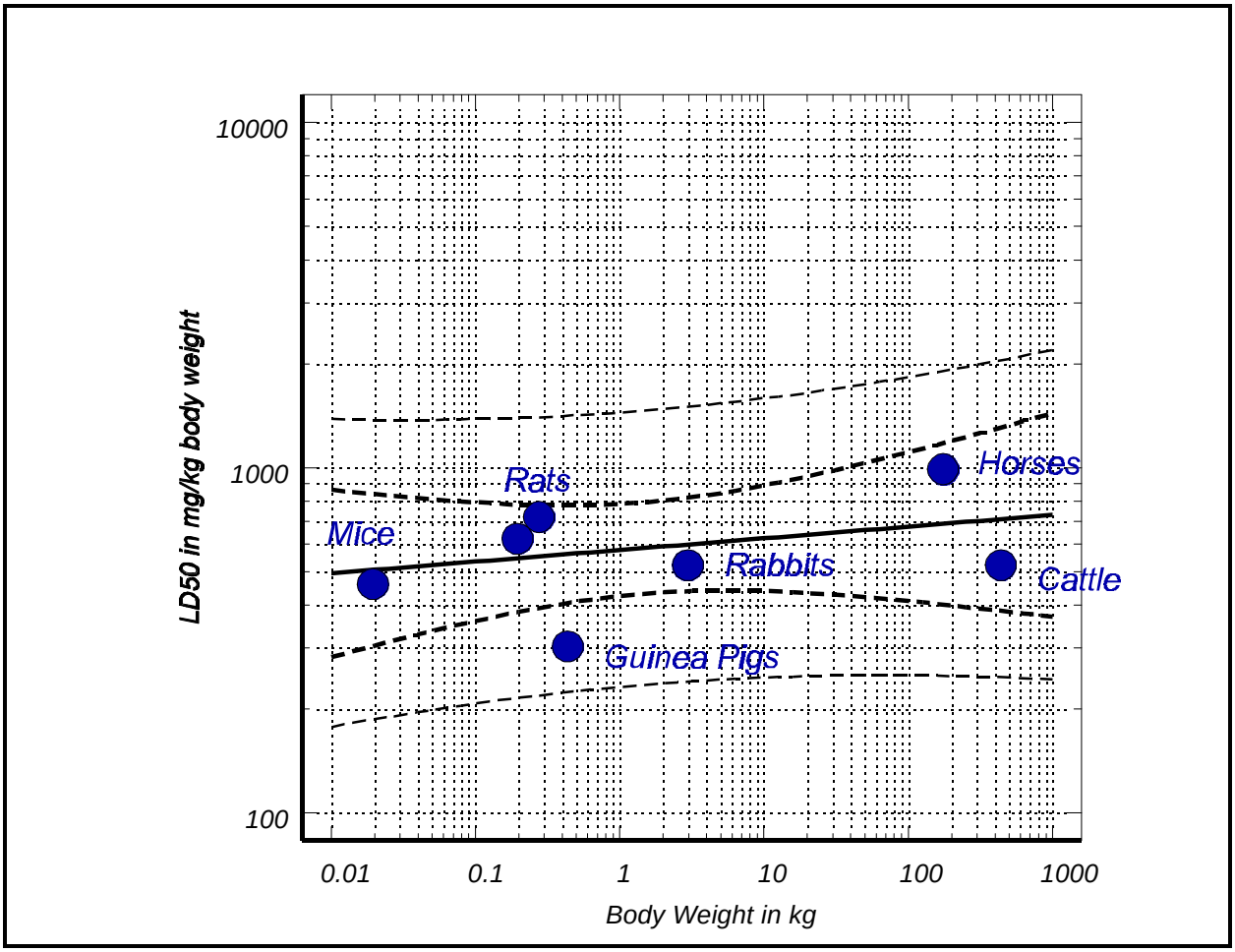


Figure 3-4. Variability of interspecies sensitivity to triclopyr (see appendix 1 for data and text for discussion).

The temporal relationship seen with the development of kidney toxicity is another factor that may modify or at least influence the qualitative interpretation of the dose-response assessment. As discussed in section 3.1.4. and discussed in Appendix 2, the dose of 2.5 mg/kg/day given to dogs is regarded as a NOAEL because it was associated with decreased PSP (phenolsulfonphthalein) urinary excretion with no effect on BUN (Quast et al. 1977). In the follow up study by Quast et al. (1988), this dose was associated with increases in serum urea nitrogen and creatinine, both of which may be associated with impaired kidney function and are regarded as AELs. A difference between these two studies is that the earlier study was conducted over a period of 183 days, or approximately 6 months, and the later study was conducted over a period of 1 year.

The information on the pharmacokinetics of triclopyr does not suggest that increasing periods of duration will be associated with increasing body burdens, which can be a key factor in dose/duration/severity relationships. For compounds such as triclopyr, which are rapidly eliminated, the time to approximate steady-state is relatively brief. For any compound, the

number of doses (*n*) required to reach a certain fraction (*f*) of the eventual plateau when administered at a certain interval (*t*), can be calculated as:

$$n = \frac{\ln(1-f)}{-k_e t}$$

(e.g., Goldstein et al. 1974, p. 321). Taking the reported halftime of 96 hours (k_e = 0.007 $hours_{-1}$ or 0.17 $days^{-1}$) for dogs (Nolan 1985) and treating the dietary doses as instantaneous, the number of days required to reach 99% of the plateau body burden would be approximately 65 days. Thus, the differences in body burden between a 6-month and 12-month study will be minimal. Nonetheless, damage to the kidney may be cumulative and progressive. This could explain why increased serum urea nitrogen was observed in the 1-year study (Quast et al. 1988) but not in the 6-month study (Quast et al. 1977).

The dose/duration/severity relationships for the effect of triclopyr on kidney function are further illustrated in Figure 3-5. The two lines drawn in this figure are log-log regressions on NOAELs (circles and solid line) and minimum observed AELs (squares and dashed line). The NOAELs are taken from the studies by Osweiler (1983): ponies, 60 mg/kg/day for 4 days; Quast et al. (1977): dogs, 2.5 mg/kg/day for 183 days; and Quast et al. (1988): dogs, 0.05 mg/kg/day for 1 year. The AELs, all of which are based on increases in BUN, are taken from the studies by Osweiler (1983): ponies, 300 mg/kg/day for 4 days; Rowe et al. (1980): cattle, 75 mg/kg/day for 7 days; Quast et al. (1976): dogs, 5 mg/kg/day for 228 days; and Quast et al. (1988): dogs, 2.5 mg/kg/day for 1 year. Without constraints, the slopes of the two lines are quite similar, -0.98 for NOAELs and -0.95 for AELs. Although the relationship for the NOAELs is not statistically significant ($p=0.12$), this is a function of few data points (n=3, 1 d.f.). For the AEL line (n=4, 2 d.f.), the relationship is statistically significant ($p=0.01$). When the lines are constrained to be parallel (n=7, d.f.=3), the relationship is statistically significant ($p<0.05$). These lines, extrapolated to a 1-day exposure, are reasonable approximations of non-lethal (NOAEL line) and lethal (AEL line) single doses, as discussed in Appendix 1.

The qualitative significance of this pattern is related to the interpretation of the protectiveness of the RfD over a life span. Dog studies conducted over a period of approximately 1 year are often classified as chronic rather than subchronic. Consequently, the uncertainty factor of 10 for extrapolating from subchronic to chronic (i.e., life span) exposures is omitted, as in the case of both of the RfDs for triclopyr derived by the U.S. EPA. While this general approach is often justified, it may be under-protective for triclopyr, based on the temporal patterns illustrated in Figure 3.5.

In the current risk assessment, many of the exposure scenarios will be for less than lifetime, such as the use of triclopyr by an applicator intermittently during a treatment season for several years. For such scenarios, it may be argued that an RfD is overly conservative because it is designed to protect an individual over a lifetime exposure. While this is the intent of the RfD for triclopyr, the dose-duration pattern illustrated in Figure 3-5 suggests that the RfD might better represent a level

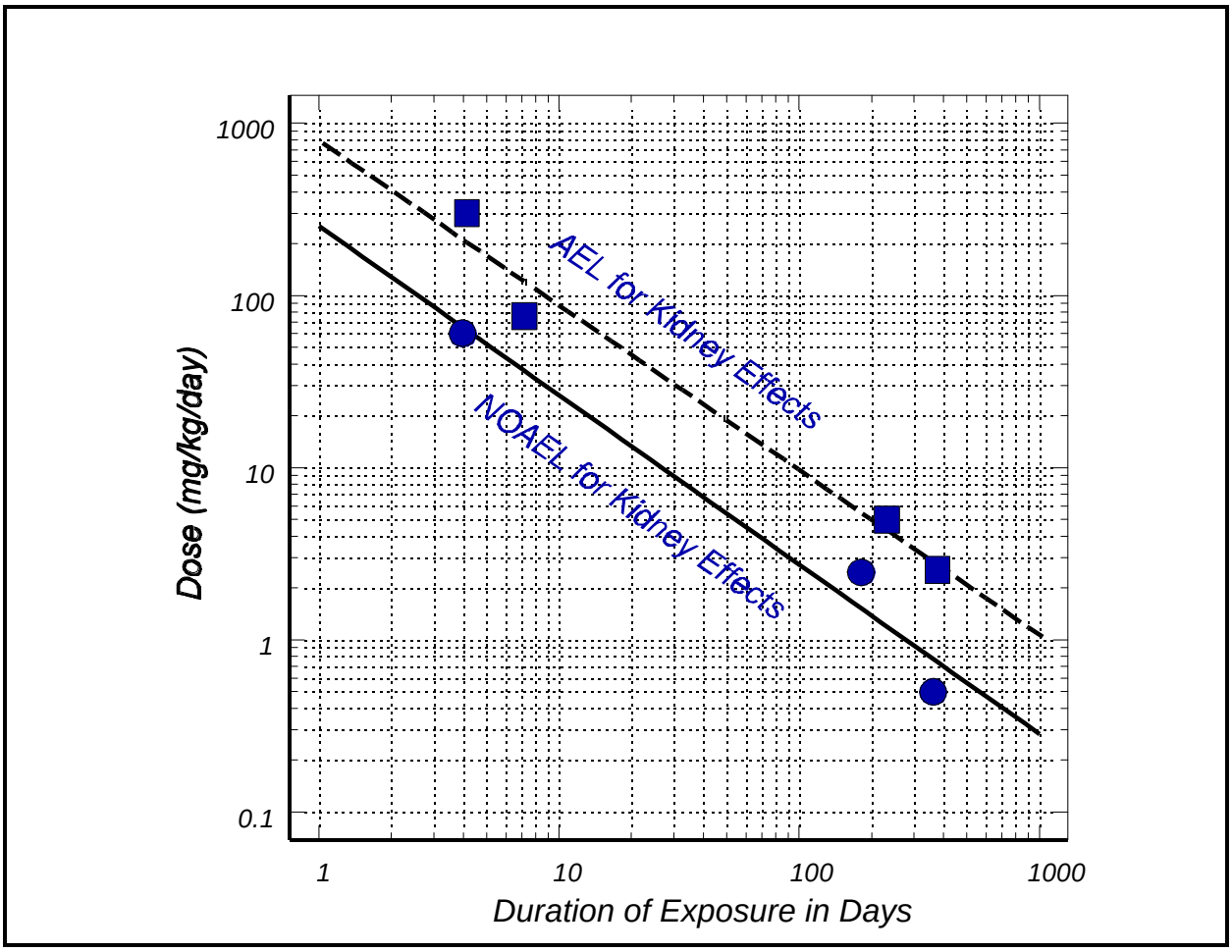


Figure 3-5. Dose/Duration Relationships for the effect of triclopyr on kidneys (see appendices 1 and 2 for data and text for discussion).

of protection over only a fraction, albeit a significant fraction, of the life span. Consequently, the RfD will be applied to workers as well as subchronic exposures to the general public without modification but with qualitative reservation.

Based on the considerations addressed above, the current RfD of 0.005 mg/kg/day may be accepted for the assessment of subchronic exposure scenarios with the qualification that excursions up to 0.015 mg/kg/day could be considered acceptable given the information on species sensitivity discussed above (i.e., using an uncertainty factor of approximately 3 rather than 10 for species extrapolation). Doses 5-fold higher than this range (0.025-0.075 mg/kg/day) would be of concern in terms of potential kidney damage because of the 5-fold spacing between the dog NOAEL and AEL in the study by Quast et al. (1988).

The temporal relationships illustrated in Figure 3-5 as well as the acute toxicity data in Appendix 1 may be used for assessing the consequences of very short-term or single exposures to

triclopyr. For several species, single doses in the range of 100 mg/kg/day have not been associated with mortality (126 mg/kg in rabbits [Olson 1967]; 200 mg/kg in rats [Henck et al. 1980]; 126 and 252 mg/kg in rats [Olson 1967]). The best study, in terms of observations for relevant endpoints, is Osweiler (1983). As noted above, four daily doses of 60 mg/kg did not cause any overt signs of toxicity in adult shetland ponies. In addition, this dose was not associated with changes in kidney function (BUN) or kidney pathology. Higher daily doses (75 mg/kg) over a somewhat longer period of exposure (7 days) were associated with gastrointestinal hypomotility and loss of appetite, mild to moderate tubular nephrosis, and increased BUN in cattle (Rowe et al. 1980). These species are not commonly used for human health risk assessments; however, the studies by Osweiler (1983) and Rowe et al. (1980) are more sensitive than the more standard bioassays in experimental mammals.

Taking an approach analogous to that for the RfD, 60 mg/kg may be taken as a 1-day NOAEL. This is somewhat conservative in that the animal NOAEL is from a 4-day exposure period. Dividing by 100, as is done with the U.S. EPA RfD, yields the adjusted value of 0.6 mg/kg for a reference 1-day exposure that should not be associated with adverse effects. As with the RfD, a 3-fold higher value, 1.8 mg/kg, could be proposed based on a less conservative but still protective species extrapolation. The AEL of 75 mg/kg, based on the data in cattle, yields a corresponding range of 0.75-2.25 mg/kg. This range of doses would not be associated with acute signs of toxicity but would be regarded as undesirable because adverse effects on the kidney might occur. The minimum dose associated with mortality in experimental mammals is 252 mg/kg in rabbits (Olson 1967). After applying an uncertainty factor of 100, the estimated dose associated with concern for acute lethal effects in humans is 2.5 mg/kg, with an upper range of 7.5 mg/kg.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. The quantitative characterization of risk is expressed as hazard quotients (HQs), the ratio of estimated exposure to some measure of acceptable exposure. The HQs in this section are based on the RfD of 0.005 mg/kg/day proposed by the U.S. EPA Office of Pesticides with an upper range of 0.015 mg/kg/day based on the apparent lack of species variability when doses are expressed in units of mg/kg.

For almost all groups of workers, the HQs reach or slightly exceed unity at an application rate of 1 lb/acre. At an application rate of 0.5 lbs a.i./acre, none of the central estimates would exceed levels of concern. At the maximum application rate of 3 lbs/acre, the central estimates of the HQs would substantially exceed unity (6 for Garlon 4 and 3 for Garlon 3A). No exposures approach levels that are likely to produce frank signs of toxicity. Nonetheless, there is a reasonable concern that workers applying the compound over a prolonged period of time in the course of a single season and/or over several seasons could be at risk of impaired kidney function.

For the general public, the potential for adverse effects from contaminated water is of relatively little concern. Similarly, the assessment for the consumption of contaminated vegetation leads to relatively little concern for acute exposures. Over a 90-day period following application, the

upper range of plausible doses moderately exceeds the RfD at an application rate of 1 lb a.i./acre. Application rates greater than 1 lb a.i./acre would result in estimated daily intakes from contaminated vegetation that are comparable to exposure levels that may affects kidney function.

3.4.2. Workers. A quantitative summary of the risk characterization for each of the job categories covered in this risk assessment is presented in Table 3-5. This table summarizes the central estimates, as well as the upper and lower ranges of worker exposure for an application rate of 1 lb a.i./acre (see section 3.2). The HQs are based on the RfD of 0.005 mg/kg/day proposed by the U.S. EPA Office of Pesticides (U.S. EPA 1995b) with an upper range of 0.015 mg/kg/day based on the apparent lack of species variability when doses are expressed in units of mg/kg (see Figure 3-4). All of the HQs are associated with application rates of 1 lb a.i./acre and would increase or decrease linearly for different application rates.

Application rates of 0.5-3 lbs/acre represent typical use by the Forest Service. At the lower range of exposure estimates, no worker groups would receive doses that approach levels of concern using either Garlon 3A or Garlon 4.

Central estimates of exposure for almost all groups of workers reach or slightly exceed HQs of unity at an application rate of 1 lb/acre. At an application rate of 0.5 lbs a.i./acre, none of the central estimates would exceed levels of concern (i.e., the HQ would be below unity). At the maximum application rate of 3 lbs/acre, the central estimates of the HQs would be substantially greater than unity (6 for Garlon 4 and 3 for Garlon 3A).

The health consequences of these HQs are likely to vary with the duration of use (see Figure 3-5). Workers who apply triclopyr only occasionally probably would not have any significant adverse effects. Workers applying the compound over a prolonged period of time in the course of a single season and/or over several seasons could be at risk of impaired kidney function.

The potential for these effects is particularly important because the RfD is based on a 1-year dog study. As noted in section 3.3.3, the dose-duration relationship for triclopyr appears to be relatively strong. Taking 12 years as the typical life span for a dog (U.S. EPA 1986), a 1-year study covers approximately 8% of the life span. A worker could be involved in the application of triclopyr over a 20-year career, approximately 30% of the human life span of 70 years. Although daily exposure probably would not occur over a 20-year career, it is not clear whether an RfD based on 8% of the life span of a test animal would be protective, given the marked dose-duration relationship for triclopyr. This concern applies equally to the interpretation of HQs in the risk characterization for the general public.

At the upper limit of exposure, the HQs for all worker groups will be substantially greater than unity. Again, the health consequences probably would not depend greatly on the duration of use. For workers using this compound over a prolonged period, some impairment of kidney function would seem plausible.

Table 3-5. Summary risk characterization for occupational exposure to triclopyr from Garlon 3A and Garlon 4 at application rate of 1 lb a.e./acre.

Treatment Method	Type of Estimate	Garlon 4		Garlon 3A	
		Daily Dose[a]	HQ[b]	Daily Dose[a]	HQ[b]
Boom spraying	Central	0.01	1-2	0.004	0.3-1
	Lower	0.0004	0.03-0.08	0.0001	0.007-0.02
	Upper	0.3	20-60	0.1	7-20
Backpack and cut surface	Central	0.006	0.4-1.0	0.002	0.1-0.4
	Lower	0.00009	0.006-0.02	0.00003	0.002-0.006
	Upper	0.3	20-60	0.1	7-20
Aerial applications (pilots and mixer/loaders)	Central	0.01	1-2	0.005	0.3-1
	Lower	0.001	0.07-0.2	0.0003	0.02-0.06
	Upper	0.2	13-40	0.08	5-16

[a]Expressed in mg/kg/day. [See Tables 3-2 and 3-3 for details of exposure estimates for Garlon 4 and Garlon 3A, respectively.]

[b] Based on RfD of 0.005 mg/kg with an upper range of 0.015 mg/kg, using less conservative assumptions in species-to-species extrapolation. Daily doses of 0.025-0.075 mg/kg/day could be associated with impaired kidney function but probably not frank signs of toxicity. Daily doses >2.5 mg/kg could be associated with frank signs of toxicity.

No exposures approach levels that are likely to produce frank signs of toxicity or death (i.e., 2.5-7.5 mg/kg). This, in a sense, is consistent with experience. Triclopyr has been used extensively without reports of acute toxic effects in workers, and, based on the above analysis, such effects would not be expected. This human experience, however, does not mitigate concern for covert kidney impairment. No epidemiology studies in workers or other individuals chronically exposed to triclopyr have been conducted that would permit the assessment of potential adverse effects on the kidney.

The accidental scenarios for workers are summarized in Table 3-6. Both of these scenarios model accidental dermal exposures over relatively brief periods. For the immersion of hands, the range of HQs is based only on the range of the estimated acute NOAEL for humans. As discussed in section 3.3, this range is based on the use of an uncertainty factor from 3 to 10, with the lower limit justified by the apparent lack of any systematic relationship of sensitivity among species. For accidental spills on the leg, the variability in the HQs also encompasses the range of the estimated

dermal absorption rates for triclopyr BEE and triclopyr acid. Neither of the exposure scenarios result in levels of exposure that are likely to be associated with any detectable adverse effect.

Table 3-6. Quantitative summary of risks for workers after accidental or incidental exposures[a]

Activity	Scenario	Dose (mg/kg/day)	HQ[b]
	Garlon 3A		
Immersion of hands	1 minute	0.0014	0.0007-0.0023
Accidental spill on lower legs	effective washing after 1 hour.	0.02-0.04	0.01-0.06
	Garlon 4		
Immersion of hands	1 minute	0.86	0.5-1
Accidental spill on lower legs	effective washing after 1 hour.	0.08-0.1	0.05-0.2

[a] See sections 3.2.2.2 and 3.2.2.3

[b] Based on an estimated human NOAEL for changes in kidney function of 0.6-1.8 mg/kg, with a corresponding LOAEL range of 0.75-2.5 mg/kg.

3.4.3. General Public. The quantitative hazard characterization for the general public is summarized in Table 3-7. Most of the exposure scenarios involve relatively short-term exposures. For these scenarios, the HQs are expressed as they were for the accidental exposures to workers. The central estimates of dose are divided by the estimated human NOAEL of 0.6-1.8 mg/kg. When ranges of dose are given, the lower range of the dose is divided by the upper range of the estimated NOAEL and the upper range of the dose is divided by the lower range of the estimated NOAEL. While this approach leads to highly variable ranges on the HQ, it most clearly illustrates uncertainties in the characterization of risk from the variability in both the exposure and dose-response assessments.

For dermal exposure scenarios, separate assessments are given for Garlon 3A and Garlon 4 because of the plausible differences in dermal absorption. None of the scenarios are of substantial concern for either formulation.

As with the risk characterization for workers, the estimates of absorbed dose from Garlon 4 formulations are associated with relatively little uncertainty, because they are based on human data. As noted in section 3.2, the risk characterizations for Garlon 3A could be regarded as

Table 3-7. Quantitative summary of risks for the general public[a]

Activity	Scenario	Formulation	Dose (mg/kg/day)	Hazard Quotient[b]
Direct spray	Naked child, entire body surface, wash after 1 hour.	Garlon 3A	0.05-0.09	0.03-0.2
		Garlon 4	0.15-0.2	0.08-0.3
	Young woman, feet and legs, wash after 1 hour.	Garlon 3A	0.004-0.008	0.002-0.013
		Garlon 4	0.01-0.02	0.006-0.03
Walking through treated area	Dermal Absorption, contaminated vegetation	Garlon 3A	0.0002-0.0004	0.0001-0.0002
		Garlon 4	0.0007-0.0009	0.0003-0.002
Contaminated water	10 kg child consuming 1 L immediately after spraying.	Both	0.25	0.1-0.4
			Highly variable. See text.	
	ambient water over 90 days		0.0001-0.004	0.007-0.8[c]
Consumption of contaminated vegetation	Berries shortly after spraying.		0.01-0.04	0.006-0.07
	Berries, time zero to day 90		0.004-0.02	0.26-4[c]

[a] Application rate of 1 lb/acre. [See section 3.2.3. for details regarding the exposure assessment.]

[b] Unless otherwise specified, the hazard quotients are based on estimated acute human NOAEL of for changes in kidney function of 0.6-1.8 mg/kg, with a corresponding LOAEL range of 0.75-2.5 mg/kg.

[c] Based on RfD of 0.005 mg/kg with an upper range of 0.015 mg/kg with levels of concern ranging from 0.025-0.075 mg/kg.

unconservative, based on the judgement that triclopyr acid will be less readily absorbed than triclopyr BEE by a factor of 3. This uncertainty, however, has almost no impact on the risk assessment because of the very low HQs associated with dermal exposure to either formulation.

For contaminated water, the exposure estimates, as discussed in section 3.2.3.4, will be highly variable, especially in standing bodies of water, depending on the application rate and depth of the water. While the halftime of triclopyr acid and triclopyr BEE are likely to differ (see Tables 2-1 and 2-2), these differences are not substantial, compared with assumptions concerning the depth of water or mixing volume. Table 3-7 presents one exposure scenario based on a contamination rate of 11.25 mg· cm/(L·lbs/acre) which corresponds to a dose rate of 1.25 mg·cm/(kg·lbs/acre) as derived in section 3.2.3.4.1. Many other exposure scenarios could be derived, based on different assumptions concerning the water depth and application rate. For example, assuming a water

depth and functional mixing depth of 1 m and an application rate of 4 lbs a.i./acre, the corresponding dose would be 0.05 mg/kg,

$$1.25 \text{ mg·cm/(kg·lbs/acre)} \cdot 4 \text{ lbs/acre} \div 100 \text{ cm}.$$

To reach a dose of 0.6 mg/kg, the lower range of the estimated human NOAEL for acute exposure, would require either extremely high application rates-far greater than those contemplated by the Forest Service—or implausibly shallow mixing depths. Thus, the potential for adverse effects from contaminated water is of relatively little concern.

Similarly, the assessment for the consumption of contaminated vegetation leads to relatively little concern for acute exposures. Over a 90-day period following application, the upper range of plausible doses moderately exceeds the RfD at an application rate of 1 lb a.i./acre. Lower application rates would not be of concern, but application rates greater than 1 lb a.i./acre would result in estimated of daily intakes that are comparable to exposure levels that may affect kidney function. This scenario is conservative in that the contaminated vegetation is consumed in large amounts (1 lb/day) on each day following the application. On the other hand, the endpoint on which the RfD is based is not extraordinarily sensitive (i.e., glomerular filtration can be reduced without increased in BUN or serum creatinine) and it is not certain that the RfD is adequately protective for longer-term exposure.

3.4.4. Sensitive Subgroups. There are no reports in the literature leading to the identification of sensitive subgroups. Furthermore, there is no indication that triclopyr causes sensitization or allergic responses. This lack of information, however, does not negate the possibility that individuals with multiple chemical sensitivity might be sensitive to these agents and many other chemicals.

Because triclopyr may impair glomerular filtration, individuals with pre-existing kidney diseases are likely to be at increased risk.

3.4.5. Connected Actions. There is very little information available on the interaction of triclopyr with other compounds. As summarized in section 3.1, the available data do not suggest a synergistic interaction between triclopyr and the other components in Garlon 3A or Garlon 4.

3.4.6. Cumulative Effects. As noted above and illustrated in Figure 3-5 (see section 3.3), this risk assessment has specifically considered the effect of repeated exposure to triclopyr. As discussed in section 3.3.3, there is an apparent and strong dose-duration relationship for triclopyr. It is uncertain that the basis of the current RfD, a NOAEL from a 1-year study in dogs, represents a reasonable approximation of a lifetime NOAEL. In this respect, exposures that approximate or exceed the current RfD are of concern, as discussed in the risk characterizations for workers and the general public.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. Standard toxicity bioassays have been conducted on several wildlife species, including mammals, birds, fish, and some terrestrial and aquatic invertebrates, as well as many species of aquatic and terrestrial plants. In addition, a number of field studies have been conducted on effects of triclopyr applications that are comparable or practically the same as those used by the Forest Service.

The toxicity studies on terrestrial animals are generally consistent with those on experimental mammals. The data on birds suggest that triclopyr and the commercial formulations of triclopyr have a low order of acute oral toxicity, with LC_{50} values ranging from 1,000 to more than 10,000 ppm. Birds appear to be no more sensitive than mammals to triclopyr. In addition to the laboratory bioassays, there are several field studies assessing the effects of triclopyr on birds and mammals. At application rates that are equal to or greater than those contemplated by the Forest Service, these studies suggest that effects on animal populations will be secondary to changes in vegetation and food supply and that these changes will either have no effect or will be beneficial to birds as well as mammals.

Triclopyr and other pyridinecarboxylic acid herbicides such as picloram mimic indole auxin plant growth hormones and cause uncontrolled growth in plants. These herbicides behave similarly to the chlorophenoxy acid herbicides such as 2,4-D and 2,4,5-T. At sufficiently high levels of exposure, the abnormal growth is so severe that vital functions cannot be maintained and the plant dies.

The toxicity of triclopyr to fish and aquatic invertebrates is relatively well characterized. Some aquatic macrophytes may be more sensitive than aquatic animals to triclopyr, but the available data, while sparse, do not suggest that algae are particularly sensitive to triclopyr. There is a major difference in the potential hazards posed by Garlon 3A and Garlon 4 to aquatic species. The difference can be attributed almost completely to differences in the inherent toxic potency of triclopyr acid and triclopyr BEE as well as an apparent antagonism of the toxicity of triclopyr by components of Garlon 3A.

4.1.2. Toxicity to Terrestrial Animals. The toxicity of triclopyr has been tested in several mammalian species (Appendices 1 and 2) and birds (Appendix 5). Like the acute bioassays in experimental mammals, the data on birds suggest that triclopyr and the commercial formulations of triclopyr have a low order of acute oral toxicity, with LC_{50} values ranging from 1,000 to more than 10,000 ppm. Birds appear to be no more sensitive than mammals to triclopyr. For both bobwhite quail and Japanese quail, the 8-day dietary LC_{50} is approximately 3,000 ppm (mg/kg diet). Assuming that quail consume food at a rate equal to approximately 10% of their body weight (USDA 1993), this level corresponds to daily doses of approximately 300 mg/kg body weight, which is similar to lethal daily doses over similar durations of exposure in cattle

(Rowe et al. 1980) and horses (Osweiler 1983). Data regarding the toxicity of triclopyr to terrestrial invertebrates were not located in the literature.

In addition to the laboratory bioassays, there are several field studies that have assessed the effects of triclopyr on birds and mammals (Appendix 4). At application rates equal to or greater than those contemplated by the Forest Service, these studies suggest that effects on animal populations will be secondary to changes in vegetation and food supply and that these changes will either have no effect (Schulz et al. 1992a,b) or will be beneficial (i.e., result in a population increases) to birds (Boren et al. 1993, Engle et al. 1991) and mammals (McMurry et al. 1993a, McMurry et al. 1994).

The only reported effect that might suggest a toxicological impact comes from the publication by Lochmiller et al. (1995). This is one of a series of studies conducted by the U.S. Fish and Wildlife Service and Oklahoma State University (Boggs et al. 1991a,b, Boren et al. 1993, McMurry et al. 1993a,b, Schulz et al. 1992a,b, Stritzke et al. 1991) that examines the effects of the aerial application of triclopyr at 2.2 kg a.i./ha. The herbicide was applied in 1983 to various sites in Cross Timbers Experimental Range (CTER) near Stillwater, Oklahoma, which is a 648-hectare area composed of blackjack oak, post oak, red cedar, savannas, and prairies. Prescribed burns were made in 1985, 1986, and 1987 in some but not all areas. Lochmiller et al. (1995) examined the effects of these treatments on cottontail rabbits. The endpoints examined included changes in body mass and dimensions, kidney fat, as well as the relative weights of the adrenals, liver, kidneys, spleen, and thymus. No effects on the kidney were noted. Compared with rabbits caught in untreated areas not subject to burns, 33% of rabbits caught in the tryclopyr only treated areas had a statistically significant increase in relative thymus weight (33%). In tryclopyr treated areas where prescribed burns were conducted, the effect was observed in 27% of the rabbits caught. When compared with control areas subject to burns, increases in thymus weight were noted (approximately 10-17%) but were not statistically significant.

The thymus has an important role in normal immune function and has a considerable capacity to regenerate (Schuurman et al. 1991). An increase in the size of the thymus could be indicative of repair after injury. Effects on the thymus, however, have not been noted in chronic studies of triclopyr in experimental mammals (Appendix 4). In addition, the lack of a statistically significant difference between rabbits from triclopyr treated areas and rabbits from areas treated only with prescribed burns suggests that the apparent effect may be an anomaly. For these reasons, the observations made by Lochmiller et al. (1995), albeit noteworthy, are not reason enough to justify a quantitative assessment or to qualitatively identify the thymus as an organ that is particularly sensitive to triclopyr.

4.1.2. Toxicity to Terrestrial Plants. Triclopyr and other pyridinecarboxylic acid herbicides such as picloram mimic indole auxin plant growth hormones and cause uncontrolled growth in plants. These herbicides behave similarly to the chlorophenoxy acid herbicides such as 2,4-D and 2,4,5-T. At sufficiently high levels of exposure, the abnormal growth is so severe that vital functions cannot be maintained and the plant dies (USDA 1989a,b,c).

Direct foliar contact, either from drift or unintended application, is the most obvious route of exposure causing effects on nontarget vegetation. As with dermal absorption in mammals, there are significant differences between the uptake of triclopyr acid and triclopyr BEE, with the ester penetrating much more rapidly than the salt. This difference has been demonstrated quantitatively in chickweed, wheat, and barley (Lewer and Owen 1990), and is likely to be true for most other plant species. Variations in species sensitivity to triclopyr BBE appear to be related directly to the rate of metabolic ester hydrolysis by the plant (Lewer and Owen 1990). As with 2,4-D and 2,4,5-T, arid conditions do not affect the rate of triclopyr absorption but do inhibit translocation and thus efficacy (Seiler et al. 1993).

In addition to direct contact, the absorption of triclopyr from contaminated soil is a potential hazard (Morash and Freedman 1989). As discussed in the exposure assessment (section 4.2) and the dose-response assessment (section 4.3), triclopyr acid and triclopyr BEE have different properties in terms of soil persistence and apparent absorption from soil into the roots of plants. Consequently, separate risk characterizations are required for Garlon 3A and Garlon 4 for this route of exposure.

4.1.3. Toxicity to Aquatic Organisms. The toxicity of triclopyr to fish and aquatic invertebrates is relatively well characterized. The acute lethal potency of triclopyr and triclopyr formulations is well defined. The available LC_{50} values can be used directly to assess the potential for acute lethal effects on aquatic fish and invertebrates. Some aquatic macrophytes may be more sensitive than aquatic animals to triclopyr; however, the available data, albeit sparse, do not suggest that algae are particularly sensitive to triclopyr.

There is a major difference in the potential hazards posed by Garlon 3A and Garlon 4 to aquatic species. As discussed in the dose-response assessment (section 4.3), this difference is attributable almost completely to differences in inherent toxic potency between triclopyr acid and triclopyr BEE as well as an apparent antagonism of the toxicity of triclopyr by components in Garlon 3A.

4.2. EXPOSURE ASSESSMENT

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

Although there are a variety of field studies regarding the effects of triclopyr on free ranging terrestrial organisms and several monitoring studies regarding the levels of triclopyr in various media after applications comparable or identical to those contemplated by the Forest Service, there are no monitoring regarding levels of triclopyr in wildlife. Based on the pharmacokinetic behavior of triclopyr in experimental mammals (see section 3.1) and the lack of or minimal bioconcentration in aquatic species (see section 3.2.3.5), bioaccumulation in wildlife is expected to be minimal.

As discussed in the dose-response assessment (section 4.3), estimates of no effect levels or lethal doses are most often expressed in units of mg/kg. For dermal exposure, the units of measure usually are expressed in milligrams of agent per centimeter of surface area of the organism, abbreviated as mg/cm^2. In estimating dose, however, a distinction is made between exposure dose and absorbed dose. *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. *Absorbed dose* is the proportion of the exposure dose that is actually absorbed by the animal. Inhalation exposure is calculated, in a similar way, as the proportion of the compound retained in the animal after exposure. Sometimes, it is appropriate to combine oral, dermal, or inhalation exposure in order to estimate the total impact on the organism, as discussed further in the risk characterization (section 4.4).

For the exposure assessments discussed below, general allometric relationships are used to model exposure. In the biological sciences, allometry is the study of the relationship of body size or mass to various anatomical, physiological, or pharmacological parameters (e.g., Boxenbaum and D'Souza 1990). Allometric relationships take the general form:

$$y = aW^x$$

where ***W*** is the weight of the animal, ***y*** is the variable to be estimated, and the model parameters are **a** and **x**. For most allometric relationships used in this exposure assessment, such as the relationship of body weight to surface area as well as the consumption of food and water, **x** ranges from approximately 0.65 to 0.75. These relationships dictate that, for a fixed level of exposure (e.g., levels of a chemical in food or water), smaller animals will be subject to a higher dose, in terms of mg/kg body weight, than larger animals.

As discussed in section 3.3, the available data on experimental and domestic animals suggest that there is no systematic relationship between species sensitivity and body weight for triclopyr. Because small animals, will receive higher doses of triclopyr for any given level of triclopyr in an environmental medium (i.e., soil, air, food, or water), generic estimates of exposure are given for a small mammal. A body weight of 20 g is used for a small animal, which approximates the body weight of small mammals such as mice, voles, shrews, and bats. All body weight values are taken from U.S. EPA (1989a), unless otherwise specified.

4.2.1.1. ***Direct Spray*** **--** In the broadcast application of any herbicide, wildlife species may be sprayed directly. This exposure scenario is similar to the accidental exposure scenarios for the general public discussed in section 3.2.2. In a scenario involving exposure to direct spray, the extent of dermal contact depends on the application rate and the surface area of the organism. As discussed in section 2 (see Table 2-5), the Forest Service uses triclopyr, either as Garlon 3A or Garlon 4, at application rates that span almost an order of magnitude, 0.4-3 lbs a.e./acre. The following calculations will be based on an application rate of 1 lb/acre or approximately 0.0112 mg a.i./cm^2. Thus, the resulting estimates of dose (mg/kg bw) may be regarded as dose rates

based on application rate (mg/kg bw per lb a.i.). The consequences of higher or low application rates are discussed in the risk characterization (section 4.4).

For mammals, surface area (*SA*) can be calculated as a function of body weight (Boxenbaum and D'Souza 1990):

$$SA\ (cm^2) = 1110 \cdot BW(kg)^{0.65}$$

where:

SA = *surface area* (cm^2)
BW = *body weight* (kg)

Thus, the calculated surface area of a 20 g mammal is approximately 87 cm^2 [1,110 · $0.020^{0.65}$] or 4.4 cm^2/g body weight. At the typical application rate of 0.0112 mg a.i./cm^2 (1 lb a.i./acre), the animal would be exposed to approximately 25 mg/kg

$$0.5 \cdot 87\ cm^2 \cdot 0.0112\ mg\ a.i./cm^2 \div 0.020\ kg = 24.36\ mg/kg.$$

Here, surface area is divided by 0.5, assuming that only 50% of the body surface is exposed to the direct spray.

The dose estimated above represents exposure dose, which is the amount of agent deposited on the organism. For most organisms, the risk characterization must be based on estimates of absorbed dose which are then compared with oral toxicity data (e.g., NOAELs and LD_{50} values). Estimating the absorbed dose from the exposure dose, requires estimates of dermal absorption rates.

As in the human health risk assessment (see section 3.2.3.2), the likely differences in dermal absorption rates of triclopyr and triclopyr BEE must be considered. For triclopyr BEE, absorption rates of 0.016 day^{-1} to 0.032 day^{-1} were used in the human health risk assessment, based on the available data regarding the dermal absorption of triclopyr BEE from Garlon 4 in humans (Carmichael et al. 1989, Carmichael 1989).

Based on the *in vitro* study by Hotchkiss et al. (1992) using skin preparations from rats and humans, greater absorption of triclopyr BEE was observed in rat skin preparations (3.7% over 72 hours) than in human skin preparations (0.7% over 72 hours). These difference were statistically significant ($p<0.05$) and seem to be substantial (i.e., a factor of about 5). The time course of absorption appeared to be linear for human skin preparations and rat skin preparations (Hotchkiss et al. 1992, Figure 1, p. 893); however, there was limited absorption over the 72-hour observation period rather than a true zero order process. The rates of absorption (k_a in $hours^{-1}$) can be calculated from the relationship:

$$M = M_0 \cdot e^{-k_a t}$$

where *M* is the amount remaining after time *t*, and M_0 is the amount applied or the amount at time zero (t_0). The above equation may be rearranged to:

$$\ln(k) = \ln(q_a) + \ln(t)$$

where q_a is simply the proportion absorbed at time *t* [$1-M_t/M_0$]. Thus, even though the differences in the proportions of triclopyr BBE absorbed by rat skin and human skin preparations are statistically significant after 72 hours, the absorption rates are almost the same, 0.01333 $hour^{-1}$ for the rat skin preparations and 0.01375 $hour^{-1}$ for the human skin preparations, and are within the range of the observed *in vivo* rates of triclopyr BEE absorption in humans.

There are no studies regarding the dermal penetration rates for triclopyr acid in wildlife species. For this exposure assessment, the rates derived in section 3.1.8 will be used, 0.005 day^{-1} to 0.01 day^{-1}. These rates assume that triclopyr is absorbed at a rate that is approximately 3 times less than triclopyr BEE absorption. As discussed in section 3.1.8, this assumption is based on the general observation that ionized molecules generally are absorbed more slowly than comparable non-ionized compounds.

Thus, for Garlon 3A, the absorbed dose after a direct spray would be about 0.12-0.24 mg/kg/day

$$24.36 \text{ mg/kg} \cdot 0.005\text{-}0.01 \text{ day}^{-1} \cdot 1 \text{ day}.$$

For Garlon 4, the absorbed dose after a direct spray would be about 0.38-0.78 mg/kg/day

$$24.36 \text{ mg/kg} \cdot 0.016\text{-}0.032 \text{ day}^{-1} \cdot 1 \text{ day}.$$

All of these estimates apply to the amount absorbed during the first 24-hour period after the direct spray event.

These estimates of absorbed doses may bracket plausible levels of exposure for small mammals. Some animals, particularly birds, groom frequently, and grooming may contribute to the total absorbed dose by the direct ingestion of the herbicide on the 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 were not located in the literature. For this exposure assessment, the assumption of complete and instantaneous absorption will be used as an upper limit of exposure to account for the effects of grooming or atypically high dermal permeability.

4.2.1.2. ***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), discussed in section 3.2.3.3, is used to estimate that the dislodgeable residue will be lower than the nominal application rate by a factor of approximately 10. Thus, at

an application rate of 1 lb a.i./acre or approximately 0.0112 mg/cm^2, the estimated dislodgeable residue will be 0.0011 mg/cm^2.

Unlike the human health risk assessment, however, no transfer rates are available for wildlife species. As discussed in Durkin et al. (1995), the transfer rates for humans are based on brief (e.g., 0.5–1 hour) exposures that measure the transfer from contaminated soil to uncontaminated skin. Wildlife, compared with humans, may spend much longer periods of time in contact with contaminated vegetation. It is reasonable to assume that for prolonged exposures an equilibrium may be reached between levels on the skin and levels on contaminated vegetation, although there are no available data regarding the kinetics of such a process. The available bioconcentration data on triclopyr (Appendix 4) suggest that triclopyr 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 residue on the animal will be equal to the dislodgeable residue on the vegetation).

The exposure dose may be estimated in a manner similar to that for direct dermal exposure (section 4.2.2.1). For a 20 g mammal with a surface area of 87 cm^2, the exposure dose is 4.8 mg/kg,

$$87 \text{ cm}^2 \cdot 0.0011 \text{ mg/cm}^2 \div 0.020 \text{ kg}.$$

Note that unlike the calculation for direct dermal exposure, this calculation assumes that 100%, rather than 50%, of the body surface is exposed to the contamination.

As in the case of the direct contact exposure scenario, the estimates of exposure dose are the upper limits of absorbed dose and may apply to animals that groom extensively or animals that have highly permeable skin. Because these exposure doses are far below any level of concern for direct toxic effects, as discussed in the risk characterization (section 4.4), this exposure scenario will not be developed further to consider the distinction between exposure dose and absorbed dose. Hence, separate exposure assessments for Garlon 3A and Garlon 4 are not necessary.

4.2.1.3. ***Ingestion of Contaminated Vegetation or Prey --*** As in the human health risk assessment, the consumption of contaminated vegetation is a plausible route of exposure. In the human health risk assessment, residues on berries of 1.6 mg/kg berry associated with the application of 1 lb a.i./acre were used. This estimate could also be applied to wildlife species that might consume berries. As indicated in several field studies (Appendix 4), however, much higher concentrations may be encountered on other types of vegetation, such as leaves near the top of the canopy.

There are three studies regarding vegetation residues and dissipation rates after aerial (Newton et al. 1990) or backpack (Thompson et al. 1994, Whisenant and McArthur 1989) applications of triclopyr that are useful for estimating initial concentrations on vegetation and rates of dissipation.

In the study by Thompson et al. (1994), Triclopyr BEE was applied by backpack sprayer (VMD of 1,089 μm and application volume of 4.32 L/min) at application rates of 0.4, 1.26, 2.12, 2.98, and 3.84 kg ai/ha to sites in New Brunswick dominated by sugar maple with other shrub species. All applications were made in July. The formulation of triclopyr BEE used in this study was RELEASE, made by DowElanco Canada Inc., and seems to correspond to Garlon 4. Foliar residues at various times after application fit the general exponential (first-order) decay model:

$$Y = \alpha \cdot e^{-k_e \cdot t} \qquad \textbf{(4-5)}$$

where ***Y*** is the mass of triclopyr per unit mass of vegetation, ***t*** is time in days, and α (residue at time zero) and k_e (dissipation rate) are model parameters. At a nominal application rate of 1.26 kg/ha (approximately 1.1 lb/acre), the average residue on vegetation immediately after spraying was approximately 302 mg/kg (Thompson et al. 1994, Table 4). When normalized for the application rate, this number corresponds to approximately 274 mg/kg per lb/acre. The halftime for triclopyr BEE was approximately 1.3 days (k_e=0.52) and the corresponding halftime for triclopyr acid was approximately 3.5 days (k_e=0.20). These values are taken as the average values for dissipation rates from Table 5 in Thompson et al. (1994) and are based on 42-day post-application monitoring.

In the other backpack study (Whisenant and McArthur 1989), triclopyr BEE with surfactant and diesel oil in water was applied by backpack sprayer at a rate of 2.3 kg a.e./ha to sites in Idaho dominated by shinyleaf Ceanothus in silt or silty loam soil during August of 1986. The commercial formulation is not specified in this publication. Initial levels on various types of vegetation ranged from 79 to 362 mg/kg. Normalized for an application rate of 1 lb/acre, these numbers correspond to residues of 39-176 mg/kg. The approximate halftime on vegetation was approximately 7 days.

Much lower initial residues but much longer halftimes are reported by Newton et al. (1990). This study involved the aerial application of triclopyr triethylamine salt (2.2 and 4.4 kg/ha) or triclopyr BEE (1.65 and 3.3 kg/ha) to Oregon brushfields on clay loam soils in late summer. The specific formulations used are not specified in the publication. Initial residues on top crown vegetation, expressed as acid equivalents, were similar for both formulations with an average of approximately 40 mg/kg per lb/applied. This residue level is about 7 times less than the residue levels reported by Thompson et al. (1994) for a ground application. Based on monitoring over a 1-year post-application period, the halftime for triclopyr BEE was approximately 94 days (k_e=0.0074) and the corresponding halftime for triclopyr acid was approximately 23 days (k_e=0.031).

For comparison, empirical relationships based on initial residues for a large number of pesticides after various application methods suggest typical residue rates of 125 mg/kg·lb a.i. on leaves and leafy crops and extreme residue rates of 240 mg/kg·lb a.i. on range grass (Hoerger and Kenaga 1972).

The observed range of residue rates is very large, 40 mg/kg per lb/applied (Newton et al. 1990) to 274 mg/kg per lb/acre (Thompson et al. 1994). Although the difference in application methods might account for some of the variability, the range of residues reported by Whisenant and McArthur (1989) in another ground application study spans the range of difference between the Newton study and the Thompson study. For this risk assessment, 300 mg/kg, a rounding of the level noted by Thompson et al. (1994) to one significant digit, will be taken as a plausible upper limit and 40 mg/kg per lb applied will be taken as the plausible lower limit. The central estimate will be taken at 100 mg/kg per lb applied. This is the geometric mean of the extreme values, rounded to one significant digit.

For estimating the effects of longer-term exposure, the large differences in halftimes/dissipation rates must be reconciled. As discussed by Thompson et al. (1994) the discrepancies between his estimates and those of Newton may be attributed to several site-specific factors as well as the use of a simple first order decay model. For this risk assessment, dissipation rates from 0.01 to 0.5 $days^{-1}$ will be used to encompass the range noted in the above studies. A rate of 0.07 $days^{-1}$, the geometric mean of this range, will be used as a central estimate. This value is also close to the rate used in the human health risk assessment from the study in berries by Siltanen et al. (1981). Although different rates for triclopyr acid and triclopyr BEE have been noted, the relative rates for these two forms of triclopyr are not consistent and these two forms are not modelled separately.

Allometric relationships and species specific data (U.S. EPA 1989a) suggest that the amount of food consumed per day by a small mammal (i.e., approximately 20 g) is equal to approximately 15% of the mammal's total body weight. Using this estimate with a residue rate of 100 mg/kg lb a.i. yields an dose estimate of 15 (6-45) mg/kg

$$0.15 \cdot 100\ (40\text{-}300)\ \text{mg/kg}\cdot\text{lb a.i} \cdot 1\ \text{lb/acre}.$$

These estimates are based on the assumption that 100% of the diet is contaminated. Under the assumption that only 10% of the diet is contaminated, the dose estimates decrease by a factor of 10. All of these dose estimates apply to levels on vegetation immediately after application.

For estimating the effects of longer-term exposure, median concentrations will be used, similar to the approach taken in the human health risk assessment (see section 3.2.3.6). Taking 90 days as a typical subchronic exposure scenario and an initial residue of 100 (40-300) mg/kg, the residue levels at day 90 after application could range from essentially zero ($2.9\cdot10^{-20}$ mg/kg) using a k_e 0.5 $days^{-1}$ to 40 (16-121) mg/kg using a k_e 0.01 $days^{-1}$. The central estimate of the range, based on a k_e 0.07 $days^{-1}$, is 0.18 (0.07-0.55) mg/kg.

Based on this exposure range, the median daily doses are 4.2 (1.7-13) mg/kg using a k_e of 0.07 $days^{-1}$ and 63(25-190) mg/kg using a k_e of 0.01 $days^{-1}$. Using the upper limit on the dissipation rate, the dose is estimated at less than $1\cdot10^{-9}$ mg/kg. As discussed in section 4.3, this lower estimate is not toxicologically significant.

4.2.1.4. ***Ingestion of Contaminated Water*** **--** Concentrations of triclopyr in water will be estimated as in the human health risk assessment. For standing bodies of water, the exposure rate is estimated at 11.25 mg · cm/(L·lbs/acre) (see section 3.2.3.4.1). In other words, a concentration of 11.25 mg/L would be expected from an application rate of 1 lb/acre over a body of water 1 cm deep. The concentration would be related directly to the application rate and related inversely to the depth of the water. Thus, at an application rate of 1 lb/acre over a shallow pond with a functional mixing depth of approximately 6 inches (15.24 cm), the initial concentration would be 0.7 mg/L,

$$11.25 \text{ mg·cm/(L·lbs/acre)} \cdot 1 \text{ lb/acre} \div 15.24 \text{ cm}.$$

Over a lake with an average mixing depth of approximately 2 m, the initial concentration would be 0.05 mg/L,

$$11.25 \text{ mg·cm/(L·lbs/acre)} \cdot 1 \text{ lb/acre} \div 200 \text{ cm}.$$

There are well-established relationships between body weight and water consumption across a wide range of mammalian species (e.g., U.S. EPA 1989a). Mice, weighing approximately 0.02 kg, consume approximately 0.005 L of water/day (i.e., 0.25 L/kg body weight/day). Thus, for the small pond scenario described above, the estimated dose for a small mammal is 0.175 mg/kg,

$$0.7 \text{ mg/L} \cdot 0.005 \text{ L} \div 0.02 \text{ kg}.$$

For the lake scenario described above, the estimated dose for a small mammal is 0.0125 mg/kg,

$$0.05 \text{ mg/L} \cdot 0.005 \text{ L} \div 0.02 \text{ kg}.$$

This range of concentrations, 0.05-0.175 mg/L, is reasonably close to the levels of 0.03 to 0.1 mg/L per lb/applied found in streams (see section 3.2.3.4.2). Hence, separate stream scenarios will not be derived.

For estimating the effects of longer-term exposures, the monitoring data of Norris et al. (1987) will be used, as in the human health risk assessment, to estimate a level of 0.001 mg/L per lb a.e./acre (see section 3.2.3.4.2). Thus, the average daily dose over a 90 day period after spraying would be approximately 0.00025 mg/kg,

$$0.001 \text{ mg/L} \cdot 0.005 \text{ L} \div 0.02 \text{ kg}.$$

4.2.2. **Terrestrial Plants.** The primary hazard to nontarget terrestrial plants is from unintended direct deposition or spray drift. Unintended direct spray will result in exposure levels equivalent to the application rate. As discussed in the dose-response assessment for terrestrial plants (section 4.3.3), such exposures are likely to result in adverse effects to many plant species. Spray drift will result in much lower levels of exposure; however, the potential for damage to

nontarget vegetation exists nonetheless. After deposition, triclopyr may contaminate soil either by runoff or leaching to soil from the roots of treated plants, and subsequent absorption by nontarget plants.

4.2.2.1. *Spray Drift*

4.2.2.1.1. Ground Applications -- Ground applications of herbicides generally will involve droplet sizes of 100 µ (or larger) sprayed from 3 feet above the ground or 400 µ (raindrop nozzles) sprayed from up to 6 feet above the ground. Stokes' law for the viscous drag on a moving sphere can be used as the basis of a conservative estimate of off-site deposition:

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

$$or$$

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

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). Using Stokes' law and ignoring the initial downward velocity of the droplet, a 100 µ droplet would remain in the air for approximately 3 seconds. Under recommended conditions of application, the wind velocity should be no more than 5 miles/hour (USDA 1989d,e, 1990), 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 could drift as far as 23 feet (3 seconds · 7.5 feet/second). At a wind speed of 15 miles/hour, applying the herbicide would constitute clear misuse. Taking this as an extreme scenario, the herbicide could drift as far as 68 feet (3 seconds · 15 · 1.5 feet/second).

These estimates are probably all variants of worst case scenarios. Using various types of nozzles with CO_2 pressurized sprayers, only 0.08-1.7% of triclopyr triethylamine salt was found to drift 0.9 m (3 feet) downwind at an average wind speed of 7.6 km/hour (4.7 miles/hours). At a distance of 2.1 m (≃7 feet) downwind of the application site, deposition was only 0.03-0.5% of the applied amount (Hatterman-Valenti et al. 1995).

The above assessment is directly relevant to spray applications but less so to cut surface treatments in which triclopyr may be translocated to the roots of plants and subsequently exuded to the surrounding soil, posing a risk to neighboring plants. This process, referred to as allelopathy, has been demonstrated for picloram, 2,4-D, and 2,4,5-T (Reid and Hurtt 1970, Webb and Newton 1972).

The most relevant field study for assessing the allelopathic potential of triclopyr is that presented by Neary et al. (1988). In this study, triclopyr was applied to oak trees using stem injectors at a dose sufficient to cause 56% defoliation in 2 months. The precise dose level per tree is not specified. Over a 1-year period, triclopyr residues in soil ranged from 0.11-2.59 mg/kg. The

levels varied over the year, with peaks occurring at 2 months (2.59 mg/kg) and 5 months (1.04 mg/kg) after application. The level of triclopyr in soil was 0.11 mg/kg at the end of month 12.

4.2.2.1.1. Aerial Applications -- Aerial applications have the potential for substantially greater drift because the higher elevation of the application and smaller droplet sizes resulting from droplet evaporation. Studies regarding the off-site deposition of triclopyr after aerial applications were not located in the literature. Initial rates of off-site deposition reflecting spray drift should be a function of application method and meteorological conditions and vary little among herbicides. Thus, for this risk assessment, the potential for off-site drift will be made by analogy to data on glyphosate, a herbicide that has been the subject of several studies on off-site deposition after aerial application.

As discussed in SERA (1996), glyphosate deposition 25 m (approximately 83 feet) downwind from the application site ranged from approximately $5 \cdot 10^{-6}$ to $7 \cdot 10^{-4}$ of the nominal application rate, based on drift deposited on Mylar fallout sheets (Yates et al. 1978, p. 600, Figure 1). During this application, wind speeds were approximately 2–4 m/second, which is approximately 4.4–8.8 miles/hour. Substantially greater drift was found by Riley et al. (1991). In this study, glyphosate was applied using a Bell 206B helicopter with a 13.1 m mid-mounted boom and operating a 21.3 m swath. The average emission rate was 4.5 liters/nozzle/minute under a pressure of 207 kPa. During the three applications, wind speeds ranged from 1.5-4.2 m/second (3.4-9.4 miles/hour). Glyphosate deposition 30 m downwind from the application site was less than 0.1 of the nominal application rate. At 200 m down wind, the deposition was less than 0.05 of the nominal application rate. Similar to the results of Riley et al. (1991), glyphosate deposition 50 m downwind from an application site was approximately 0.1 of the nominal application rate at a release height of 10 m with wind speeds ranging from 2.2 to 5.7 m/second (4.9-12.8 miles/hour). At 200 m down wind, the deposition was less than 0.002-0.005 of the nominal application rate (Payne 1993).

For this risk assessment, off-site deposition will be taken as 0.1 of the nominal application rate 30-50 m downwind (Riley et al. 1991, Payne 1993) and 0.002-0.005 of the nominal application rate at 200 m downwind (Payne 1993), recognizing that under some conditions, much less drift may occur (Yates et al. 1978).

4.2.2.2. *Soil Contamination* -- As summarized in Appendix 4, the behavior of triclopyr acid, triclopyr BEE, and triclopyr formulations has been extensively studied in soil (Deubert and Corte-Real 1986, Johnson and Lavy 1994, Lee et al. 1986, Neary et al. 1988, Newton et al. 1990, Norris et al. 1987, Norris et al. 1987, Pusino et al. 1994, Stephenson et al. 1990). Based on soil column studies, triclopyr BEE is more mobile in sand than triclopyr acid but neither form of triclopyr is very mobile in loamy soil. Residues of triclopyr were found only in the top 10 cm of loam after 54 days. Most (85%) of triclopyr metabolized to 3,,5,6-trichloro-2-pyridinol with some formation (10%) of 2-methoxy-3,5,6-trichloropyridine. In sand, 65% of the applied triclopyr (acid) leached through a 40 cm column after 54 days. All triclopyr BEE leached

through a 40 cm sand column by day 34 (Lee et al. 1986). For triclopyr acid, soil adsorption decreases with decreasing organic matter and increasing pH (Pusino et al. 1994).

Comparable halftimes have been reported for triclopyr in soil after applications of Garlon 3A (10-39 days, k_e = 0.07-0.02 $days^{-1}$) (Deubert and Corte-Real 1986) and Garlon 4 (approximately 14 days in clay or sand, k_e = 0.05 $days^{-1}$) (Stephenson et al. 1990). Soil halftimes of approximately 10 days at 2 or 20 cm (silty loam soil) and approximately 39 days at 60 cm (silty clay loam) have been reported for soil preparations containing triclopyr (salt or formulation not specified) at initial levels of 2.5 ppm (Johnson and Lavy 1994).

Long-term field studies (i.e., those conducted over approximately 1 year) have found very little indication that triclopyr will leach substantially either laterally or vertically in loamy soil (Norris et al. 1987, Newton et al. 1990). These studies have also reported somewhat longer soil halftimes for triclopyr, approximately 60-80 days, than the laboratory studies summarized above.

Some of the apparent discrepancies in soil halftime as well as the apparent similarity of triclopyr salt and triclopyr BEE may be partly due to the use of a simple exponential model for calculating the halftime. This is suggested by the results of Newton et al. (1990), who examined triclopyr soil residues after aerial application of triclopyr triethylamine salt (2.2 and 4.4 kg/ha) or triclopyr BEE (1.65-3.3 kg/ha) to Oregon brushfields on clay loam soils. In this study, soil samples were analyzed at various depths after 37, 79, 153, and 325 days. Both forms of triclopyr tended to stay in the top 15 cm (≃6 inches) of soil. While Newton et al. (1990) do not present a formal kinetic analysis, the reported soil residue data (Table IV, p. 581 of Newton et al. 1990) yield similar halftimes for both triclopyr amine (73 and 63 days) and triclopyr BEE (75 and 82 days). At both application rates, the kinetic data on the triclopyr salt fit an exponential decline model ($p=0.006$ and 0.02). For triclopyr BEE, however, the model gave a very poor fit ($p=0.12$ and 0.4), and visual inspection of the data suggests two first order processes, an initial rapid decay between day 34 and day 79, followed by a much slower decay.

For this risk assessment, maximum soil residues will be taken from levels reported in various field studies and expressed as mg/kg soil (ppm) per lb a.i. applied. As noted in the field studies by both Newton et al. (1990) and Norris et al. (1987) these maximum residues do not necessarily occur and probably will not occur at day 0 (i.e., the day of application). Soil residues will probably increase after application due to washoff or litter fall. In this respect, none of the available field studies may provide estimates of true maximum values. For this reason, the highest levels of both triclopyr salt and triclopyr BEE will be used. For both of these forms, the highest rate is approximately 0.3 mg/kg per lb a.i. applied (Norris et al. 1987 for triclopyr isopropylamine and Newton et al. 1990 for triclopyr BEE). Both of these levels apply to about the top 6 inches of soil.

The available data on soil persistence suggests that a first order model is appropriate for triclopyr salt, with approximately 80 days as a conservative estimate of a halftime. This would apply to loam or clay soils, with more rapid dissipation being likely in sandy soils. For triclopyr BEE, the

reported halftime of approximately 14 days given by Stephenson et al. (1990) for Garlon 4 in both sand and clay seems to be a reasonable approximation for an initial rate of decay. Based on the results of Newton et al. (1990), much lower decay rates over more prolonged periods are plausible.

4.2.3. Aquatic Organisms. The exposure assessment used for aquatic organisms will be almost the same as the exposure assessment used for terrestrial organisms (see section 4.2.1.4). For a standing body of water, an initial contamination rate of 11.25 mg·cm/(L·lbs/acre) will be used. This yields estimates of 0.7 mg/L for a small pond and 0.05 mg/L for a lake at an application rate of 1 lb/acre. As noted in section 4.2.1.4, these levels also correspond closely to anticipated levels in oversprayed streams.

For estimating the effects of longer-term exposure, the estimated concentrations in water will be estimated from the rate of 0.001 mg/L per lb a.e./acre, as in the human health risk assessment (see section 3.2.3.4.2) and the assessment of effects on terrestrial animals (see section 4.2.1.4).

The effect of application rate on potential risk is discussed in the risk characterization for aquatic species (section 4.4.3).

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Terrestrial Animals. As summarized in the human health risk assessment (see section 3.3), triclopyr has a low order of acute toxicity to mammals. As noted in the hazard identification for ecological effects (section 4.1.2), there is relatively little information regarding the toxicity of triclopyr to other terrestrial mammals. The information on birds (Appendix 5) suggests that the acute lethal potency of triclopyr to birds and mammals is similar. The most important quantitative consideration for the dose-response assessment of terrestrial animals is the apparent lack of a systematic relationship between body weight and toxicity (see section 3.3.3). This apparent lack of an allometric relationship for acute toxic potency is somewhat confounded by the information suggesting that the dog is atypically sensitive. As discussed in section 3.3.3, however, the differences in the pharmacokinetics of the dog and other species may not be directly or simply related to subsequent toxic effects. Furthermore, the dose/duration/severity relationships do not suggest that the dog is unusually sensitive to triclopyr.

For nontarget terrestrial species, the approach will be similar to that taken in the human health risk assessment, except that uncertainty factors will not be used because data are available on nontarget species. Thus, for assessing the effects of acute exposures, the 1-day NOAEL of 60 mg/kg will be taken as an estimate of acceptable short-term exposures. Adverse effects could be expected at somewhat higher doses, 75 mg/kg, but lethality would not be expected unless doses approached approximately 250 mg/kg (see section 3.3.3). Because these estimates are based on relatively small experiments, in terms of the numbers of animals used, they may not be sufficiently protective for exposures involving large numbers of animals. Conversely, these dose estimates may be extremely conservative because they approach levels that have not been associated with

frank adverse effects in longer-term feeding studies, as discussed in the following paragraph. These factors are qualitatively considered in the risk characterization for terrestrial organisms (section 4.4.2).

To assess the potential for longer-term toxic effects, the NOAEL of 0.5 mg/kg/day will be used, consistent with the derivation of the RfD for the protection of human health (see section 3.3.2). Decrements in kidney function might be expected in sensitive species at the corresponding LOAEL, 2.5 mg/kg/day. Nonetheless, chronic dietary intake of doses up to 250 mg/kg/day have led to histological changes in the kidney but no grossly observable effects over 90-day exposure periods in rodents (Landry et al. 1984). At dietary levels resulting in doses of 350 mg/kg/day, histological changes have been observed in the liver and kidney but the only grossly observable effect was a decrease in body weight (Barna-Lloyd et al. 1992).

4.3.2. Terrestrial Plants. As discussed in the exposure assessment for terrestrial plants (see section 4.2.2), there are two types of exposure to be considered: direct contact (i.e., either direct spray or drift) and soil contamination. As discussed in section 4.4.2, a different dose-response assessment is required to determine the consequences of both types of exposure.

4.3.2.1. ***Direct Spray*** **--** For direct spray or drift, the relevant exposure metameter is the application rate or functional rate of deposition expressed in units of toxicant weight per unit area (e.g., lb a.i./acre). In some respects, the product labels for triclopyr (DowElanco 1992 and 1993a) provide useful information on effective levels of application and suggest differences in species or life-stage sensitivity. As discussed in section 2.4, applications of Garlon 3A at 6-9 lbs a.e./acre or Garlon 4 at 4-8 lbs a.e./acre will control most species of woody plants and are above the levels necessary to control broadleaf weeds.

The dose-response assessment for direct spray can also be developed based on field studies with triclopyr, as summarized in Appendix 4. Application rates in the range of 0.3-0.6 lb/acre are likely to affect sensitive species such as rice (Pantone and Baker 1992, Street et al. 1992). Cotton appears to be very sensitive to triclopyr. Application rates as low as 0.03 kg/ha (0.027 lb/acre) have been shown to lower crop yield, and rates of 0.06 kg/ha (0.054 lb/acre) cause visible damage when applied at the pin-head square stage (Snipes et al. 1991).

Pine is relatively resistant to triclopyr; however, applications of up to 4.5 kg/ha (4 lbs/gallon) can cause severe effects, particularly during the summer, with much less injury after annual growth has ceased and during periods of high water stress (King and Radosevich 1985).

In general, triclopyr is less likely to affect grasses than broadleaf vegetation, although both types of vegetation may increase after triclopyr applications of 2.2 kg/ha (2 lbs/acre) because of damage to overstory vegetation (Boggs et al. 1991a,b, Engle et al. 1991, Lochmiller et al. 1995). Depending on the application rate, triclopyr may favor the development of grasses over broadleaf weeds. At rates of 0.56 kg/ha (0.5 lbs/acre), Meyer and Bovey (1990) noted no substantial effect on either type of vegetation 15 months after application. At a rate of 1.12 kg/ha (1 lb/acre), total

grasses increased by a factor of approximately 2 over control plots and total broadleaf cover decreased to approximately 60% of that noted in control plots.

Droplet size may influence damage to nontarget species. At low application/deposition rates, small droplets ($\simeq 100\mu$) tend to be more toxic than larger droplets ($\simeq 600\mu$). This effect is not apparent at high application rates (Prasad and Cadogan 1992).

4.3.2.2. ***Soil Exposures*** **--** As discussed in section 4.1, the environmental fate of triclopyr in soil has been studied extensively. The most relevant exposure metameter for this type of exposure is soil concentrations. Only one bioassay involving the response of plants to varying levels of triclopyr in soil was located (Morash and Freedman 1989). In this laboratory study, soil from a mixed wood clear cut was treated with triclopyr, as Garlon 4, at levels of 10, 50, 100, 500, 1,000, and 5,000 ppm (a.i. dry weight). The emergence of seedlings naturally occurring in the soil taken from an 8-year old mixed wood clearcut was monitored. The seedlings were classified as *Rubus* species, other dicots, and monocots. As illustrated in Figure 4-1, substantial inhibition of *Rubus* species, other dicots, and monocots was observed at concentrations ≥ 50 mg/kg soil. No seed germination was apparent at soil concentrations of 500-5,000 mg/kg soil. Inhibition of germination at 10 mg/kg soil was not statistically significant. The concentration of 10 mg/kg soil is essentially a NOEL and 50 mg/kg soil is a FEL for all three groups of seeds.

Coffman et al. (1993) report substantial differences in sensitivity among species to triclopyr soil levels for some commercial crops. In this study, triclopyr (a commercial formulation of 480 g triclopyr/L, consistent with Garlon 4) was applied to silt loam soil at rates of 3.4, 6.7, and 10.1 kg/ha by ground sprayer. Different kinds of vegetation were planted at various times after application and observed for damage. No soil residues were determined. Wheat tolerated all applications by day 8 after application (8 DAA) in terms of visual assessment of injury; however, the yield from untreated plots was about twice as much as that from treated plots. Kidney beans tolerated 3.4 and 6.7 kg/ha applications 82 DAA, there was no effect on yield. Corn tolerated 3.4, 6.7, and 10.1 kg/ha by 8, 47, and 82 DAA. At 3.4 kg/ha, yield was reduced to approximately 80% of the control level. By 82 DAA, squash emerged and grew normally at 3.4 kg/ha. Earlier plantings often resulted in emergence and subsequent plant death. At 3.4 kg/ha, the yield of okra sowed 8 DAA was not affected. Potato plant fresh weights from 436 DAA of triclopyr at 3.4 kg/ha were only moderately less (6%) than untreated controls. There was evidence of injury to banana crops at all application rates. After 2 years, all sites were covered by indigenous species with no apparent differences between treated and untreated sites. By that time, all crops, except bananas, tolerated triclopyr residues in soil.

4.3.3. Aquatic Organisms.

4.3.3.1. ***Fish --*** Information regarding the toxicity of various forms of triclopyr as well as the commercial formulations are presented in Appendix 6. The most extensive comparative study on the toxicity of these agents was conducted by Wan et al. (1989). This publication summarizes a series of static bioassays on several species of salmonids that were conducted over a

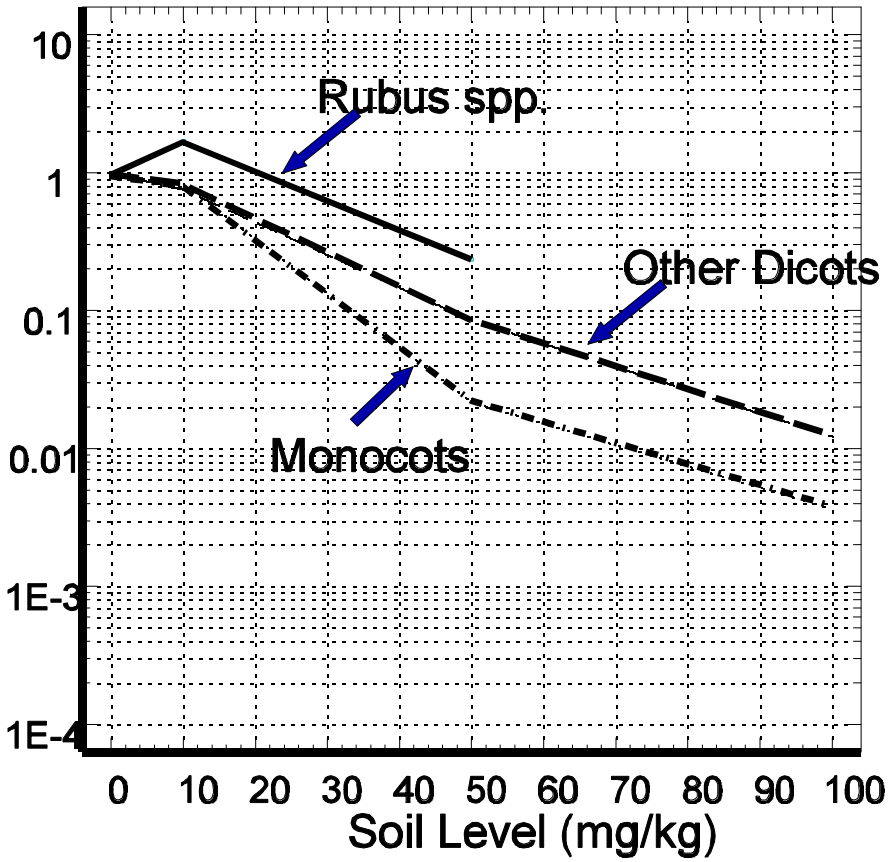


Figure 4-1: Relationship of triclopyr soil levels to the inhibition of seed generation [data from Table 1, p. 348 of Morash and Freedman 1989].

4-month period in 1986 and a 2-month period in 1987. The 96-hour LC_{50} values for triclopyr acid, triclopyr BEE, Garlon 3A, and Garlon 4 are summarized in Table 4-1. This table also presents the expected LC_{50} values for Garlon 3A and Garlon 4 based on the concentrations and toxicities of triclopyr acid and triclopyr BEE, respectively, in these formations. Wan et al. (1989) also present LC_{50} values at 24, 38, 72, and 96 hours. Since no strong time/response relationship is apparent, the shorter term results are not discussed further.

There are no remarkable differences among species in terms of sensitivity to the various agents covered in this risk assessment. Wan et al. (1989) do not provide confidence intervals on the LC_{50} values; however, given that the acute bioassays were conducted at different times over a prolonged period and the differences in LC_{50} values among species are relatively slight, this lack of information does not represent a significant data gap. Nonetheless, there is a substantial difference between the toxicity of triclopyr acid and the toxicity of triclopyr BEE, and the difference is reflected in the toxicities of the Garlon formulations. As indicated in Table 4-1,

Table 4-1. Acute toxicity of triclopyr and related compounds to various species of salmonids[a].

Test Compound	Species	A: 96-hour LC_{50} values	B: Expected LC_{50} values[b]	A÷B
Garlon 3A	coho salmon	463	26	18
	chum salmon	267	21	13
	sockeye salmon	311	21	15
	rainbow trout	420	21	20
	chinook salmon	275	27	10
Garlon 4	coho salmon	2.1	1.6	1.3
	chum salmon	1.7	0.5	3.4
	sockeye salmon	1.4	0.6	2.3
	rainbow trout	2.7	1.8	1.5
	chinook salmon	2.7	1.8	1.5
	pink salmon	1.2	0.8	1.5
Triclopyr acid (not amine salt)	coho salmon	9.6	N/A	N/A
	chum salmon	7.5		
	sockeye salmon	7.5		
	rainbow trout	7.5		
	chinook salmon	9.7		
	pink salmon	5.3		
Triclopyr BEE	coho salmon	1.0	13	0.08
	chum salmon	0.3	10	0.03
	sockeye salmon	0.4	10	0.04
	rainbow trout	1.1	10	0.1
	chinook salmon	1.1	13	0.08
	pink salmon	0.5	7.4	0.06

[a]Source: Wan et al. (1987). All bioassays conducted at 8-14°C, 10 fish/concentration. Static with aeration. LC_{50} based on measured, rather than, nominal concentrations. Photo-period and lighting conditions not specified.

[b]For Garlon 4, the observed LC_{50} of triclopyr BEE divided by the proportion of Garlon 4, 0.616, which consists of triclopyr BEE. For Garlon 3A, the observed LC_{50} of triclopyr acid divided by the proportion of Garlon 3A, 0.360, which consists of triclopyr acid. For triclopyr BEE, the observed LC_{50} of triclopyr acid divided by the proportion of triclopyr BEE, 0.72, which consists of triclopyr acid.

triclopyr BEE is more toxic than triclopyr acid, in terms of acid equivalents, by factors ranging from approximately 10 (rainbow trout, 1÷0.1) to 30 (chum salmon, 1÷0.03). Because the bioassays were conducted at different times, this range of differences may not be significant; however, the magnitude of the difference is substantial and reasonably consistent across species.

The results of Wan et al (1987) appear to be expressed in terms of the formulation. The expected LC_{50} values for these formulations, given in the fourth column of Table 4-1, are simply the reported LC_{50} values for the active agent divided by the proportion of the agent in the formulation (see footnote in Table 4-1 for details). Garlon 4 is more toxic than Garlon 3A by a factor of about 200 (150-230). This difference in toxicity is substantially greater than the difference in toxicity between triclopyr BEE and triclopyr acid. As indicated in the last column of Table 4-1, this increased difference appears to be attributable to the less than expected toxicity of Garlon 3A, based on the level of triclopyr acid in this formulation. The level of triclopyr BEE in Garlon 4 appears to account for practically all of the toxicity of Garlon 4 (i.e., the ratios of observed to predicted LC_{50} values do not vary remarkably from unity for Garlon 4). Although Garlon 4 contains kerosene (see section 2.2), the toxicity of kerosene to aquatic species is approximately 100-1,000 fold less than triclopyr BEE [LC_{50} values of approximately 200-3,000 mg/L (CHEMBANK 1995)], supporting the observation that the toxicity of Garlon 4 can be completely accounted for by the toxicity of triclopyr BEE.

The Wan et al. (1987) study is supported by more recent flow-through toxicity assays on Garlon 4 with reported LC_{50} values for salmonids of 0.79-1.76 mg/L (Kreutzweiser et al. 1994) and 0.84 mg/L (Johansen and Geen 1990). As indicated in Appendix 6, Kreutzweiser et al. (1994) report a strong time-response relationship between exposure periods of 1-24 hours. This is not inconsistent with the results of Wan et al. (1989) but simply indicates that increasing body burdens occur during the first 24 hours of exposure.

The sublethal effects of Garlon 4 on salmonid (rainbow trout) has been examined by Johansen and Geen (1990) using flow-through systems. At concentrations of 0.32-0.43 mg/L, about a factor of 2 below the 96-hour LC_{50} determined by these investigators, fish were lethargic. At levels $\leq$0.1 mg/L, fish were hypersensitive over 4-day periods of exposure. This is reasonably consistent with the threshold for behavioral changes in rainbow trout for Garlon 4 of 0.6 mg/L (Morgan et al. 1991). The corresponding threshold for behavioral changes to Garlon 3A was 200 mg/L (Morgan et al. 1991) is consistent with the relative acute lethal potencies of these two agents.

The limited acute toxicity data on non-salmonid species, also summarized in Appendix 6, suggest that these species are about as sensitive to the various forms of triclopyr as salmonids.

Subchronic toxicity data are available only on the triethylamine salt of triclopyr. At 140 mg/L, approximately 0.25 of the LC_{50} in salmonids, over an exposure period of 28 days, the survival of fathead minnows (embryo-larval stages) was significantly reduced, compared with control animals (Mayes et al. 1984).

For this risk assessment, a level of 0.6 mg/L will be taken as a functional NOEL for Garlon 4 exposures. That is, no frank toxic effects should be apparent in fish. Based on the time course data of Kreutzweiser et al. (1994) and the earlier work of Wan (Wan et al. 1987), acute exposures to Garlon 4 at levels of 1 mg/L for 24 hours or 20 mg/L for 1 hour would be associated with substantial mortality.

For Garlon 3A, an acute NOEL of 200 mg/L could be taken based on the threshold for behavioral changes (Morgan et al. 1991) but this value is too close to lethal levels reported by other investigators. A judgmental estimate of 50 mg/L over a 1-day exposure period will be used as the estimated NOEL for fish. This is below the lower limit of any reported LC_{50} values. Substantial lethality could be expected in some fish species at concentrations >200 mg/L.

4.3.3.2. ***Aquatic Invertebrates --*** Information regarding the toxicity to aquatic invertebrates of various forms of triclopyr as well as the commercial formulations are presented in Appendix 7. The available LC_{50} values, while not as extensive as those for fish, suggest that most invertebrates are somewhat less sensitive than fish to the various forms of triclopyr. Some families of invertebrates (Ephemeroptera, Plecoptera, Trichoptera, Odonata) are much more resistant than fish to Garlon 4 (Kreutzweiser et al. 1992) (Appendix 7). Given this pattern, and the limited levels of exposure in streams (section 4.2), the dose-response assessment for fish will be used to encompass effects on invertebrates. Special considerations, such as the induction of invertebrate drift in streams, are discussed in the risk characterization.

4.3.3.3. ***Aquatic Plants --*** The only available information regarding the toxicity of triclopyr to aquatic algae is the study by Peterson et al. (1994). A summary of this study is presented in Appendix 8. Assaying toxicity as an inhibition of carbon fixation, these investigators noted no or relatively little inhibition at concentrations of triclopyr acid of 2.6 mg/L. Data regarding the effects of Garlon formulations on algae were not located in the literature.

One study has been encountered on the effect of Garlon 3A on aquatic macrophytes. This laboratory study was designed to determine the efficacy of Garlon 3A for the control of eurasian watermilfoil, an aquatic macrophyte and involved levels of 0.25-2.5 mg a.e./L (as Garlon 3A) over time periods of 2-48 hours. Very little effect at any concentration was seen for exposure periods <6 hours. At 0.25 mg/L, effective control was associated with exposure periods of 24 (partially effective) to 72 (very effective) hours (Netherland and Getsinger 1992). These results are substantially below exposure levels associated with toxicity in fish or aquatic invertebrates.

4.4. RISK CHARACTERIZATION

4.4.1. **Overview.** For terrestrial animals, there is little indication that dermal exposure or exposure from the consumption of contaminated water will to lead to exposure levels that approach levels of concern. The consumption of contaminated vegetation is the only scenario in which the HQ exceeds unity. Immediately after the application of triclopyr, small mammals that consume contaminated vegetation exclusively are likely to intake levels that may exceed an HQ of 1. Although signs of frank effects are not likely to occur at these levels of exposure, kidney function could be impaired.

For terrestrial plants, direct deposition, either through unintentional direct spraying or spray drift presents a plausible hazard. If plants are accidentally sprayed at the application rates used by the Forest Service, the plants, with the possible exception of grasses, are likely to be damaged,

particularly in the upper ranges of anticipated application rates. This may be regarded as an accidental scenario, which is relatively easy to control with proper management and application. Spray drift could cause detectable damage to nontarget plants within approximately 30 m downwind of a spray zone. At distances >30 m, detectable damage is unlikely.

Based on conservative assumptions regarding exposure, it is reasonable to assume that the maximum levels of triclopyr in soil associated with treatments contemplated by the Forest Service are likely to be far less those associated with damage to nontarget plants. This characterization is tempered somewhat by a field study indicating that application rates of Garlon 4 at approximately 3-10 lbs/acre can lead to decreased germination and plant growth for periods of approximately 8-80 days after application.

At plausible levels of acute exposure in standing water and streams, 0.07-0.5 mg/L, Garlon 3A is not likely to have any effect on fish, aquatic invertebrates, and most algae. Some sensitive macrophytes might be affected. At an application rate of 1 lb/acre, Garlon 4 could cause transient behavioral changes in some aquatic species at the upper range of estimated exposure levels at an application rate of 1 lb/acre. At application rates of 2 lbs/acre or higher, the upper range of exposure could result in mortality in fish and perhaps in some sensitive invertebrates.

4.4.2. Terrestrial Animals. The risk characterization for terrestrial animals is summarized in Table 4-2. The top part of Table 4-2 summarizes each of the quantitative exposure assessments made in section 4.2.1. for the small (20 g) mammal. The bottom part of the Table 4-2 summarizes the dose-response relationships discussed in section 4.3.1. For each of the exposure assessments, the last column in the table gives the highest HQ relevant to the exposure assessment. The derivation of each of these HQs and an explanation of the term *relevance* is provided in the following paragraphs. Because the individual components of the exposure assessments are pathway specific, this section ends with a discussion of concern for multi-pathway exposures.

There are two risk characterizations for dermal exposure. One involves direct spray, and the other involves dermal contact with contaminated vegetation. For the direct spray scenario, application rates of either Garlon 3A or Garlon 4 at 1 lb a.i./acre are not toxicologically significant. As indicated by the HQs, these exposures would remain far below levels of concern at application rates greatly in excess of 10 lbs a.i./acre.

As with dermal exposure, water contamination is not likely to lead to levels of exposure that approach a level of concern.

The consumption of contaminated vegetation is the only scenario in which the HQ exceeds unity. Immediately after the application of triclopyr, small mammals that consume contaminated vegetation exclusively are likely to intake levels of triclopyr result in an HQ that exceeds unity. No signs of frank effects are likely to occur at these levels of exposure, but kidney function could be impaired.

Table 4-2. Summary risk characterization for a 20 g terrestrial mammal after exposure to triclopyr at an application rate of 1 lb a.i./acre

Media/scenario	Exposure Estimates (mg/kg)	Highest Relevant HQ
	Small mammal (20 g)	
Direct spray, dermal		
Garlon 3A	0.12-0.24	0.002-0.004[a]
Garlon 4	0.38-0.78	0.006-0.01[a]
Indirect dermal contact		
100% dermal absorption	4.8	0.08[a]
Consumption of vegetation		
Extreme exposure assumptions (t_0)		
10% of diet contaminated	10(4-30)	0.2(0.07-0.5)[a]
100% of diet contaminated	100(40-300)	2(0.7-5)[a]
Typical exposure assumptions (t_{90})		
k_e = 0.07 $days^{-1}$	4.2(1.7-13)	8(3-30)[b]
k_e = 0.01 $days^{-1}$	63(25-190)	130(50-380)[b]
Consumption of water		
Maximum ambient levels	0.05-0.2	<0.004[a]
Typical ambient levels (0.001 mg/L)	0.00025	0.0005[b]
ESTIMATES OF PLAUSIBLE NO-EFFECT LEVELS		
Non-lethal acute dose	60	
Longterm NOEL	0.05	

[a] HQ based on nonlethal acute dose.

[b] HQ based on long-term NOEL.

As noted in Section 4.2.1.3, data regarding the persistence of triclopyr on contaminated vegetation is highly variable both for Garlon 3A and Garlon 4. For this risk assessment, separate exposure assessments for these two formulations are not justified because of the variability and inconsistencies in the data on these two formulations. Nonetheless, relatively typical exposure and persistence assumptions lead to estimates of doses that exceed the NOAEL even at the lower ranges of the estimated dose. As with acute exposures, the consequences of all of these exposures are likely to be impaired renal function that would not lead to signs of frank toxic effects. The only effect that might be observed at the upper range of these doses is decreased

body weight. This is consistent with the available field studies summarized in Appendix 4, which do indicate the occurrence of adverse effects.

The characterization of risk from the consumption of contaminated vegetation is based on an application rate of 1 lb/acre. Nonetheless, at all application rates used by the Forest Service, the consumption of contaminated vegetation would lead to HQs that exceed unity. No other HQs would be of comparable concern. Because the consumption of contaminated vegetation dominates the exposure assessment, considerations of multiple simultaneous pathways would have a negligible impact on the characterization of risk.

4.4.3. Terrestrial Plants. Direct deposition, from unintentional direct spraying or from spray drift is a plausible hazard for most herbicides, including those containing triclopyr. If plants are sprayed accidentally at the application rates used by the Forest Service, the plants, with the possible exception of grasses, are likely to be damaged, particularly in the upper ranges of anticipated application rates. This exposure scenario may be regarded as accidental and is relatively easy to control with proper management and application. The extent and duration of the resulting damage will depend on the time of application and the plant species.

The extent of drift depends on specific conditions during application, such as wind speed, wind direction, topography, the distance from the ground at which the herbicide is applied, and the droplet size of the herbicide spray. Aerial applications are likely to generate greater drift, compared with ground applications, as illustrated by Yates et al. (1978). Even for aerial applications conducted under relatively unfavorable conditions, however, off-site deposition at 30-50 m is likely to be <0.1 of the nominal application rate. At 200 m downwind, the levels are likely to be only 0.002-0.005 of the nominal application rate.

The lowest adverse effect level for triclopyr is 0.03 lbs/acre. This level of exposure was associated with a lower crop yield of cotton but no visible damage. Levels of 0.3-0.6 have been associated with visible damage to rice. Thus, at a distance <30 m, some damage to nontarget vegetation is plausible due to drift. At distances $\geq$30 m, no detectable damage is likely.

Using very conservative exposure assumptions (i.e., based on the most conservative estimates from monitoring studies) the maximum levels of triclopyr in soil are likely to be no greater than 0.3 mg/kg soil at an application rate of 1 lb/acre. This is far below the apparent NOAEL, 10 mg/kg soil, for dicots and monocots. While there are substantial uncertainties in comparative fate of triclopyr from Garlon 3A versus Garlon 4, these have no impact on the characterization of risk. This characterization, however, is somewhat tempered by a field study (Coffman et al. 1993) indicating that application rates of Garlon 4 at approximately 3-10 lbs/acre can lead to decreased germination and plant growth for periods of approximately 8-80 days after application, depending on the species.

4.4.4. Aquatic Organisms. At plausible levels of acute exposure in standing water and streams, 0.07-0.5 mg/L, Garlon 3A is not likely to have any effect on fish, aquatic

invertebrates, and most algae. Some sensitive macrophytes might be affected. Currently, information is available only on eurasian watermilfoil. This species is adversely affected if water concentrations remain above 0.25 mg/L for more than 24 hours. Such concentrations are not plausible in streams but could be maintained in small standing bodies of water.

Garlon 4 could cause adverse effects on aquatic species at the upper range of estimated exposure levels, 0.07-0.5 mg/L, associated with an application rate of 1 lb/acre. These effects would probably consistent of transient behavioral changes. At application rates $\geq$2 lbs/acre, the upper range of exposure could be lethal to fish and perhaps to some sensitive invertebrates.

As noted in Appendix 4 (Kreutzweiser et al. 1995, Thompson et al. 1995), application rates comparable to those contemplated by the Forest Service have resulted in increases of invertebrate drift in streams. These effects, however, were transient and did not affect invertebrate abundance.

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6. GLOSSARY

Absorption -- The process by which the agent is able to pass through the body membranes and enter the bloodstream. The main routes by which toxic agents are absorbed are the gastrointestinal tract, lungs, and skin.

Acute exposure -- A single exposure or multiple exposure occurring within a short time (24 hours or less).

Additive Effect -- A situation in which the combined effects of two chemicals is equal to the sum of the effect of each chemical given alone. The effect most commonly observed when two chemicals are given together is an additive effect.

Adjuvant(s) -- Formulation factors used to enhance the pharmacologic or toxic agent effect of the active ingredient.

Adrenergic -- A type of nerve which uses an adrenaline like substance as a neurotransmitter.

Adsorption -- The tendency of one chemical to adhere to another material.

Adverse-Effect Level (AEL) -- Signs of toxicity that must be detected by invasive methods, external monitoring devices, or prolonged systematic observations. Symptoms that are not accompanied by grossly observable signs of toxicity. In contrast to Frank-effect level.

Aerobes -- Organisms that require oxygen.

Allelopathic Effects -- Literally *reciprocal pathology*. In plant pathology, the term is used to describe the release of substances from one plant that may have an adverse effect on another plant.

Allometric -- pertaining to allometry, the study and measure of growth. In toxicology, the study of the relationship of body size to various physiological, pharmacological, pharmacokinetic, or toxicodynamic processes among species.

Anaerobes -- Organisms that do not require oxygen.

Assay -- A kind of test (noun); to test (verb).

Biologically Sensitive -- A term used to identify a group of individuals who, because of their developmental stage or some other biological condition, are more susceptible than the general population to a chemical or biological agent in the environment.

Broadleaf weed -- A nonwoody dicotyledonous plant with wide bladed leaves designated as a pest species in gardens, farms, or forests.

Cancer Potency Parameter -- A model-dependent measure of cancer potency $(mg/kg/day)^{-1}$ over lifetime exposure. [Often expressed as a q_1^* which is the upper 95% confidence limit of the first dose coefficient (q_1) from the multistage model.]

Carcinogen -- A chemical capable of inducing cancer.

Carcinoma -- A malignant tumor.

Carrier -- In commercial formulations of insecticides or control agents, a substance added to the formulation to make it easier to handle or apply.

Chronic Exposure -- Long-term exposure studies often used to determine the carcinogenic potential of chemicals. These studies are usually performed in rats, mice, or dogs and extend over the average lifetime of the species (for a rat, exposure is 2 years).

Confounders -- A term used in discussions of studies regarding human populations (epidemiology studies) to refer to additional risk factors that if unaccounted for in a study, may lead to erroneous conclusions.

Conifer -- An order of the Gymnospermae, comprising a wide range of trees, mostly evergreens that bear cones and have needle-shaped or scalelike leaves; timber commercially identified as softwood.

Connected Actions -- Exposure to other chemical and biological agents in addition to exposure to the control agent during program activities.

Contaminants -- For chemicals, impurities present in a commercial grade chemical. For biological agents, other agents that may be present in a commercial product.

Controls -- In toxicology or epidemiology studies, a population that is not exposed to the potentially toxic agent under study.

Cumulative Exposures -- Exposures that may last for several days to several months or exposures resulting from program activities that are repeated more than once during a year or for several consecutive years.

Cytosolic -- Found in the cytoplasm of a cell.

Dams -- Female rats.

Degraded -- Broken down or destroyed.

Degrees of freedom -- In statistics, the number of data elements minus the number of parameters being estimated by a model.

Dermal -- Pertaining to the skin.

Dislodgeable Residues -- The residue of a chemical or biological agent on foliage as a result of aerial or ground spray applications, which can be removed readily from the foliage by washing, rubbing or having some other form of direct contact with the treated vegetation.

Dose-response Assessment -- A description of the relationship between the dose of a chemical and the incidence of occurrence or intensity of an effect. In general, this relationship is plotted by statistical methods. Separate plots are made for experimental data obtained on different species or strains within a species.

Drift -- That portion of a sprayed chemical that is moved by wind off a target site.

EC_{50} -- A concentration that causes 50% inhibition or reduction. As used in this document, this values refers to a 50% inhibition of growth.

EC_{100} -- A concentration that causes complete inhibition or reduction. As used in this document, this values refers to a complete inhibition of growth.

Elimination -- In pharmacokinetics, a term that is usually reserved for decreases in blood and other body tissue due to excretion, distribution, and metabolism.

Empirical -- Refers to an observed, but not necessarily fully understood, relationship in contrast to a hypothesized or theoretical relationship.

Enzymes -- A biological catalyst; a protein, produced by an organism itself, that enables the splitting (as in digestion) or fusion of other chemicals.

Epidemiology Study -- A study of a human population or human populations. In toxicology, a study which examines the relationship of exposures to one or more potentially toxic agent to adverse health effects in human populations.

Exposure assessment -- The process of estimating the extent to which a population will come into contact with a chemical or biological agent.

Extrapolation -- The use of a model to make estimates outside of the observable range.

First order kinetics -- A characteristic of a model in which the proportion of an element such as the amount absorbed, eliminated, or remaining changes at a fixed rate with respect to time.

Formulation -- A commercial preparation of a chemical including any inerts or contaminants.

Frank effects -- Obvious signs of toxicity.

Frank-effect Level (FEL) -- The dose or concentration of a chemical or biological agent that causes gross and immediately observable signs of toxicity.

Gavage -- The placement of a toxic agent directly into the stomach of an animal, using a gastric tube.

Genotoxic -- Causing direct damage to genetic material. Associated with carcinogenicity.

Geometric Mean -- The measure of an average value often applied to numbers for which a log normal distribution is assumed.

Gestation -- The period between conception and birth; in humans, the period known as pregnancy.

Half-time or Half-life -- For compounds that are eliminated by first-order kinetics, the time required for the concentration of the chemical to decrease by one-half.

Hazard Quotient (HQ) -- The ratio of the estimated level of exposure to the RfD or some other index of acceptable exposure.

Hazard identification -- The process of identifying the array of potential effects that an agent may induce in an exposed human population.

Hematological -- Pertaining to the blood.

Hematology -- One or more measurements regarding the state or quality of the blood.

Henry's law constant -- An index of the tendency of a compound to volatilize from aqueous solutions.

Herbaceous -- A plant that does not develop persistent woody tissue above the ground (annual, biennial, or perennial, but whose aerial portion naturally dies back to the ground at the end of a growing season. They include such categories as grasses and grass-like vegetation.

Herbicide -- A chemical used to control, suppress, or kill plants, or to severely interrupt their normal growth processes.

Histopathology -- Signs of tissue damage that can be observed only by microscopic examination.

Hydrolysis -- Decomposition or alteration of a chemical substance by water.

Hydroxylation -- The addition of a hydrogen-oxygen or hydroxy (-OH) group to one of the rings. Hydroxylation increases the water solubility of aromatic compounds. Particularly when followed by conjugation with other water soluble compounds in the body, such as sugars or amino acids, hydroxylation greatly facilitates the elimination of the compound in the urine or bile.

Hyperemia -- An increase in the amount of blood in an organ or region of the body with distention of the blood vessels. This may be caused either by an increase in dilation of the blood vessels (active hyperemia) or a hindrance of blood drainage from the site (passive hyperemia).

Hypoactivity -- Less active than normal.

In vivo -- Occurring in the living organism.

In vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

Inerts -- Adjuvants or additives in commercial formulations that do not directly effect the target species although they may enhance the effectiveness of the active ingredient(s).

Interpolation -- The use of mathematical models within the range of observations

Intraperitoneal -- Injection into the abdominal cavity.

Invertebrate -- An animal that does not have a spine (backbone).

Irritant Effect -- A reversible effect, compared with a corrosive effect.

Lethal Concentration$_{50}$ (LC_{50}) -- A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.

Lethal Dose$_{50}$ (LD_{50}) -- The dose of a chemical calculated to cause death in 50% of a defined experimental animal population over a specified observation period. The observation period is typically 14 days.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of a chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Malignant -- Cancerous.

Metabolite -- A compound formed as a result of the metabolism or biochemical change of another compound.

Metameter -- Literally, the unit of measure. Used in dose-response or exposure assessments to describe the most relevant way of expressing dose or exposure.

Microorganisms -- A generic term for all organisms consisting only of a single cell, such as bacteria, viruses, and fungi.

Microsomal -- Pertaining to portions of cell preparations commonly associated with the oxidative metabolism of chemicals.

Minimal Risk Level (MRL) -- A route-specific (oral or inhalation) and duration- specific estimate of an exposure level that is not likely to be associated with adverse effects in the general population, including sensitive subgroups.

Most Sensitive Effect -- The adverse effect observed at the lowest dose level, given the available data. This is an important concept in risk assessment because, by definition, if the most sensitive effect is prevented, no other effects will develop. Thus, RfDs and other similar values are normally based on doses at which the most sensitive effect is not likely to develop.

Multiple Chemical Sensitivity -- A syndrome that affects individuals who are extremely sensitive to chemicals at extremely low levels of exposure.

Mutagenicity -- The ability to cause genetic damage (that is damage to DNA or RNA). A mutagen is substance that causes mutations. A mutation is change in the genetic material in a body cell. Mutations can lead to birth defects, miscarriages, or cancer.

Nontarget -- Any plant or animal that a treatment inadvertently or unavoidably harms.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of a chemical at which no statistically or biologically significant increases in frequency or severity of adverse effects were observed between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

No-Observed-Effect Level (NOEL) -- The dose of a chemical at no treatment-related effects were observed.

Normal Distribution -- One of several standard patterns used in statistics to describe the way in which variability occurs in a populations.

Octanol-Water Partition Coefficient (K_{ow}) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Ocular -- Pertaining to the eye.

Parenteral -- Any form of injection.

Partition -- In chemistry, the process by which a compound or mixture moves between two or more media.

Pathway -- In metabolism, a sequence of metabolic reactions.

Perennial -- A plant species having a lifespan of more than 2 years.

pH -- The negative log of the hydrogen ion concentration. A high pH (>7) is alkaline or basic and a low pH (<7) is acidic.

Phenolsulfonphthalein -- An organic acid (pK_a = 7.9) used to test kidney function. The compound, which is essentially a non-toxic dye with very well characterized pharmacokinetics, is typically injected into the animal and the rate of elimination in the urine is monitored. A substantial change in the elimination rate may be indicative of an effect on kidney function.

pK_a -- The negative log of the hydrogen ion concentration or pH at which 50% of a weak acid is dissociated.

pK_b -- The negative log of the hydrogen ion concentration or pH at which 50% of a weak base is dissociated.

Pharmacokinetics -- The quantitative study of metabolism (i.e., the processes of absorption, distribution, biotransformation, elimination).

Plasma -- The fluid portion of the blood in which particulates are suspended.

Precommercial thinning -- Cutting in immature stands to improve the quality and growth of the remaining stand.

Prospective -- looking ahead. In epidemiology, referring to a study in which the populations for study are identified prior to exposure to a presumptive toxic agent, in contrast to a retrospective study.

PSP -- see phenolsulfonphthalein.

Release -- A work done to free desirable trees from competition with overstory trees, less desirable trees or grasses, and other forms of vegetative growth.

Reference Dose -- Oral dose (mg/kg/day) not likely to be associated with adverse effects over lifetime exposure, in the general population, including sensitive subgroups.

Reproductive Effects -- Adverse effects on the reproductive system that may result from exposure to a chemical or biological agent. The toxicity of the agents may be directed to the reproductive organs or the related endocrine system. The manifestations of these effects may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions dependent on the integrity of this system.

Resorption -- Removal by absorption. Often used in describing the unsuccessful development and subsequent removal of post-implantation embryos.

Retrospective -- looking behind. In epidemiology, referring to a study in which the populations for study are identified after exposure to a presumptive toxic agent, in contrast to a prospective study.

RfD -- A daily dose which is not anticipated to cause any adverse effects in a human population over a lifetime of exposure. These values are derived by the U.S. EPA.

Right-of-way -- a corridor of low growing shrubs or grasses that facilitate the maintenance and protection of utility power lines and provide transport pathways for humans or wildlife.

Route of Exposure -- The way in which a chemical or biological agent enters the body. Most typical routes include oral (eating or drinking), dermal (contact of the agent with the skin), and inhalation.

Scientific Notation -- The method of expressing quantities as the product of number between 1 and 10 multiplied by 10 raised to some power. For example, in scientific notation, 1 kg = 1,000 g would be expressed as 1 kg = 1 x 10^3 g and 1 mg = 0.001 would be expressed as 1 mg = 1 x 10^{-3}.

Sensitive subgroup -- Subpopulations that are much more sensitive than the general public to certain agents in the environment.

Site preparation -- The removal of competition and conditioning of the soil to enhance the survival and growth of seedlings or to enhance the seed germination.

Species to Species Extrapolation -- A method involving the use of exposure data on one species (usually an experimental mammal) to estimate the effects of exposure in another species (usually humans).

Subchronic Exposure -- An exposure duration that can last for different periods of time, but 90 days is the most common test duration. The subchronic study is usually performed in two species (rat and dog) by the route of intended use or exposure.

Substrate -- With reference to enzymes, the chemical that the enzyme acts upon.

Synergistic Effect -- A situation is which the combined effects of two chemicals is much greater than the sum of the effect of each agent given alone.

Systemic Toxicity -- Effects that require absorption and distribution of a toxic agent to a site distant from its entry point at which point effects are produced. Systemic effects are the obverse of local effects.

Teratogenic -- Causing structural defects that affect the development of an organism; causing birth defects.

Teratology -- The study of malformations induced during development from conception to birth.

Threshold -- The maximum dose or concentration level of a chemical or biological agent that will not cause an effect in the organism.

Toxicity -- The inherent ability of an agent to affect living organisms adversely.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD and similar values from experimental data. UFs are intended to account or (1) the variation in sensitivity among members of the human population; (2) the uncertainty in extrapolating animal data to the case of humans; (3) the uncertainty in extrapolating from data obtained in a study that is less than lifetime exposure; and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10. See table 2-4 for additional details.

Urinalysis -- Testing of urine samples to determine whether toxic or other physical effects have occurred in an organism.

Vehicle -- A substance (usually a liquid) used as a medium for suspending or dissolving the active ingredient. Commonly used vehicles include water, acetone, and corn oil.

Vertebrate -- An animal that has a spinal column (backbone).

Volatile -- Referring to compounds or substances that have a tendency to vaporize. A material that will evaporate quickly.

Xenobiotic -- A chemical that does not naturally occur in an organism. Often applied generically to all synthetic or man-made chemicals.

7. SUBJECT INDEX

APPENDICES

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

Species	Exposure	Response	Reference
		ORAL	
Triclopyr			
Guinea Pig	Single oral (gavage) dose at 126, 252, 500, 1000, or 2000 mg/kg; five male mice per dose; two week post-treatment observation period.	LD_{50} = 310 mg/kg One death at 252 mg/kg and 5/5 deaths at 500 mg/kg.	Olson 1967
Horse Adult Shetland pony geldings, 151-203 kg 3 in control and 6 in each dosed group.	Acid administered by gavage in corn oil:acetone vehicle. Vehicle controls used. Daily doses of 0, 60, and 300 mg/kg for 4 days. Six day post-treatment observation period.	No clinical signs of toxicity at 60 mg/kg [Cumulative dose of 240 mg/kg]. At 300 mg/kg [Cumulative dose of 1200 mg/kg], signs of toxicity included depression and recumbency. Decrease GI activity. Increased and labored respiration with cyanotic mucus membranes in some animals. Ataxia, stiffness and weakness with fine tremors. Slight changes in blood urea nitrogen, blood glucose, serum calcium, and serum iron. Pale liver and swollen kidneys. Mild to moderate hepatosis and cellular swelling and fatty changes around the central veins of the liver. Vacuolar swelling and cast formation in the renal tubules at 300 mg/kg. At 300 mg/kg, 2/6 ponies died on days 5 and 6 of study and a third pony was euthanized on day 5. Another pony, moderately affected, was euthanized on day 6. The remaining 2 ponies were only mildly affected. Estimated LD_{50} = ≃1000 mg/kg.	Osweiler 1983
Mouse, COBS CF_1	Single oral (gavage) dose at 126, 252, 500, 1000, or 2000 mg/kg; five male mice per dose; two week post-treatment observation period.	LD50 = 471 mg/kg	Henck et al. 1979

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

Species	Exposure	Response	Reference
Triclopyr, ORAL (continued)			
Rabbit	Single oral (gavage) dose at 126, 252, 500, 1000, or 2000 mg/kg; five animals per dose; two week post-treatment observation period.	LD_{50} = 550 mg/kg One death at 252 mg/kg; 2/5 deaths at 500 mg/kg; 4/5 deaths at 1000 mg/kg; 5/5 deaths at 2000 mg/kg.	Olson 1967
Rat, Sprague-Dawley	Single oral (gavage) dose at 0, 200, 400, 630, 800, or 1600 mg/kg; 6 rats/sex/dose level; two week post-observation period.	Males: LD_{50} = 729 mg/kg. NOEL ≤ 200 mg/kg LEL = 200 mg/kg Females: LD_{50} = 630 mg/kg. LEL = 200 mg/kg All males at 630 mg/kg had diarrhea; at 800 mg/kg all exhibited lethargy, diarrhea and piloerection. All females at 200 mg/kg exhibited lethargy, piloerection, and a dark exudate around the nose occurred at 630 mg/kg.	Henck et al. 1980
Rat	Single oral (gavage) dose at 126, 252, 500, 1000, or 2000 mg/kg; five rats/sex/dose; two week post-observation period.	LD_{50} = 713 mg/kg No deaths in either sex at or below 500 mg/kg; at 1000 mg/kg, 5/5 deaths in both males and females.	Olson 1967

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

Species	Exposure	Response	Reference
Trichlopyr, butyl ester ether, ORAL (continued)			
Cattle, 2 year old Hereford and Hereford-Angus steers weighting 397-452 kg, 3/dose	Product characterized as 93% TEE. Seven consecutive daily doses of 75 or 150 mg/kg and 5-7 daily doses at 300 mg/kg.	At 75 mg/kg/day [Cumulative dose of 525 mg/kg], GI hypomotility and anorexia in 2/3 animals but no mortality. At 150 mg/kg [Cumulative dose of 1050 mg/kg], anorexia, GI hypomotility, CNS depression, tremors, and rapid respiration. All three animals died on days 9-13 of the study. At 300 mg/kg [Cumulative dose of 1500-2100 mg/kg], anorexia, GI hypomotility, CNS depression, tremors, and rapid respiration. All three animals died on days 5-7 of the study. All but 2 steers at 75 mg/kg/day lost body weight of at least 5% or more. Histopathological examination revealed mild to moderate toxic tubular nephrosis and hepatosis in all fatally exposed animals. Biochemical signs of toxicity included elevated BUN and creatinine, hypokalemia, hypocalcemia and elevated CPK, SGOT, and LDH. All observations in surviving animals made at 15-17 days after the initiation of treatment. Estimated LD_{50}, 742 mg/kg as cumulative dose of $[525 \cdot 1050^{0.5}]$ or about 534 mg/kg expressed as acid equivalents.	Rowe et al. 1980

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

Species	Exposure	Response	Reference
Garlon 3A, ORAL			
Cattle 3/dose	Seven consecutive daily doses of 169 or 338 mg/kg. 5-6 daily doses of 676 mg/kg [Doses as acid equivalents given as 75, 150, and 300 mg/kg.]	At 169 mg/kg/day [Cumulative dose of 1183 mg/kg], GI hypomotility and anorexia but no mortality. At 338 mg/kg [Cumulative dose of 2366 mg/kg], GI hypomotility, anorexia, tremors, malaise, and 1/3 deaths at day 10 of study. At 676 mg/kg [Cumulative dose of 3380-4056 mg/kg], GI hypomotility, anorexia, tremors, weakness, recumbency, and 3/3 deaths within days 5-6 of study. All observations in surviving animals made at 15-17 days after the initiation of treatment.	Anon, no date, form Dow Chemical Company 1987 [appears to be summary of study conducted by Rowe before the cattle study]
Goats, Spanish 3/dose	Seven consecutive daily doses of 225 and 450 mg/kg. 3-5 daily doses of 901 mg/kg [Doses as acid equivalents given as 100, 200, and 400 mg/kg.]	No signs of toxicity and no mortality at daily doses of 225 and 450 mg/kg [cumulative doses of 1575 and 3150 mg/kg]. All animals died after 3-5 doses at 901 mg/kg [Cumulative dose of 2703-4505 mg/kg.] Signs of toxicity included anorexia, weakness, tremors, depression, and recumbency. All observations in surviving animals made at day 17 of study.	Anon, no date, form Dow Chemical Company 1987 [appears to be summary of study conducted by Rowe before the cattle study]

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

Species	Exposure	Response	Reference
Rat	Single oral (gavage) dose at 500, 1000, 2000, 3980, or 7950 (males only) mg/kg; five rats/sex/dose level; two-week post-treatment observation period.	Males: LD_{50} = 2830 mg/kg NOEL = 2000 mg/kg LEL = 3980 mg/kg Female: LD_{50} = 2140 mg/kg NOEL = 1000 mg/kg LEL = 2000 mg/kg Rats of both sexes at 3980 mg/kg and females at 2000 mg/kg dose levels exhibited lethargy and piloerection, with tremors and convulsions in one female each at 3980 and 2000 mg/kg. In males, 0/55 deaths at 2000 mg/kg and 5/5 deaths at 3980 mg/kg.	Keeler et al. 1974

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

Species	Exposure	Response	Reference
Garlon 4, ORAL			
Cattle 3/dose	Seven consecutive daily doses of 122 or 244 mg/kg. 5-6 daily doses of 487 mg/kg [Doses as triclopyr equivalents given as 75, 150, and 300 mg/kg.]	At 122 mg/kg/day [Cumulative dose of 854 mg/kg], GI hypomotility and anorexia in all animals and diarrhea in one animal but no mortality. At 244 mg/kg [Cumulative dose of 1708 mg/kg], GI hypomotility, anorexia, weakness, depression, tremors, diarrhea (in 2 animals), and recumbancy. All animals were euthanized when moribund on days 7-9 of study. At 487 mg/kg [Cumulative dose of 2435-2922 mg/kg], GI hypomotility, anorexia, weakness, depression, tremors, recumbency, and 3/3 deaths within on day 6 of study. All observations in surviving animals made at 15-17 days after the initiation of treatment.	
Goats, Spanish 3/dose	Seven consecutive daily doses of 162 and 325 mg/kg. 2-7 daily doses of 647 mg/kg [Doses as acid equivalents given as 100, 200, and 400 mg/kg.]	Anorexia and diarrhea but no deaths at 162 mg/kg [Cumulative dose of 1134 mg/kg]. Death in 2/3 animals at 325 mg/kg after last dose on day seven [Cumulative dose of 2275 mg/kg]. Death in all 3 animals at 647 mg/kg after 2-7 days [Cumulative doses of 1294-4529 mg/kg]. At these two higher dose levels, signs of toxicity included Anorexia, weakness, tremors, diarrhea, depression and recumbency. All observations in surviving animals made at day 17 of study.	Anon, no date, form Dow Chemical Company 1987 [appears to be summary of study conducted by Rowe before the cattle study]

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

Species	Exposure	Response	Reference
Garlon 4, ORAL (continued)			
Rat	Single oral (gavage) dose at 252, 500, 1000, 2000 or 3980 mg/kg; five rates/sex/dose; two week post-treatment observation period.	Males: LD_{50} = 2460 mg/kg NOEL = 1000 mg/kg LEL = 2000 mg/kg Female: LD_{50} = 2140 mg/kg NOEL = 1000 mg/kg LEL = 2000 mg/kg Rats of both sexes at 3980 mg/kg exhibited lethargy; females at 2000 and 3980 mg/kg had diarrhea.	Lichy et al. 1975
		DERMAL	
Triclopyr			
Rabbit	Single dermal application to shaved intact skin at 2000 mg/kg.	No deaths reported.	Olson 1967
Rabbit	Repeated application of undiluted material to intact and abraded skin; treated area covered.	Essentially non-irritating to intact or abraded skin.	Olson 1967
Garlon 3A			
Rabbit	Single dermal application to shaved intact skin at 3980 mg/kg; 2/sex/dose; two-week post-treatment observation period.	No deaths reported; only slight erythema observed; not other signs of toxicity.	Keeler et al. 1974
Rabbit	Repeated application of 0.5 ml or undiluted material, once daily for 3 days, to intact and abraded skin; treated area covered, 6 animals tested.	Slight erythema and edema.	Keeler et al. 1974

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

Species	Exposure	Response	Reference
Garlon 4, DERMAL			
Rabbit	Single dermal application to shaved intact skin at 3980 mg/kg; 2/sex/dose; two-week post-treatment observation period.	No deaths reported; moderate erythema; severe edema, very slight necrosis; no other signs of toxicity.	Lichy et al. 1975
Rabbit	Repeated application of 0.5 ml or undiluted material, once daily for 3 days, to intact and abraded skin; treated area covered, 6 animals tested.	Slight to moderate erythema, slight edema, slight to moderate necrosis.	Lichy et al. 1975
	OCULAR		
Triclopyr			
Rabbit	undiluted	mild irritation. Slight, transient conjunctival erythema and corneal irritation	Olson 1987 (Shipp et al. 1986)
Garlon 3A			
Rabbit	undiluted	severe conjunctival irritation and moderate to severe corneal damage that persisted at seven days post-instillation	Keeler et al 1974 (Shipp et al. 1986)
Garlon 4			
Rabbit	undiluted	no irritation	Lichy et al. 1975 (Shipp et al. 1986)

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

Species	Exposure	Response	Reference
		INHALATION	
Triclopyr			
Rat	5.34 ppm for 1 hour	no effect	Keeler et al. 1974 (Shipp et al. 1986)
Garlon 3A			
No information available.			
Garlon 4			
Rat	0.82 ppm (particle size = 10 μ) for four hours	nasal irritation; no mortality.	Yakel and Johnson 1980 (Shipp et al. 1986)

Material safety data sheet states that inhalation exposures to Garlon 4 may cause CNS depression attributable to kerosene.

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Dog, Beagle	Exposure: In the diet at concentrations resulting in 0, 5, 10, or 20 mg/kg bw/day for 228 days. Four dogs/sex/dose. Response: At all doses, decreased body weight gain and food consumption, alterations in clinical chemistry enzymes suggestive of altered liver and kidney function, and microscopic changes in liver and kidney morphology; possible transient.	Quast et al. 1976 (MRID 00071793)
Dog, Beagle	Exposure: In the diet at concentrations resulting in doses of 0, 0.1, 0.5, and 2.5 mg/kg bw/day for 183 days. Five doses/sex/dose group. Response: At the highest dose, decreased PSP urinary excretion as well as reduced absolute and relative kidney weight. Complete hematology, chemistry, and histopathology revealed no other treatment-related toxicity. Specifically, there was no increase in serum urea nitrogen at 2.5 mg/kg.	Quast et al. 1977 (MRID 00071794)
Dogs, Beagle	Exposure: In the diet at concentrations resulting in doses of 0, 0.5, 2.5, or 5.0 mg/kg bw/day for 1 year. Triclopyr triethylamine salt, 98%. Response: Significant increases in serum urea nitrogen and creatinine at 2.5 mg/kg. There effects were more pronounced at 5 mg/kg. No effects at 0.5 mg/kg. **This is the basis for the OPP/RfD.**	Quast et al. 1988 (MRID No. 4120031)

Measurements of BUN

	PRE-TREATMENT		AFTER TREATMENT	
Dose	Males	Females	Males	Females
0.0	16	14	16	17
0.5	13	15	18	19
2.5	14	13	22	20
5.0	13	15	27	23

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Monkey, Rhesus	Exposure: Groups of two females/dose were administered 0, 10, 20, or 30 mg/kg bw/day by nasogastric intubation, for 20 days. Response: No treatment-related toxicity or alterations in parameters evaluated.	Molello et al. 1976 (from Shipp et al. 1986)
Mouse, CF-1, 30/dose	Exposure: In the diet at concentrations resulting in doses of 0, 3, 15, or 70 mg/kg bw/day to male mice for nine weeks (63 days). Response: Males mated to two groups of untreated females for one week. Females sacrificed and uterine contents examined for evidence of increased resorptions. No effects on reproductive parameters: fertility indices, average numbers of implantations, and average number of resportions.	Hanley et al. 1980
Mouse, Swiss-Cox, males and females	Exposure: In the diet at concentrations resulting in doses of 0, 6, 20, or 60 mg/kg bw/day for 90 days. Response: In males, slight reduction in relative liver weight at 60 mg/kg. No effects in any other group.	Dow Chemical Co. 1983a
Mouse, 60/sex/dose	Exposure: Triclopyr acid (98%) at dietary levels of 0, 50, 250, and 1250 ppm for 22 months. Resulted in doses of 7.5, 37.5, 187.5 mg/kg bw/day. Response: A 10% decrease in body weight gain at the highest dose. No other signs of toxicity.	Tsuda et al. 1992 (MRID 40356601)
Mouse, CDF_1/Cox, 50/sex/dose	Exposure: Dietary levels of 0, 24, 80, and 240 ppm in the diet (equivalent to 0, 3, 10, or 30 mg/kg bw/day) for two years. Response: Comparable incidence of non-tumor pathology in all groups. Statistically significant increase in benign alveologenic adenomas in male mice at all doses and female mice at the highest dose when compared to study controls.	Molello et al. 1979

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Rabbit, New Zealand 15 females /dose group. 25 females in control group.	Exposure: Daily oral (gavage) doses at 0, 25, 50, or 100 mg/kg bw/day from day 6-18 of gestation period. Response: High maternal mortality at all doses. No evidence of fetotoxicity or teratogenicity in fetuses of surviving does. Teratogenic evaluation not done on fetuses of does that died prior to the 29th day of gestation period.	Smith et al. 1977 (from Shipp et al. 1986)
Rabbit, New Zealand, 2.8-3.8 kg, 20 females/dose group.	Exposure: Daily oral (gavage) doses at 0, 10, or 25 mg/kg bw/day from day 6-18 of gestation period. Response: Some maternal deaths, primarily attributed to enteric disorder but toxicity could not be ruled out in the 25 mg/kg/day dose group. Decrease (not statistically significant) in body weight gain in does at 10 and 25 mg/kg/day. No fetotoxic or teratogenic effects in fetuses attributable to treatment.	Hanley et al. 1984
Rabbit	Exposure: 0, 10, 30, and 100 mg/kg bw/day by gavage as triethlyamine salt (46.5% purity, doses corrected for purity) on days 6-18 of gestation. 16 dams/dose group. Response: Maternal toxicity (decreased body weight gain and decrease food efficiency) at 100 mg/kg. Fetal effects at 100 mg/kg included decreased number of live offspring and increased fetal death.	Bryson 1994b (MRID No. 43217603, U.S. EPA 1995)
Rabbit	Exposure: 0, 10, 30, and 100 mg/kg bw/day by gavage as butoxyethyl ester (96.9% purity, doses corrected for purity) on days 6-18 of gestation. Equivalent to 0, 7, 22, and 72 mg/kg acid equivalents. 16 dams/dose group. Response: Maternal toxicity (some dams died) at 100 mg/kg. Fetal effects at 100 mg/kg included decreased numbers of live fetuses in total and per dam, fetal death, and post-implantation losses. Decreased skeletal ossification in live offspring.	Bryson 1994c (MRID No. 43217601, U.S. EPA 1995)

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, Sprague-Dawley	Exposure: Daily oral (gavage) doses of triclopyr (98.5%) at 0, 50, 100 or 200 mg/kg bw/day from day 6-15 of gestation; 25 females/dose group. Response: Excessive salivation occasionally with dyspnea was associated with incidental deposition of the test material in the oral cavity. Reduced maternal weight gain at 200 mg/kg (17%) and 100 mg/kg (13) accompanied by reduced food consumption. In the 200 mg/kg group, 2 of 277 fetuses had major malformations. Also at 200 mg/kg, delayed ossification of skull bones was statistically significant.	Hanley et al. 1984
Rat	Exposure: 0, 30, 100, 300 mg/kg bw/day by gavage as triethlyamine salt (46.5% purity, doses corrected for purity) on days 6-15 of gestation. 25 dams/dose group. [Doses as acid equivalents: 21.6, 72, 216 mg/kg bw/day.] Response: Maternal toxicity (salivation and one death) at 300 mg/kg. Fetal effects at 300 mg/kg including decreased ossification and skeletal malformations.	Bryson 1994a (MRID No. 43217602, U.S. EPA 1995)
Rats, males and females	Exposure: In the diet at concentrations resulting in doses of 0, 30, 100, 200, or 300 mg/kg bw/day for 14 days. Response: Decreased weight gain at 100 mg/kg in males and at 200 and 300 mg/kg in males and females.	EPA 1984 (from Shipp et al. 1986)
Rat, Sprague-Dawley	Exposure: Three generation feeding study at dietary levels which resulted in daily doses of 0, 3, 10, or 30 mg/kg bw/day. Response: No treatment-related effect on reproductive capacity, litter viability, fetotoxicity, teratogenicity, or growth and maturation of offspring.	Hanley et al. 1976 (MRID 400057084)

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Rat, Sprague-Dawley 23 females and 11-12 male/dose in F_0	Exposure: Dietary levels which resulted in daily doses of 0, 3, 10, or 30 mg/kg bw/day for 8 weeks prior to breeding. Diet maintained during breeding, gestation, and lactation. F_1 and F_2 animals maintained on test diet for 10 weeks prior to breeding. [Use 38 weeks for duration.] Response: No treatment-related effects in terms of toxicity or reproductive ability in any generation.	Hanley et al. 1984
Rat, Sprague-Dawley, males and females	Exposure: Administered in the diet at concentrations which resulted in doses of 0, 3, 10, 30, or 100 mg/kg bw/day diet for 90 days. Response: No treatment related effects in females. In males at 100 mg/kg, decreased growth rate, decreased food consumption, decreased liver weight, and increased relative kidney and brain weights. No treatment related effects in males at doses $\leq$30 mg/kg.	Humiston et al. 1975 (from Shipp et al. 1986)
Rats, F344	Exposure: Administered in the diet at concentrations which resulted in doses of 0, 7, 28, 70, and 350 mg/kg bw/day as butoxyethyl ester for 90 days. 9 animals/sex/dose. Response: Decreased body weight and hematologic changes in males in high dose group. Increased relative kidney and liver weight in males at 28 and 70 mg/kg. Hematologic changes as well as increases in relative liver and kidney weight in females at 7 mg/kg/day. Histopathological changes in the liver and kidney of males at 70 and 350 mg/kg and in females at 350 mg/kg. Systemic LEL of 28 mg/kg for males and $\leq$ 7 mg/kg for females.	Barna-Lloyd et al. 1992 (MRID No. 42274901, U.S. EPA 1995)

Appendix 2: Toxicity of triclopyr after repeated oral administrations.

Species	Exposure/Response	Reference
Rats, F344, 10/sex/dose	Exposure: Administered in the diet at concentrations which resulted in doses of 0, 5, 20, 50, or 250 mg/kg bw/day for 13 weeks (91 days). Response: No overt signs of toxicity. Slight decrease in body weight in females at 250 mg/kg and in males at 50 and 250 mg/kg. Dose/severity related degeneration of the proximal tubules of the kidneys at dose $\geq$20 mg/kg. This was accompanied by an increase in kidney weight. Slight functional changes in kidneys at 250 mg/kg. Centrilobular liver cells of male rats at 250 mg/kg were slightly more eosinophilic than controls. This was accompanied by a slight elevation of SGPT and a decrease in serum proteins.	Landry et al. 1984
Rat, Charles River	Exposure: Administered in the diet to groups of 50 rats per sex per dose at levels which resulted in doses of 0, 3, 10, or 30 mg/kg bw/day for 2 years. Response: No significant differences between control and treated groups of both sexes in mortality, hematology, clinical chemistry, or histopathology. No treatment-related tumors observed.	Dunn et al. 1980 (from Shipp et al. 1986)
Rats, F344, 50/sex/dose	Exposure: Administered in the diet at concentrations which resulted in doses of 3, 12, or 36 mg/kg bw for two years. Response: Significant decrease in hemoglobin, hematocrit, and erythrocyte values, and a significant increase in absolute and relative kidney weights in high-dose males. No carcinogenic effects.	Eisenbrandt et al. 1987 (MRID 40107701, 41200302, 92189021, 921890221)

Appendix 3: Mutagenicity studies on triclopyr.

Organism	Exposure Level	Assay System	Effects	Reference
E. coli	not specified	gene mutation assay systems (not specified)	negative results	Dow Chemical Co. 1983b in U.S. EPA 1995
Salmonella typhimurium	not specified	gene mutation assay systems (not specified)	negative results	Dow Chemical Co. 1983b in U.S. EPA 1995
B. subtillis	not specified	DNA damage assays	negative results	U.S. EPA 1995
Salmonella typhimurium	≤5000 µg/plate	Ames assay	negative results with strains TA98 and TA100	Moriya et al. 1983
rat	not specified	unscheduled DNA synthesis with rat hepatocytes	negative results	U.S. EPA 1995
hamster	not specified	chromosomal aberration test in Chinese hamster cells	negative results	U.S. EPA 1995
hamster	600, 800, 1000, 1200, 1500 µg/mL	CHO/HGPRT assay	negative results	Linscombe and Gollapudi 1988
not specified	not specified	cytoplasmic assays (not specified)	no mutagenicity	Dow Chemical Co. 1983b
mice	0, 28, 90, 280 mg/kg bw	mouse bone marrow micronucleus test for genotoxic activity	no significant increases in the frequencies of micronucleated polychromatic erythrocytes, compared with negative controls; positive controls showed significant increases in polychromatic erythrocytes	Bruce et al. 1985

Appendix 3: Mutagenicity studies on triclopyr.

Organism	Exposure Level	Assay System	Effects	Reference
rats	$5x10^{-3}$, $1.56x10^{-3}$, $5x10^{-4}$, $1.56x10^{-4}$, $5x10^{-5}$, $1.56x10^{-5}$, $5x10^{-6}$M	rat hepatocyte unscheduled DNA synthesis	toxicity to hepatocyte cultures, manifested as granular appearance of hepatocytes, occurred at $1.56x10^{-5}$M and increased in dose related manner until no cells remained viable at $5x10^{-3}$M. Triclopyr did not elicit significant DNA repair in primary cultures	Mendrala and Dryzga 1986

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

Application	Observations	Reference
Triclopyr (not otherwise specified) at 2.2 kg a.i./ha applied in 1983 with and without prescribed burning in 1985, 1986, and 1987. Area: Cross Timbers Experimental Range (CTER) near Stillwater, Oklahoma, 648 ha area composed of blackjack oak, post oak, red cedar, savannas, and prairies.	Increase in the population of cotton rats in all treated areas attributed to improved habitat for the cotton rat - i.e. increase in understory cover and more abundant food. This increase was more pronounced on burned areas. Decrease in numbers of rats with helminth infections in treated areas - more pronounced in areas treated with both herbicide and burning.	Boggs et al. 1991a
see description under Boggs et al. 1991a above	Prevalence of *Cuterebra* (larvae of bot flies) infestations in small mammals (white-footed deer mice, eastern woodrats, harvest mice, and cottontail rabbits) was significantly greater on unburned sites compared to burned sites. This effect could be associated with high soil temperatures during burning.	Boggs et al. 1991b
see description under Boggs et al. 1991a above	Herbaceous forage (forbs and grasses) increased after herbicide application. No effect on nutritional status of bobwhite quail.	Boren et al. 1993

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

Application	Observations	Reference
Triclopyr (commercial formulation of 480 g/L, consistent with Garlon 4) applied to soil (Elkton silt loam - plowed, disced, and harrowed) at rates of 3.4, 6.7, and 10.1 kg/ha by ground sprayer. Treated in May 1988. Site in Prince George's County, MD. Different types of vegetation planted at varying periods after application.	Wheat tolerated all applications by day 8 after application (8 DAA) in terms of visual assessment of injury but yield from untreated plots was about twice that of treated plots. Kidney beans tolerated 3.4 and 6.7 kg/ha applications 82 DAA and no effect on yield was noted. Corn tolerated 3.4 6.7 and 10.1 kg/ha by 8, 47, and 82 DAA. At 3.4 kg/ha, yield was reduced to about 80% of control level. By 82 DAA, squash emerged and grew normally at 3.4 kg/ha. Earlier plantings often resulted in emergence and plant death. At 3.4 kg/ha, the yield of okra sowed 8 DAA was not effected. Potato plant fresh weights from 436 DAA of triclopyr at 3.4 kg/ha were only moderately less (6%) than untreated controls. Bananas evidence signs of injury at all application rates. After 2 years, all cites were covered by indigenous species with no apparent differences between treated and untreated cites. By this time, all crops except bananas tolerated triclopyr residues in soil.	Coffman et al. 1993
Selective foliar application of Garlon 3A at 0.6 and 6 lb a.e./acre to understory vegetation to simulate runoff form targets in an area with very porous soil, a 9% slope, clay content <0.5%.	Estimated soil half time of about 10 days with most residues in the top 10 inches of soil. Very little residue at 10-20 inches. Residues in the top 4 inches of soil at t_0 were about 0.42 ppm.	Deubert and Corte-Real 1986
Pastures treated with triclopyr at 2.2 kg/ha in June of 1983 and burned in late spring of 1985, 1986, and 1987. Stillwater, Oklahoma.	Frequency of horseweed, rosette panicgrass, and little bluestem increased with treatment due to reduction in woody overstory. Pronounced increase in the production of forbs and browse which would likely be beneficial for wildlife habitat.	Engle et al. 1991

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

Application	Observations	Reference
Triclopyr formulation not specified. Soil degradation study in crowley silt loam soil used for growing rice [see Table 1, p. 558 for soil characteristics at different depths.]	Initial soil residues of about 2.4 ppm (mg/kg soil). Soil half lives of about 10 days at 2 cm or 20 cm (silty loam soil) and about 39 days at 60 cm (silty clay loam).	Johnson and Lavy 1994
Triclopyr BBE (probably Garlon 4 or equivalent) at rates of 0.28, 0.56, and 1.12 kg ai/ha on a pasture by backpack sprayer.	Efficacy study on the control of souther wax myrtle. The highest application rate, substantial defoliation and mortality.	Kalmbacher et al. 1993

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

Application	Observations	Reference
Triclopyr (not otherwise specified) at a rate of 4.5 kg ai/ha on pine stands by backpack sprayer at monthly intervals from April to October of 1981. Location: Sierra Nevada Mountains, elev. 1300 m.	Assayed effects on various conifer species. Jeffery Pine: Severe (>60%) damage on all dates of application, and no difference in herbicide tolerance between application dates. A slight tendency for less severe effects with applications in April and may, before new leaves began the rapid phase of growth. Sugar Pine: Maximum damage after June and October applications. Minimum damage after September application. Damage highly correlated with xylem pressure potential. Red Fir: Less injury with applications in spring and most damage from applications in summer. White Fir: Most injury during summer applications with less in May and September. Douglas Fir: Most injury with applications in May and June (period of leader growth) and least injury after applications during a time of maximum water stress. High tolerance	King and Radosevich 1985

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

Application	Observations	Reference
Field evaluation of triclopyr ester (TBEE) toxicity to trout. Lake enclosures treated by backpack application at level of 0.25 to 7.6 mg a.e./L.	Median dissipation times of 4-8 days. Cages Rainbow Trout: All rainbow trout died by day 3 at initial concentrations of 0.69-7.6 mg/L and partial mortality at 0.45 mg/L. No mortality at 0.25 mg/L. At both 0.25 and 0.45 mg/L, significant adverse effects on growth rate of surviving fish. These concentrations represent the maximum-expected concentrations in 5-- and 15 mc deep bodies of water when directly oversprayed at an application rate of 3.84 kg/ha. Native Uncaged Brook Trout: No indication of mortality or changes in population density. Some indication, however, that growth of may have been inhibited. Native Invertebrates: Only transient increase in drift. At a stream collection station 15 m downstream from the lake, the maximum measured concentration of TBEE was 0.61 mg/L, which declined to <0.05 mg/L within 40 minutes.	Kreutzweiser et al. 1995
Soil column leaching studies with loam or quartz sand with triclopyr salt (99.1%), triclopyr BEE, or Garlon 4. Water added to every column every other day to simulate 2.5 cm of precipitation.	Residues found only in top 10-cm of loam soil after 54 days. Most (85%) of triclopyr metabolized to 3,,5,6-trichloro-2-pyridinol with some (10%) formation of 2-methoxy-3,5,6-trichloropyridine. In sand, 65% of the applied triclopyr (acid) leached through column after 54 days. All TBEE leached through the sand column by day 34. Very little metabolism in sand for either compound.	Lee et al. 1986

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

Application	Observations	Reference
Leaf uptake studies of triclopyr and TBEE in wheat, barley, and chickweed.	Hydrolysis of TBEE essentially complete after 3 days and half-life TBEE was <12 hours in each species. The sensitivity of each species appeared to be best associated with the rate of metabolism of the triclopyr acid for wheat (12 hour, tolerant), barley (24 hour, moderately tolerant), and chickweed (48 hour, sensitive).	Lewer and Owen 1990
Triclopyr, ^{14}C-labeled on the pyridine ring at 2.5 mg/L in water.	Blue gill sunfish exposed for 96 hours had maximum residues in edible flesh of 0.13 mg/kg (BCF=0.0.05). The maximum whole body residue was 2.33 mg/kg (BCF $\simeq$ 1). The principal metabolites were the pyridinol and pyridine analogues.	Lickly and Murphy 1987
see description under Boggs et al. 1991a above	Oak overstory replaced by elm and eastern red cedar. Understory dominated by pioneer forbs and grasses. Effects on cotton tail rabbits examined. Compared to untreated controls, triclopyr did not influence body mass or size of rabbits and had no effect on kidney fat or relative kidney weight. A slight but statistically significant increase in relative mass of the spleen on triclopyr treated areas with or without burning compared to untreated area. This difference was not significant when compared to burned areas without herbicide treatments.	Lochmiller et al. 1995
Combination of Garlon/Tordon at 11.7 L/ha and 18.7 L/ha. Formulation of Garlon not specified. Applied along a power-line corridor in Ohio in late June of 1990.	After one year, less plant coverage relative to control. A lesser but still noticeable effect after two years. Treatment favored germination of annuals rather than perennial herbs and vines. Relatively rapid recovery of trees.	Luken et al. 1993

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

Application	Observations	Reference
see description under Boggs et al. 1991a above	Increase in population density of woodrats on triclopyr treated site compared to control site associated with an increase in forage and nest-building material. No significant differences in sex and age ratios between triclopyr and triclopyr/burn sites. No effect on reproductive activity. No effect on testes or seminal vesicle gland weights for either triclopyr and triclopyr/burn sites compared to controls. No effect of treatment on body mass or stomach content weights.	McMurry et al. 1993a
As above.	Detailed study of rat diets in treated and untreated areas. In general, forb and browse diet classes were used in accordance with availability - i.e. eastern woodrats are opportunistic feeders.	McMurry et al. 1993b
As above.	Increase in population density and reproductive activity of cotton rats. This was associated with an increase in herbaceous dicots, compared to the untreated plot. Nutritional quality of herbaceous vegetation may have been enhanced by annual burning.	McMurry et al. 1994
Hand sprayer application of triclopyr BEE at rates of 0.56, 1.12, and 2.24 kg/ha. [Whether these are acid equivalents is not specified. Assume not for risk assessment.] Area: Washington, Texas, huisache plants about 1-2 meters tall (about 800/ha) on a Bleiblerville clay.	Triclopyr BEE caused no mortality in target plant (huisache) but caused a modest reduction in canopy at the two high application rates. Grasses were favored over broadleafs at the middle dose but no effect on either was seen at the low dose.	Meyer and Bovey 1990

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

Application	Observations	Reference
Laboratory studies on washoff using Garlon 4.	When applied in a manner simulating 2.24 kg ai/ha in 28 liters of water and allowed to dry for one hour, 62% of applied triclopyr could be washed off. When allowed to dry for 2 days, only 11-17% could be washed off after simulated rains of 0.75-3.5 mm.	Michael et al. 1992
Laboratory study with soil from a mixed wood clear cut. Triclopyr, as Garlon 4) added at levels of 10, 50, 100, 500, 1000, and 5000 ppm (dry weight). Emergence of seedlings naturally occurring in the soil was monitored.	Substantial inhibition of *Rubus* spp, other dicots and monocots at all concentrations of 50 ppm and above. No substantial inhibition at 10 ppm. At levels of 500 ppm and above, no germination. The concentration of 10 ppm is essentially a NOEL and 50 ppm a FEL. Apparently, a very steep dose/response relationship.	Morash and Freedman 1989
Stem injection of oak trees. Application rate as wgt/area not specified.	Soil levels of triclopyr peaked after 2 months at 2.59 mg/kg (dry weight) associated with defoliation. A lesser peak at about 1 mg/kg after 5 months, could have come from bark or small branch litterfall.	Neary et al. 1988
Laboratory efficacy study to control eurasian watermilfoil, an aquatic macrophyte. Levels of 0.25-2.5 mg a.e./L (as Garlon 3A) over time periods of 2-48 hrs.	Very little effect at any concentration for exposure periods less than 6 hours. At 0.25 mg/L, effective control was associated with exposure periods of 24 (partially effective) to 72 (very effective) hours.	Netherland and Getsinger 1992

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

Application	Observations	Reference
Aerial application of triclopyr salt (2.2 and 4.4 kg/ha) or triclopyr BEE (1.65-3.3 kg/ha) to Oregon brushfields on clay loam soils.	Foliar $t_{½}$s ranging from about 20 to almost 300 days, depending on formulation and type of residue (crown, browse, and litter). Average initial concentrations - including both forms as well as 2,4-D and picloram) on crowns was 44 mg/kg per kg/ha applied. Residues were lower on browse (17.1) and litter (32.1). No evidence of soil leaching from an adjacent up-slope treatment area. Soil concentrations of triclopyr (both forms) ranged from about 0.3-0.7 mg/kg at 37 days to not detectable to about 0.03 mg/kg by 325 day. Somewhat higher levels of ester than amine salt (Table V, p. 581).	Newton et al. 1990
Garlon 3A, 2.2 and 4.4 kg/ha by aerial application.	Vegetative hardwood and shrub cover over 1.5 meters in height virtually eliminated. Differences in height and cover were apparent at 9 years after application.	Newton et al. 1992a [NJAF 9:126]
Garlon 3A, 2.2 and 4.4 kg/ha by aerial application.	Conifers dominated over hardwoods. Some injury to conifers at the higher application rate.	Newton et al. 1992b [NJAF, 9:130]
Triclopyr (formulation not specified) at 3.4 kg a.e./ha with a polyglycol surfactant by helicopter. A hill-pastures in western Oregon with a 34% slope and silt clay loam soils. Stream adjacent to application site. No spray boundary used.	Initial soil residues of about 0.02 mg/kg which increased on day 180 to 0.93 mg/kg, presumably due to washoff. [Kinetic data at different depths given.] Soil half time of about 75 days. Most residues in the top 15 cm of soil. Only trace amounts of metabolites detected. Stream levels peaked at 95μg/L in the first 20 hours after application. In the first significant rain after application, maximum residues were 12 μg/L. The peak level over several months was 15 μg/L.	Norris et al. 1987

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

Application	Observations	Reference
Triclopyr at 10.1 kg a.e./ha with a polyglycol surfactant by hand held boom sprayer. A hill-pastures in western Oregon with a 15% slope and silt clay loam soils.	Initial triclopyr grass levels of 527 mg/kg. Levels of pyridinol and pyridine metabolites were about 0.5% and 0.02%, respectively, of those of triclopyr. Half time of < 7 days [kinetic data given] in grass. By one year after treatment, grass levels of triclopyr were about 1.3 mg/kg. Initial soil residues of about 0.55 mg/kg which peaked on day 28 to 3.1 mg/kg, presumably due to washoff. Soil half time of about 81 days. Most residues in the top 15 cm of soil. [Kinetic data at different depths given.] Only trace amounts of metabolites detected.	Norris et al. 1987 This is the same paper as the previous entry but a different site.
Triclopyr at 0.4 and 0.8 kg ai/ha by backpack sprayer to 3 cultivars of rice.	Moderate injury (primarily leaf necrosis, chlorosis, and stunting) to all three cultivars at both rates of application with a dose/dependent decrease in yield.	Pantone and Baker 1992
Triclopyr (RELEASE/TBEE) at nominal rates of 0.4, 1.26, 2.12, 2.98, and 3.84 kg a.e./ha by backpack sprayers (VMD=1089 μm) in early fall to clear-cuts in New Brunswick.	Plots assayed two growing seasons after application evidenced shallow dose/response patterns in terms of decreased crown area.	Pitt et al. 1993
Soil adsorption studies.	Adsorption decreased as organic matter deceased and pH increased.	Pusino et al. 1994
see above description for Boggs et al. 1991a	No treatment related effects on bird density. Types of birds varied from control based on habitat preference.	Schulz et al. 1992
see description under Boggs et al. 1991a above	Greater bird density and species richness in autumn and winter on herbicide plots.	Schulz and Leslie 1992

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

Application	Observations	Reference
Triclopyr BEE at 1.9 kg/ha by aerial application on whole-tree clearcut in north Maine.	Stream water draining from clearcut had peak concentration of 56 μg/L, immediately after application, and 48 μg/L after an 11-mm rain which occurred 6 days after application. Below a 450 m buffer, the highest stream concentration was 11 μg/L. Over a 298 day monitoring period, estimated losses to watershed were estimated at 0.02% of applied triclopyr.	Smith and McCormack 1988
Triclopyr at 1.9 kg/ha by aerial application on whole-tree clearcut in north Maine.	Treatment increased the concentration of nitrate and Ca in the water of moderately well drained soils and in streams. Effect is secondary to decreased vegetation.	Smith et al. 1988
Triclopyr rates of 0.03 and 0.06 kg/ha on cotton to simulate drift. Fine sandy loam soil in Mississippi.	Higher application rate decrease height of cotton when applied to pin-head square but not early-bloom. Effects not seen at lower application rate. Both application rates delayed crop maturity and lowered yield.	Snipes et al. 1991
Garlon 4E (butoxyethanol ester, 480 g a.e./L) at nominal application rate of 3 kg/ha to sand and clay soils (slope of 7-8%) in northern Ontario.	Actual application rates estimated at 3.28 and 2.85 kg/ha on sand and clay sites, respectively. $t_{½}$ for both soil types was about 2 weeks. After four weeks, however, soil levels were less than 10% of t_0 levels and did not decline further of the 48 week observation period [about 55 μg/kg in sand and 35 μg/kg in clay]. More than 97% of the applied triclopyr remained in the top 15 cm of soil, even after heavy rains. No evidence of lateral soil transport. Very low concentrations of triclopyr in runoff water (<1μg/L) from 1-150 days after treatment.	Stephenson et al. 1990
Triclopyr at 0.3, 0.4, or 0.6 kg/ha plus X-77, a surfactant, applied to cotton.	When applied to early booting stage, there was a dose/related decrease in yields. When applied to three- to four-leaf rice, hyponasty was observed.	Street et al. 1992

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

Application	Observations	Reference
see description under Boggs et al. 1991a above	Effective control of dominant overstory brush species, blackjack oak and post oak. Less effective against American elm, gum burnelia, hackberry, roughleaf dogwood, buckbrush, and eastern redcedar.	Stritzke et al. 1991
Garlon 4, aerial application at 3.67 kg a.e./ha over a forest stream.	Initial peak water levels of 0.23-0.35 mg/L as TBEE. Average concentration in stream during first 12-14 hours was 0.05-0.11 mg/L. Within 72 hours, residues were <0.001 mg/L, the limit of detection. No pyridinol residues were found at the limit of detection, 0.05 mg/L.	Thompson et al. 1991
Triclopyr BEE (RELEASE) applied by backpack sprayer (VMD of 1089 μm and application volume of 4.32 L/min) at application rates of 0.4, 1.26, 2.12, 2.98, and 3.84 kg ai/ha to sites predominated by sugar maple with other shrub species.	Good kinetic description of foliar deposition and residues [see Table 4, p. 2256 of paper]. Foliar half times of 1.1-1.4 days for BEE and 2.6-5.7 days for triclopyr acid.	Thompson et al. 1994
Garlon 4 directly applied to stream as a point source to yield initial concentrations in water of 0.8 and 2.7 mg/L. This was intended to mimic bodies of water 50 and 15 cm deep inadvertently sprayed with TBEE at a rate of 4 kg/ha.	Maximum concentrations of TBEE in stream water of 0.848 and 0.949 mg/L. TBEE rapidly converted to triclopyr. Periods of exposure to concentrations in excess of 0.001 mg/L were less than or equal to 120 minutes, depending on the speed of the stream flow. Invertebrate drift was increased by 3-4 fold but invertebrate abundance was not affected. Species monitored included *Plecoptera*, *Trichoptera*, *Chironemidae*, *Ceratopagonidae*, and *Tipulidae*.	Thompson et al. 1995

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

Application	Observations	Reference
Triclopyr BEE at 2.3 kg a.e./ha (with surfactant and diesel oil in water) applied to sites in Idaho dominated by shinyleaf ceanothus. Silt or silty loam soil.	Initial foliar residues of 362 mg/kg with a 42% decline in one day [see Table 1, p 663 of paper for residues and kinetic data for different plant species. Also see Table 2, p. 554, for kinetic analyses].	Whistenant and McArthur 1989
Garlon 3A applied to lake in Georgia at a rate of 2.5 mg a.e./L.	Day 0 concentration close to nominal application rate. First order $t_{½}$s of 3.3, 3.5, and 0.4 days on different plots. Variability in decay rates attributed to different hydrodynamic conditions and native vegetation. Only trace amounts of pyridinol metabolite found. Sediment residues of 0.1-0.64 mg/kg. Some bioconcentration by aquatic plants (3.3-5.7 mg/kg) with first order dissipation ($t_{½}$ of about 4 days). No detectable residues in fish (<0.1 mg/kg). The pyridinol metabolite was detected in trace quantities (<0.05 mg/kg). Minor bioconcentration in crayfish (4.87 mg/kg on day 0) with first order elimination ($t_{½}$ of about 7 days). Also some bioconcentration in clams (2.5 mg/kg on day 0) with first order elimination ($t_{½}$ of about 2 days).	Woodburn et al. 1993

Appendix 5. Acute Toxicity of Triclopyr to Birds

Formulation	Species	Nature of Exposure	Exposure Time	Effects	Reference
Triclopyr	mallard duck	acute oral	NS	LD_{50} = 1698 ppm	WSSA 1983
Garlon 3A	mallard duck	acute oral	NS	LD_{50} = 3176 ppm	WSSA 1983
Garlon 4	mallard duck	acute oral	NS	LD_{50} = 4640 ppm	WSSA 1983
Triclopyr	mallard duck	subchronic oral	8 days	LC_{50} >5000 ppm	Dow Chemical Co. 1983a
Triclopyr	bobwhite quail	subchronic oral	8 days	LC_{50} = 2935 ppm	Dow Chemical Co. 1983a
Triclopyr	Japanese quail	subchronic oral	8 days	LC_{50} = 3278 ppm	Dow Chemical Co. 1983a
Triclopyr (triethylamine salt)	mallard duck	subchronic oral	8 days	LC_{50} >10,000 ppm	Dow Chemical Co. 1983a
Garlon 3A	bobwhite quail	subchronic oral	8 days	LC_{50} = 11,622 ppm	Dow Chemical Co. 1983a
Triclopyr (triethylamine salt)	mallard duck	subchronic oral	8 days	LC_{50} >10,000 ppm	Dow Chemical Co. 1983a
Garlon 3A	bobwhite quail	subchronic oral	8 days	LC_{50} = 9026 ppm	Dow Chemical Co. 1983a

NS = Not specified.

Appendix 6. Toxicity of Triclopyr to Fish and Amphibians

Formulation	Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
			FISH		
Triclopyr (butoxyethyl ether)	rainbow trout	static bioassay	96 hours	LC_{50} = 0.74 ppm	Dow Chemical Co. 1983a
Triclopyr (triethylamine salt)	rainbow trout	static bioassay	96 hours	LC_{50} = 552 ppm	Dow Chemical Co. 1983a
Garlon 3A	bluegill	static bioassay	96 hours	LC_{50} = 891 ppm	Dow Chemical Co. 1983a
Garlon 4	coho salmon (juvenile)	static bioassay	96 hours	LC_{50} = 2.7 ppm	Wan et al. 1991
Garlon 4	pink salmon (juvenile)	static bioassay	96 hours	LC_{50} = 1.3 ppm	Wan et al. 1991
Garlon 4	rainbow trout (juvenile)	static bioassay	96 hours	LC_{50} = 1.8 ppm	Wan et al. 1991
Garlon 4	sockeye (fingerling)	static bioassay	96 hours	LC_{50} = 1.4 ppm	Servizi et al. 1987
Garlon 4	sockeye (fry)	static bioassay	96 hours	LC_{50} = 1.2 ppm	Servizi et al. 1987
Garlon 4	rainbow trout (fry)	static bioassay	96 hours	LC_{50} = 2.2 ppm	Servizi et al. 1987
Garlon 4	coho salmon (fry)	static bioassay	96 hours	LC_{50} = 2.2 ppm	Servizi et al. 1987
Garlon 4	rainbow trout	flow-through	1 hour 6 hours 24 hours	LC_{50} = 22.5 ppm LC_{50} = 1.95 ppm LC_{50} = 0.79 ppm	Kreutzweiser et al. 1994
Garlon 4	chinook salmon	flow-through	1 hour 6 hours 24 hours	LC_{50} = 34.6 ppm LC_{50} = 4.7 ppm LC_{50} = 1.76 ppm	Kreutzweiser et al. 1994
Garlon 4	coho salmon (juvenile)	flow-through	96 hours	LC_{50} = 0.84 ppm	Johansen and Green 1990

Appendix 6. Toxicity of Triclopyr to Fish and Amphibians

Formulation	Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Garlon 4 (ethylene glycol butyl ether ester formulation)	coho salmon (juvenile)	flow-through respirometer	96 hours	lethargy occurred at concentrations >0.56 mg/L then regressed to highly distressed condition characterized by elevated oxygen uptake and death; at 0.32-0.43 mg/L fish were lethargic with reduced oxygen uptake; at concentrations ≤0.10 mg/L fish were hypersensitive to stimuli and activity levels and oxygen uptake were increased during photoperiod transitions	Johansen and Green 1990
Triclopyr (triethylamine salt)	fathead minnow	static bioassay	96 hours	LC_{50} = 245 ppm (224-269 ppm)	Mayes et al. 1984
Triclopyr (triethylamine salt)	fathead minnow	flow-through test	96 hours	LC_{50} = 120 ppm (104-140 ppm)	Mayes et al. 1984
Triclopyr (triethylamine salt)	fathead minnow	flow-through test	192 hours	LC_{50} = 101 ppm (88.5-116 ppm)	Mayes et al. 1984

Appendix 6. Toxicity of Triclopyr to Fish and Amphibians

Formulation	Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Triclopyr (triethylamine salt)	fathead minnow (embryo-larval stages)	flow-through test	31 days	at 114 ppm (measured), larval survival (2.1% at 28 days) significantly less than controls (79% at 28 days). No difference between treatment groups and controls in day-to-hatch (day 3), hatchability of embryos, normal larvae at hatch, and growth	Mayes et al. 1984
Triclopyr	rainbow trout	static bioassay	96 hours	LC_{50} = 117 ppm	Dow Chemical Co. 1983a
Triclopyr	bluegill	static bioassay	96 hours	LC_{50} = 148 ppm	Dow Chemical Co. 1983a
Garlon 3A	rainbow trout	static bioassay	96 hours	LC_{50} >100 ppm	Johnson and Finley 1980
Garlon 3A	bluegill	static bioassay	96 hours	LC_{50} >100 ppm	Johnson and Finley 1980
Garlon 3A	coho salmon, juvenile	static bioassay	96 hours	LC_{50} = 400 ppm	Janz and Farrel 1991
Garlon 3A	coho salmon, juvenile	static bioassay	96 hours	LC_{50} = 2.4 ppm	Janz and Farrel 1991
Garlon 3A	Rainbow trout	static for lethality studies, flow through Y-maze for avoidance studies	96 hours for LC_{50}s and 0.5 hours for avoidance test	Threshold for behavioral changes = 200 ppm LC_{50} = 400 ppm Threshold for avoidance response = 800 ppm	Morgan and Vigers 1991

Appendix 6. Toxicity of Triclopyr to Fish and Amphibians

Formulation	Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
Garlon 4	Rainbow trout	static bioassay for LC_{50}, flow through Y-maze for avoidance studies	96 hours for LC_{50}s and 0.5 hours for avoidance test	Threshold for behavioral changes = 0.6 ppm LC_{50} = 2.4 ppm Threshold for avoidance response = 19.2 ppm	Morgan and Vigers 1991

See also Table4-1 in text adapted from Wan et al.1987.

Appendix 6. Toxicity of Triclopyr to Fish and Amphibians

Formulation	Species	Nature of Exposure	Exposure Time	Effects[a]	Reference
			AMPHIBIANS		
Garlon 4	Embryos and tadpoles of *Rana pipiens* (leopard frog), *Rana clamitans* (green frog), and *Rana catesbeiana* (bullfrog).	static with aeration, 15° in darkness (to prevent hydrolysis of triclopyr BEE)	Exposures to 0.6, 1.2, and 4.6 ppm (triclopyr a.e.). Little evidence of hydrolysis. No effect on hatching success, malformations, or subsequent avoidance behavior of embryos. Newly hatched tadpoles died or became immobile after exposure to the two higher concentrations. Approximate EC_{50} for response to prodding was between 1.2 and 4.6 ppm after a 24 hour exposure period.	Berrill et al. 1994

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

Appendix 7. Toxicity of Triclopyr to Aquatic Invertebrates

Formulation, type of assay	Species	Exposure Time	Effects[a]	Reference
Garlon 3A, static	shrimp (crustacea)	96 hours	LC_{50} = 895 ppm	Ghassemi et al. 1981, WSSA 1983
Garlon 3A, static	crab (crustacea)	96 hours	LC_{50} >1000 ppm	Ghassemi et al. 1981, WSSA 1983
Garlon 3A, static	oyster (molusca)	48 hours	56 ppm < LC_{50} < 87 ppm	Ghassemi et al. 1981, WSSA 1983
Garlon 4, static test	*Daphnia pulex*	96 hours	EC_{50} = 1.2 ppm	Servizi et al. 1987
Triclopyr (triethylamine salt), static test	cladocera (*Daphnia magna*; crustacea)	48 hours	LC_{50} = 1170 ppm (1030-1340 ppm) no animals killed at <336 ppm; all died at >2000 ppm; water pH = 7.7-8.0; temperature = 66.7-68.5°F (19.6-20.3°C)	Gersich et al. 1984
Triclopyr (triethylamine salt), static renewal (3 times/week)	cladocera (*Daphnia magna*; crustacea)	21 days	LC_{50} = 1140 ppm (950-1590 ppm) water pH = 7.8-8.1; temperature = 66.2-69.8°F (19-21°C)	Gersich et al. 1984
Triclopyr, NOS, artificial stream	Epeorus sp., aquatic insect	up to 2 hours	32 mg/L - increased drift, about 20%, a factor of 2 over controls by 2 hours. 320 mg/L - increased drift, about 60%, a factor of 6 over controls by 2 hours.	Kreutzweiser and Capell 1992
Triclopyr, NOS, artificial stream	Isogenoides and Hydropsyce (caddisfly) sp.	24 hours	32 mg/L - no significant increase in mortality. 320 mg/L - Significant increase in mortality	Kreutzweiser and Capell 1992

Appendix 7. Toxicity of Triclopyr to Aquatic Invertebrates

Formulation, type of assay	Species	Exposure Time	Effects[a]	Reference
Garlon 4 (units of exposure as ester), flow through system	Ephemeroptera *Heptagenia flavescens* *Isonychia sp.* *Epeorus vitrea* Plecoptera *Acroneuria abnormis* *Pteronarcys sp.* *Paragnetina sp.* *Isogenoides sp.* Trichoptera *Pycnopsyche guttifer* *Dolophilodes distinctus* (6 hr) *Hydropsyche sp.* Odonata *Ophiogomphus carolus* Diptera *Simulium sp.*	1 hour exposure, mortality assessed at 48 hours except as noted, 6 hours for *D. distinctus* because of high mortality at 24 hours.	LC_{50} > 320 mg/L LC_{50} > 320 mg/L LC_{50} > 320 mg/L LC_{50} > 320 mg/L LC_{50} > 290 mg/L LC_{50} > 320 mg/L LC_{50} 302.9 (249-370) slope = 3.38 LC_{50} > 290 mg/L LC_{50} 61.7 (21.8-126) LC_{50} > 290 mg/Lslope = 2.22 LC_{50} > 320 mg/L LC_{50} 0.6 (0.07-1.27) slope = 1.14	Kreutzweiser et al. 1992
Garlon 4 (units of exposure as ester), artificial stream.	*Isonychia sp.*, *Epeorus vitrea*, *Hydropsyche sp.*, and *Isogenoides sp.*	1 hour exposures	320 mg/L - Significant increase in stream drift for all species except *Hydropsyche* sp. Significant increase in mortality for *Epeorus vitrea* and *Isogenoides* sp. 32 mg/L - Significant increase in stream drift only for *Isogenoides* sp. Not seen in this species at 3.2 mg/L.	Kreutzweiser et al. 1992
Garlon 4 (units of exposure as ester), artificial stream	*Dolophilodes distinctus*	1 hour exposures	Significant increase in stream drift at 3.2 mg/L but not at 0.32 mg/L.	

[a]Values in parentheses are 95% confidence limits.
NS = Not specified.

Appendix 8: Toxicity of triclopyr and to aquatic algae

Species	Endpoint	Reference
	Triclopyr	
Cyclotella meneghiana, green algae	-15% inhibition at 2.6 mg/L	Peterson et al. 1994 [Inhibition of carbon fixation after 24 hours. Negative values indicate stimulation.]
Nitzschia sp., green algae	-4% inhibition at 2.6 mg/L	
Scenedesmus quadricauda, green algae	13% inhibition at 2.6 mg/L	
Selenastrum capricornutum, green algae	-24% inhibition at 2.6 mg/L	
Microcystis aeruginosa, cyanobacter	-10% inhibition at 2.6 mg/L	
Microcystis aeruginosa, cyanobacter	-2% inhibition at 2.6 mg/L	
Oscillatoria sp., cyanobacter	-9% inhibition at 2.6 mg/L	
Pseudoanabaena sp, cyanobacter	13% inhibition at 2.6 mg/L	
Anabaena inaequalis, cyanobacter	-4% inhibition at 2.6 mg/L	
Aphanizomenon flos-aquae, cyanobacter	-34% inhibition at 2.6 mg/L	
Lemna minor, duckweed	23% inhibition at 2.6 mg/L	