Clopyralid (Transline) - Final Report

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TABLE OF CONTENTS

TABLE OF CONTENTS (*continued*)

TABLE OF CONTENTS (*continued*)

APPENDICES

WORKSHEETS

LIST OF TABLES

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

a.e.	acid equivalents
a.i.	active ingredient
AEL	adverse-effect level
ACGIH	American Conference of Governmental Industrial Hygienists
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
F	female
F_1	first filial generation
g	gram
HQ	hazard quotient
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	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
mM	millimole
MW	molecular weight
MOS	margin of safety
MSDS	material safety data sheet
NCI	National Cancer Institute
NIOSH	National Institute for Occupational Safety and Health

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NOS	not otherwise specified
NRC	National Research Council
OPP	Office of Pesticide Programs
OPPTS	Office of Pesticide Planning and Toxic Substances
OSHA	Occupational Safety and Health Administration
ppm	parts per million
RBC	red blood cells
RfD	reference dose
ROW	right-of-way
UF	uncertainty factor
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
WHO	World Health Organization
µ	micron
>	greater than
≥	greater than or equal to
<	less than
≤	less than or equal to
=	equal to
≃	approximately equal to
~	approximately

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

To convert ...	Into ...	Multiply by ...
acres	hectares (ha)	0.4047
acres	square meters (m^2)	4,047
atmospheres	millimeters of mercury	760
centigrade	Fahrenheit	1.8C°+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 acre (lb/acre)	mg/square meter (mg/m^2)	112.1
pounds per acre (lb/acre)	µg/square centimeter ($µg/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

Program Description

The USDA Forest Service uses the herbicide, clopyralid, in its vegetation management programs. Only one commercial formulation, Transline, is used by the Forest Service. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using clopyralid in future Forest Service programs.

Clopyralid is a selective herbicide used primarily in the control of broadleaf weeds. The Forest Service uses only a single commercial formulation of clopyralid, Transline. Transline is a liquid formulation of clopyralid that is manufactured by DowAgro and contains 40.9% clopyralid as the monoethanolamine salt and 59.1% inert ingredients. One of the inerts is identified as isopropyl alcohol. The amount of isopropyl alcohol in the formulation as well as the identity of the other inerts is considered proprietary. The Forest Service uses Transline almost exclusively in noxious weed control. Relatively minor uses include rights-of-way management, wildlife openings, and facilities maintenance. Although clopyralid may be applied as the sole herbicide in some situations, it is also sometimes applied by the Forest Service in combination with 2,4-D or 2,4-D and picloram. The most common methods of ground application for Transline involve backpack (selective foliar) and boom spray (broadcast foliar) operations. Although Transline is registered for aerial applications, the Forest Service does not and does not intend to use Transline in aerial applications. The typical application rate in Forest Service programs is 0.1 lb a.e./acre. The range of application rates that are likely to be used in Forest Service programs is 0.01 to 1 lb a.e./acre.

Technical grade clopyralid contains hexachlorobenzene and pentachlorobenzene as contaminants. Nominal or average concentrations of hexachlorobenzene are less than 2.5 ppm. Nominal or average concentrations of pentachlorobenzene are less than 0.3 ppm. Because hexachlorobenzene is classified as a potential human carcinogen and because it is very persistent in the environment, the consequences of this contamination is addressed quantitatively in the human health risk assessment.

Human Health Risk Assessment

Although no information is available on the toxicity of clopyralid to humans, the toxicity of clopyralid has been relatively well-characterized in mammals. All of this information is contained in unpublished studies submitted to the U.S. EPA as part of the registration process for clopyralid.

Two different manufacturing processes may be used for clopyralid: the penta process and the electrochemical process. The limited available information indicates that technical grade clopyralid samples from the electrochemical process may be somewhat more toxic (LD50 values in the range of about 3000 mg/kg) than the penta process (LD50 > 5000 mg/kg). These differences, however, are not substantial and may be due to random variability. Clopyralid also has a low order of chronic toxicity. On chronic or subchronic exposures, no effects have been

observed in laboratory mammals as doses of 50 mg/kg/day or less. At doses of 100 mg/kg/day or greater, various effects have been observed in different species and different bioassays. These effects include weight loss, changes in the weight of the liver and kidney, thickening of epithelial tissue, irritation of the lungs, and decreases in red blood cell counts.

Although technical grade clopyralid has been subject to several chronic bioassays for carcinogenicity and none of the bioassays have shown that clopyralid has carcinogenic potential, technical grade clopyralid does contain low levels of hexachlorobenzene. Hexachlorobenzene has shown carcinogenic activity in three mammalian species and has been classified as a potential human carcinogen by the U.S. EPA.

No occupational exposure studies are available in the literature that involve the application of clopyralid. Consequently, worker exposure rates are estimated from an empirical relationship between absorbed dose per kilogram of body weight and the amount of chemical handled in worker exposure studies on nine different pesticides (Rubin et al. 1998). Separate exposure assessments are given for backpack and boom spray ground applications. For these two groups, the central estimates and also the lower and upper estimates of exposure are similar: 0.0013 mg/kg/day for backpack workers and 0.0022 mg/kg/day for boom spray applicators. Although some clopyralid formulations are labeled for aerial application, the Forest Service is not using and does not plan to use that application method. Consequently, aerial applications are not considered in this risk assessment.

For the general public, all of the chronic or longer term exposure scenarios lead to levels of exposure that are below those for workers. The highest dose associated with any of the longer term exposure scenarios for the general public involves the consumption of contaminated fruit with exposure estimates of 0.0005 (0.00004 to 0.059) mg/kg/day. The accidental exposure scenario involving the consumption of contaminated water results in a central estimate of exposure of up to 0.023 mg/kg/day with an upper range of 0.51 mg/kg/day. The other accidental exposure scenarios for the general public result in central estimates of dose from 0.00009 to 0.0033 mg/kg/day with estimates of the upper ranges of exposure between 0.0068 and 0.067 mg/kg/day. All of the accidental exposure scenarios involve relatively brief periods of exposure and most should be regarded as extreme, some to the extent of limited plausibility.

Because of the potential carcinogenicity of hexachlorobenzene a separate exposure assessment for this compound is provided. General and incidental worker exposure scenarios as well as acute exposure scenarios for the general public follow the same general methods used for clopyralid. Chronic exposure scenarios for the general public are based on modeling the runoff of hexachlorobenzene from a treated site to nearby vegetation or water.

Hexachlorobenzene is a persistent ubiquitous environmental pollutant. Estimates of hexachlorobenzene release to the environment exceed 240,000 kg/year. Based on the amount of clopyralid currently used in Forest Service programs and the proportion of hexachlorobenzene in clopyralid, the amount of hexachlorobenzene released each year in Forest Service programs is

about 0.0034 kg. Thus, Forest Service programs contribute very little to the background levels of hexachlorobenzene in the environment - i.e., about one part in one-hundred million (100,000,000) parts.

ATSDR (1998) reports that general background contamination of the environment with hexachlorobenzene results in long-term daily national average doses of about 0.000001 mg/kg/day for the general public. The exposure assessments based on the use of clopyralid by the Forest Service result in long-term dose estimates for the general public that are below this amount by factors of about 25,000 to several million. In the normal application of clopyralid, workers will be exposed to greater amount of hexachlorobenzene than members of the general public. Nonetheless, the central estimates of worker exposure under normal conditions to hexachlorobenzene are below the background levels of exposure by factors of about one thousand. Upper ranges of worker exposure are below background levels of exposure by factors of about 3 to 5. Thus, there is no basis for asserting that the use of clopyralid by the Forest Service will result in substantial increases in the general exposure of either workers or members of the general public to hexachlorobenzene.

Accidental exposure scenarios for both workers and members of the general public do result in short term exposures that are above the background dose of 0.000001 mg/kg/day. The highest dose estimate is about 0.002 mg/kg, the upper range of exposure for a worker wearing contaminated gloves for one-hour. For members of the general public, the highest dose estimate is about 0.001 mg/kg and is associated with the short term consumption of contaminated fish. As with the exposure scenarios for clopyralid, all of the accidental exposure scenarios for hexachlorobenzene involve relatively brief periods of exposure and most should be regarded as extreme.

The Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.5 mg/kg/day for clopyralid. This RfD is based on a chronic rat NOAEL of 50 mg/kg/day and an uncertainty factor of 100. The rat NOAEL is well-supported by chronic NOAELs in dogs and mice as well as additional chronic NOAEL in rats. The NOAELs for chronic toxic effects are below the NOAELs for reproductive effects. Thus, doses at or below the RfD will be at or below the level of concern for reproductive effects.

The only ambiguity in the dose-response assessment for clopyralid concerns the critical effect - i.e., the adverse effect which will occur at the lowest dose level. No specific adverse effect has been consistently observed in the available studies. Different studies in rats, mice, and dogs have noted general decreases in body weight, increases in liver and kidney weight, as well as a thickening in some epithelial tissue. Decreases in body weight and changes in organ weight are commonly observed in chronic toxicity studies and can indicate either an adaptive or toxic response. Changes in epithelial tissue are less commonly observed and the toxicologic significance of this effect is unclear.

The data on the toxicity of clopyralid are adequate for additional dose-response or dose-severity modeling. Because none of the anticipated exposures substantially exceed the RfD and the great majority of anticipated exposures are far below the RfD, such additional modeling is not necessary for the characterization of risk.

The contamination of technical grade clopyralid with hexachlorobenzene and pentachlorobenzene can be quantitatively considered to a limited extent. The U.S. EPA has derived RfDs for both pentachlorobenzene and hexachlorobenzene and a cancer potency factor for hexachlorobenzene. Based on the levels of contamination of technical grade clopyralid with these compounds and the relative potencies of these compounds to clopyralid, this contamination is not significant in terms of potential systemic toxic effects. This assessment, however, does not reduce concern for the potential carcinogenicity associated with hexachlorobenzene and this risk is quantitatively considered.

The risk characterization for potential human health effects associated with the use of clopyralid in Forest Service programs is relatively unambiguous. Based on the estimated levels of exposure and the criteria for chronic exposure developed by the U.S. EPA, there is no evidence that typical or accidental exposures will lead to dose levels that exceed the level of concern. In other words, all of the anticipated exposures - most of which involve highly conservative assumptions - are at or below the RfD. The use of the RfD - which is designed to be protective of chronic or lifetime exposures - is itself a very conservative component of this risk characterization because the duration of any plausible and substantial exposures is far less than lifetime.

Irritation and damage to the skin and eyes can result from exposure to relatively high levels of clopyralid - i.e., placement of clopyralid directly onto the eye or skin. From a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling clopyralid. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of clopyralid.

The only reservation attached to this assessment of clopyralid is that associated with any risk assessment: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated.*** No chemical, including clopyralid, has been studied for all possible effects and the use of data from laboratory animals to estimate hazard or the lack of hazard to humans is a process that is fraught with uncertainty. Prudence dictates that normal and reasonable care should be taken in the handling of this or any other chemical. Notwithstanding these reservations, the use of clopyralid does not appear to pose any identifiable hazard to workers or the general public in Forest Service programs.

The contamination of clopyralid with hexachlorobenzene does not appear to present any substantial cancer risk. Administratively, the Forest Service has adopted a cancer risk level of one in one-million (1÷1,000,000) as a trigger that would require special steps to mitigate exposure or restrict and possibly eliminate use. Based on relatively conservative exposure assumptions, the risk levels estimated for members of the general public are below this trigger level. The highest

risk level is estimated at about 8 in 100 million, about a factor of 12 below the level of concern. The exposure scenario associated with this risk level involves the consumption of contaminated fish by subsistence populations - i.e., groups that consume relatively large amounts of contaminated fish. The consumption of fish contaminated with hexachlorobenzene is a primary exposure scenario of concern because of the tendency of hexachlorobenzene to bioconcentrate from water into fish. This is also consistent with the general observation that exposure to hexachlorobenzene occurs primarily through the consumption of contaminated food.

For workers, the only cancer risk level that approaches a level of concern involves workers wearing contaminated gloves for one-hour. In this instance, the risk level is about one in ten-million, a factor of 10 below the Forest Service trigger level of one in one-million. As with the fish consumption scenario for members of the general public, the contaminated glove scenario for workers leads to relatively high risks because of the tendency of hexachlorobenzene to partition into fatty tissue.

Both of these relatively high risk scenarios are based on upper ranges of plausible exposures. Based on central estimates of exposure, the cancer risk levels are below the trigger level by factors of about one-thousand (1000) to ten-million (10,000,000). In other words, the cancer risk estimates based on central or most likely estimates of exposure are in the range of about 1 in one-billion (1÷1,000,000,000) to less than 1 in one-trillion (1÷1,000,000,000,000).

In terms of potential toxic effects, the only scenarios of marginal concern with hexachlorobenzene are the scenarios that approach the level of concern for cancer risk: consumption of contaminated fish by members of the general public and workers wearing contaminated gloves. In all cases, however, projected exposures are below the RfD by at least a factor of five.

The simple verbal interpretation of this risk characterization is that, in general, the contamination of clopyralid with hexachlorobenzene does not appear to pose a risk to the general public. The prolonged use of clopyralid at the highest plausible application rate, 1 lb a.e./acre, could approach a level of concern in areas with small ponds or lakes used for fishing and in areas with local conditions that favor runoff. In such cases, site-specific exposure assessments and/or monitoring of hexachlorobenzene concentrations in water could be considered.

Ecological Risk Assessment

The toxicity of clopyralid is relatively well characterized in experimental mammals but few wildlife species have been assayed relative to the large number of non-target species that might be potentially affected by the use of clopyralid. Within this admittedly substantial reservation, clopyralid appears to be relatively non-toxic to terrestrial or aquatic animals, is highly selective in its toxicity to terrestrial plants, and relatively non-toxic to aquatic plants. Thus, the potential for substantial effects on non-target species appears to be remote. Consistent with this assessment of toxicity to non-target species, one long-term field study has been conducted that indicates no substantial or significant effects on species diversity.

The toxicity to non-target terrestrial animals is based almost exclusively on toxicity studies using experimental mammals - i.e., the same studies used in the human health risk assessment. Some additional studies are available on birds, bees, and earthworms that generally support the characterization of clopyralid as relatively non-toxic. An additional study of the toxicity of clopyralid to non-target invertebrates also suggests that clopyralid has a low potential for risk. A caveat in the interpretation of this study is the limited detail in which the experimental data are reported. As with terrestrial species, the available data on aquatic species, both plants and animals, suggest that clopyralid is relatively non-toxic.

The toxicity of clopyralid to terrestrial plants has been examined in substantial detail in studies that have been published in the open literature as well as studies that have been submitted to the U.S. EPA to support the registration of clopyralid. Clopyralid is a plant growth regulator and acts as a synthetic auxin or hormone, altering the metabolism and growth characteristics of the plant and causing a proliferation of abnormal growth that interferes with the transport of nutrients throughout the plant. This, in turn, can result in gross signs of damage and the death of the plant. The phytotoxicity of clopyralid is relatively specific to broadleaf plants because clopyralid is rapidly absorbed across leaf surfaces but much less readily absorbed by the roots of plants. For the same reason, clopyralid is much more toxic/effective in post-emergent treatments (i.e., foliar application) than pre-emergent treatment (i.e., application to soil).

Clopyralid does not bind tightly to soil and thus would seem to have a high potential for leaching. While there is little doubt that clopyralid will leach under conditions that favor leaching - i..e., sandy soil, a sparse microbial population, and high rainfall - the potential for leaching or runoff is functionally reduced by the relatively rapid degradation of clopyralid in soil. A number of field lysimeter studies and one long-term field study indicate that leaching and subsequent contamination of ground water are not likely to be substantial. This conclusion is also consistent with a short-term monitoring study of clopyralid in surface water after aerial application.

For terrestrial mammals, the dose-response assessment for clopyralid is based on the same data as the human health risk assessment (i.e., a NOAEL of 50 mg/kg/day from a 2-year rat feeding study). None of the exposure scenarios, acute or longer-term, result in exposure estimates that exceed this NOAEL. The very limited data on toxicity to birds suggest that birds may be somewhat more sensitive than mammals. The data on birds, however, are not as extensive or of the same detail as the data on experimental mammals. The available data on terrestrial invertebrate are also less complete than the data on mammals. Nonetheless, there is no indication that clopyralid is highly toxic to birds or terrestrial invertebrates.

The toxicity of clopyralid to terrestrial plants can be characterized relatively well and with little ambiguity. Clopyralid is more toxic to broadleaf plants than grains or grasses and is more toxic in post-emergence applications - i.e., foliar spray - than pre-emergence applications - i.e., soil treatment. Many non-target species - especially grains, grasses, and several types of trees - are not likely to be affected by clopyralid even if the plants are sprayed at application rates of 0.1 lb a.e./acre or greater. When applications are made prior to emergence - i.e., directly to the soil

before the germination of the plant seeds - NOAELs for sensitive species such as soybeans, snap beans, tomatoes, and sunflowers are in the range of 0.028 to 0.056 kg/ha. When applied directly to the foliage - i.e., post-emergence - the NOAELs are about 0.00056 kg/ha. This difference is attributable to the very rapid absorption of clopyralid after direct foliar application.

Based on the results of acute bioassays, fish and aquatic invertebrates are equally sensitive to clopyralid. While there are no chronic studies available in fish, a chronic reproductive NOAEL of about 20 mg/L has been determined in Daphnia magna, a common aquatic invertebrate test species. Given the low levels of plausible exposure to clopyralid in water, this NOAEL can be used to characterize risk to both fish and aquatic invertebrates. Aquatic plants are somewhat more sensitive than aquatic animals to clopyralid. The lowest reported LC_{50} for aquatic algae is 6.9 mg/L, about a factor of 3 below the chronic NOAEL in Daphnia.

Clopyralid is a herbicide and the most likely damage to non-target species will involve terrestrial plants. As is the case with any herbicide, the likelihood of damage to non-target plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential non-target species. In this respect, the apparent selectively of clopyralid substantially narrows the number of non-target plants that might be affected. With clopyralid, some sensitive post-emergent plants could be adversely effected by off-site drift over a relatively narrow band. Most species of trees, grains, or grasses, however, are not likely to be affected by off-site drift or even direct spray. This risk characterization is conservative in that the off-site drift estimates are derived from studies involving aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no substantial or detectable impact on off-site plant species outside of a very narrow range - i.e., less than and perhaps much less than 25 feet.

Soil contamination by runoff, which could potentially harm off-site plant species, does not appear to be a major concern with clopyralid. Rains are most likely to cause clopyralid to leach into the soil column rather than wash-off. The best available estimate of runoff is on the order of 0.015 (1½%) of the applied amount. Because clopyralid is less effectively absorbed from roots than from leaf surfaces, the consequences of runoff are likely to be less severe than those of drift. In addition, once in the soil column, clopyralid will be rapidly degraded except in arid soils with low microbial populations. Thus, while damage to off-site plants from runoff cannot be ruled-out under conditions that would be highly favorable to runoff, this is not likely to be a major problem with clopyralid.

The potential for adverse effects on other non-target species appears to be remote. The weight of evidence suggests that no adverse effects in terrestrial or aquatic animals are plausible using typical or even very conservative worst case exposure assumptions. Some inhibition of growth in aquatic plants would be possible in cases involving accidental spills. Such effects, however, would be transient.

As with the human health risk assessment, this characterization of risk must be qualified by the general reservation in any risk assessment: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated.*** Clopyralid has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging non-target animals or some populations of non-target plants. Notwithstanding this limitation, the available data do not indicate that adverse effects are likely in terrestrial or aquatic animals from the use of this compound in Forest Service programs. Under normal and proper conditions of application, effects on non-target vegetation would likely be confined to sensitive plant species in or very near to the treatment area.

1. INTRODUCTION

The USDA Forest Service uses the herbicide, clopyralid, in its vegetation management programs. Only one commercial formulation, Transline, is used by the Forest Service. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using clopyralid 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 clopyralid and its commercial formulation, an assessment of potential exposure to the product, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These are the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

Although this is a technical support document and addresses some specialized technical areas, an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 1998). Furthermore, the technical terms are defined in the glossary to this risk assessment. Some of the more complicated terms and concepts are defined, as necessary, in the text.

The human health and ecological risk assessments presented in this document are not, and are not intended to be, comprehensive summaries of all of the available information. No published reviews regarding the human health or ecological effects of clopyralid have been encountered. Moreover, almost all of the mammalian toxicology studies and most of the ecotoxicology studies are unpublished reports submitted to the U.S. EPA as part of the registration process for this compound.

Because of the lack of a detailed, recent review concerning clopyralid and the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA files was conducted. Full text copies of relevant studies were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies were reviewed, discussed in sections 3 and 4 as necessary, and synopses of the most relevant studies are provided in the appendices to this document.

In the interest of economy, an updated chemical background statement has not been prepared with the current risk assessment. The information presented in the appendices and the detailed discussions in sections 2, 3, and 4 of the risk assessment are intended to be detailed enough to support an independent review of the risk analyses; however, they are not intended to be as detailed as the information generally presented in Chemical Background documents.

For the most part, the risk assessment methods used in this document are similar to those used in risk assessments previously conducted for the Forest Service as well as risk assessments conducted by other government agencies. Details regarding the specific methods used to prepare the human health risk assessment are provided in SERA (1998), while detailed explanations of specific methods used in estimating occupational exposure are provided in Rubin et al. (1998). Similar documentation for methods used in assessing dermal absorption are provided in Durkin et al. (1998).

Risk assessments are usually expressed with numbers; however, the numbers are far from exact. *Variability* and *uncertainty* may be dominant factors in any risk assessment, and these factors should be expressed. Within the context of a risk assessment, the terms *variability* and *uncertainty* signify different conditions.

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

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

In considering different forms of variability, almost no risk estimate presented in this document is given as a single number. Usually, risk is expressed as a central estimate and a range, which is

sometimes very large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations.

Most of the calculations are relatively simple, and the very simple calculations are included in the body of the document. Some of the calculations, however, are cumbersome. For those calculations, worksheets are included as an attachment to the risk assessment. The worksheets provide the details for the estimates cited in the body of the document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on non-target organisms. Because of the importance of hexachlorobenzene, a contaminant in technical grade clopyralid, to the human health risk assessment, a separate subset of worksheets for hexachlorobenzene are provided that detail the calculations involved in assessing the health effects of hexachlorobenzene.

2. PROGRAM DESCRIPTION

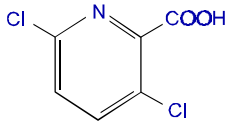
2.1. OVERVIEW

Clopyralid is a selective herbicide used primarily in the control of broadleaf weeds. The Forest Service uses only a single commercial formulation of clopyralid, Transline. Transline is a liquid formulation of clopyralid that is manufactured by DowAgro and contains 40.9% clopyralid as the monoethanolamine salt and 59.1% inert ingredients. One of the inerts is identified as isopropyl alcohol. The amount of isopropyl alcohol in the formulation as well as the identity of the other inerts is considered proprietary. The Forest Service uses Transline almost exclusively in noxious weed control. Relatively minor uses include rights-of-way management, wildlife openings, and facilities maintenance. Although clopyralid may be applied as the sole herbicide in some situations, it is also sometimes applied by the Forest Service in combination with 2,4-D or 2,4-D and picloram. The most common methods of ground application for Transline involve backpack (selective foliar) and boom spray (broadcast foliar) operations. Although Transline is registered for aerial applications, the Forest Service does not and does not intend to use Transline in aerial applications. The typical application rate in Forest Service programs is 0.1 lb a.e./acre. The range of application rates that are likely to be used in Forest Service programs is 0.01 to 1 lb a.e./acre.

Technical grade clopyralid contains hexachlorobenzene and pentachlorobenzene as contaminants. Nominal or average concentrations of hexachlorobenzene are less than 2.5 ppm. Nominal or average concentrations of pentachlorobenzene are less than 0.3 ppm (Lade 1998).

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Clopyralid is the common name for 3,6-dichloro-2-pyridinecarboxylic acid:



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

There are two different manufacturing processes used in the synthesis of clopyralid: the penta process and the electrochemical process. The penta process is the original method used in the manufacturing of clopyralid. The electrochemical process is a new procedure. The two processes yield “slightly different ingredient profiles” (Dow AgroSciences 1998). Details of these methods have been submitted to the U.S. EPA but are considered proprietary and are not detailed in this risk assessment. Nonetheless, some comparative information is available on the acute toxicity of clopyralid produced by both the penta and electrochemical processes and these data are summarized in sections 3 and 4.

Technical grade clopyralid contains hexachlorobenzene and pentachlorobenzene as contaminants. Nominal or average concentrations of hexachlorobenzene are less than 2.5 ppm. Nominal or average concentrations of pentachlorobenzene are less than 0.3 ppm (Lade 1998). The impact of these contaminants to this risk assessment is detailed in section 3.

Transline is the only formulation of clopyralid used by the Forest Service. Transline is produced by Dow AgroSciences and is formulated as a liquid containing the monoethanolamine salt of clopyralid (40.9% w/v). This is equivalent to a concentration of 3 lb a.e./gallon. The remaining 59.1% of the formulation consists of inerts. The identity of the inerts in Transline is proprietary with the exception of isopropyl alcohol. This inert is listed on the Transline MSDS, but the amount of isopropyl alcohol in the formulation is not disclosed (C&P Press 1998). The potential significance of the inerts in Transline to this risk assessment is discussed further in section 3.1.9.

Transline is labelled for use only in non-crop and non-timber areas. It has no labeled uses on crops. The uses for Transline recommended on the product label include selective, postemergence control of broadleaf weeds on rights-of-way and the maintenance of wildlife openings, wild parkland and wildlife management areas, and forest spot applications adjacent to such areas (C&P Press 1998).

2.3. APPLICATION METHODS

Detailed descriptions regarding the use of herbicides in silviculture and the various methods of herbicide application are available in the general literature [e.g., Cantrell and Hyland (1985)] and in earlier risk assessments conducted by the Forest Service (USDA 1989a,b,c). The following summary focuses on those aspects of application that are most relevant to the exposure assessments (sections 3.2 and 4.2).

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

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

Although Transline is registered for aerial applications (C&P Press 1998), the Forest Service does not and does not intend to use Transline in aerial applications.

Table 2-1: Identification and Physical/Chemical Properties of Clopyralid and the Monethanolamine salt of Clopyralid.

Property	Value	Reference
Synonyms	3,6-dichloro-2-pyridinecarboxylic acid, 3,6-dichloropyridine-2-carboxylic acid, 3,6-dichloropicolinic acid, 3,6-DCP, Dowco 290 Formulations: Lontrel, Reclaim, Shield, Stinger, Transline	Budavari 1989 C&P Press 1998 Dow AgroSciences 1998
CAS Number	001702-17-6 (acid) 057754-85-5 (salt)	Budavari 1989 C&P Press 1998
EPA Registration Number	62719-83	C&P Press 1998
MW	192 (acid) 253 (salt)	Budavari 1989
pK_a	2.33 2.0	Bidlack 1982 Dow AgroSciences 1998
Melting Point	151-152°C	Budavari 1989
Vapor pressure at 25°C	1.2×10^{-5} mm Hg	Budavari 1989
Water solubility	≈1000 mg/L	Budavari 1989
	9,000 mg/L @20°C	Baloch-Haq et al. 1993
Log_{10} $K_{o/w}$ pH 5 pH 7 pH 9	-1.81 -2.63 -2.55	Dow AgroSciences 1998
Soil $t_{1/2}$ (field dissipation)	25 (8-250) days	Dow AgroSciences 1998
Soil leaching in undisturbed soil columns	0.001 to 0.006 of applied dose center of mass movement: 6-18"	Dow AgroSciences 1998
$K_{o/c}$ (ml/g)	10 0.4-29.8	Bidlack 1982 Dow AgroSciences 1998

2.4. MIXING AND APPLICATION RATES

The specific application rates used in a ground application vary according to local conditions and the nature of the target vegetation. Application rates of 0.09-0.5 lb a.e./acre are recommended on the product label (C&P Press 1998). The product label further specifies that the lower range of the application rate is appropriate only under highly favorable conditions when the plants are no more than three to six inches tall. The upper range of the labelled rates are recommended for

Table 2-2. Uses of clopyralid by the Forest Service in 1997 (USDA 1998).

Herbicide or Herbicide Mixture	Use	Acres Treated	Amount Used (lbs a.e.)	lbs a.e./acre[1]
Clopyralid as sole herbicide	facilities maintenance	8	0.12	0.015
	noxious weed control	2755.8	296.5	0.11
	nursery weed control	1.44	1.44	1
	ROW management	91	5.36	0.059
	wildlife habitat improvement	0.3	0.01	0.033
	sole herbicide subtotal	2856.54	303.43	0.11
with 2,4-D	noxious weed control	1352.70		
with 2,4-D and picloram	noxious weed control	148		
	mixture subtotal	1500.7		
Total (sole herbicide plus mixture subtotals)		4357.24		

[1] For clopyralid as the sole herbicide, this column is calculated at the total number of pounds used divided by the total number of acres treated - i.e., average application rate. For tank mixtures, the Forest Service statistics do not specify the amount or proportion of each herbicide in the mixture. Thus, average application rates for clopyralid or other herbicides are not calculated.

Canada thistle or knapweeds.

The use of clopyralid by the Forest Service in 1997, the most recent year for which statistics are available, is summarized in Table 2-2. As indicated in this table, the Forest Service treated about 3000 acres with about 300 lbs of clopyralid as the only herbicide for an average application rate of about 0.1 lb/acre. About half again as much of this acreage was treated with mixtures containing clopyralid with either 2,4-D or 2,4-D and picloram, all for noxious weed control. Virtually all of the clopyralid applied by the Forest Service in 1997 involved noxious weed control (97.7%, [{2755.8+1500.7}÷4357.24]).

For this risk assessment, application rates used to construct the various exposure scenarios range from 0.01 lb a.e./acre to 1.0 lb a.e./acre with a typical rate taken as 0.1 lb a.e./acre. The typical application rate is the average application rate that the Forest Service used in 1997, when clopyralid was applied as the sole herbicide (see Table 2-2), rounded to one significant figure. Although this rate is near the lower end of the labelled application rate of 0.09 lb a.e./acre, the rate of 0.11 lb a.e./acre is typical for most Forest Service programs. As indicated in Table 2-2, this is the rate used on about 96% of the acres treated by the Forest Service in 1997 [2755.8÷2856.54].

The lower limit of the application rate is taken as 0.01 lb a.e./acre, somewhat below the lowest reported use by clopyralid by the Forest Service in 1997.

The upper end of the range of application rates is taken as 1 lb clopyralid a.e./acre. This is above the highest labeled application rate (0.5 lb a.e./acre) but is used in this risk assessment because a rate of 1.0 lb a.e./acre was used by the Forest Service in 1997 for nursery weed control.

For ground applications, spray volumes of 20 gallons or more per acre are recommended. For this risk assessment, 20 gallons per acre is taken as the minimum spray volume. A spray volume of 40 gallons per acre is taken as an upper range. Based on these application rates and spray volumes, the typical field concentration - i.e., the concentration of clopyralid in solution after mixing and dilution - is taken as 0.4 mg/L with a range of 0.03 mg/L to 6 mg/L. These values are summarized in worksheet B02 and the calculations for these values are given in the text that follows worksheet B01.

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview. Although no information is available on the toxicity of clopyralid to humans, the toxicity of clopyralid has been relatively well-characterized in mammals. All of this information is contained in unpublished studies submitted to the U.S. EPA as part of the registration process for clopyralid.

Two different manufacturing processes may be used for clopyralid: the penta process and the electrochemical process. The limited available information indicates that technical grade clopyralid samples from the electrochemical process may be somewhat more toxic (LD_{50} values in the range of about 3000 mg/kg) than the penta process (LD_{50} > 5000 mg/kg). These differences, however, are not substantial and may be due to random variability. Clopyralid also has a low order of chronic toxicity. On chronic or subchronic exposures, no effects have been observed in laboratory mammals as doses of 50 mg/kg/day or less. At doses of 100 mg/kg/day or greater, various effects have been observed in different species and different bioassays. These effects include weight loss, changes in the weight of the liver and kidney, thickening of epithelial tissue, irritation of the lungs, and decreases in red blood cell counts.

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

3.1.2. Acute Toxicity. Although the mechanism of phytotoxic action of clopyralid is characterized in some detail (section 4.1), the mechanism of toxic action in mammals or other animal species is not well characterized. Standard acute toxicity studies have been conducted with rats using clopyralid produced from both the penta process, the original method used in the manufacture of clopyralid, and the electrochemical process, a more recently developed method for the commercial synthesis of clopyralid (appendix 1). As summarized in Dow AgroSciences (1998), the LD_{50} of clopyralid from the penta process is >5000 mg/kg and the LD_{50} of clopyralid from the electrochemical process is 3738 mg/kg for male rats and 2675 mg/kg for female rats. This information appears to be a summary of the studies by Jeffrey et al. (1987b) and Gilbert and Crissman (1995) on the penta and electrochemical samples, respectively, detailed in Appendix 1. While these data suggest that clopyralid from the newer electrochemical process may be somewhat more toxic than the clopyralid from the older penta process, this assessment is based on only one study for each type of clopyralid. In addition, these studies were conducted at different times, and the results of acute toxicity studies will vary both among and within laboratories when assays of the same compound are conducted at different times (Streibig et al. 1995). Thus, the apparent differences between the two studies should not be overly interpreted.

Gilbert and Crissman (1995) observed gross changes in the stomach of rats that died after being given clopyralid (electrochemical) by gavage at a dose of 5000 mg/kg. This effect is not reported in this study at lower dose levels - i.e., 500 mg/kg or 2000 mg/kg.

3.1.3. Subchronic or Chronic Systemic Toxic Effects. As summarized in appendix 1, several subchronic and chronic studies have been conducted on clopyralid. These studies were submitted to the U.S. EPA in support of the registration of clopyralid, and none of the studies are published in the open peer-reviewed literature. In the preparation of this risk assessment, full copies of most of studies submitted to the U.S. EPA were obtained from EPA and reviewed. In some cases, as specified in appendix 1, summaries of the studies are based on the recent review by Dow AgroSciences (1998).

The most consistent effects associated with dietary exposures to clopyralid are decreased body weight (Barna-Lloyd et al. 1986; Dow AgroSciences 1998; Humiston et al. 1977; Young et al. 1986) and increases in relative kidney weight (Barna-Lloyd et al. 1986; Dow AgroSciences 1998) and relative liver weight (Barna-Lloyd et al. 1986; Breckenridge et al. 1984; Dow AgroSciences 1998). In addition, Barna-Lloyd et al. (1986) report hyperplasia and thickening of the gastric epithelium of rats after dietary exposures to clopyralid that resulted in daily doses of 150 mg/kg/day.

As discussed further in section 3.3, the U.S. EPA has identified a rat NOEL of 50 mg/kg/day as the basis for the RfD (U.S. EPA 1988a; U.S. EPA 1997a) with a corresponding LOAEL of 150 mg/kg/day based on decreased body weight in female rats (Humiston et al. 1977; Dow AgroSciences 1998) that is also supported by a LOAEL based on epithelial hyperplasia at 150 mg/kg/day (Barna-Lloyd et al. 1986). The rat NOEL of 50 mg/kg/day is supported by another rat NOEL of 100 mg/kg/day from the study by Young et al. (1986).

Based on the study by Breckenridge et al. (1984), a dose of 100 mg/kg/day is also a NOEL in dogs, although the endpoint, changes in hematologic parameters, is different from the endpoint seen in rats. In the Breckenridge et al. (1984) study, six beagle dogs per sex were used at each nominal/target dose levels: 0 (control), 100, 320 and 1000 mg/kg/day. Actual doses based on measured food consumption and body weights were 99, 301, and 983 mg/kg/day for males and 99, 319, and 977 mg/kg/day for females. The primary toxic effect noted was a significant reduction in red blood cell counts in males and females at the 320 and 1000 mg/kg/day nominal dose levels. These effects were not statistically significant in the 100 mg/kg/day dose groups. Significant decreases in total protein, serum albumin and serum globulin were also noted in high dose males and females at 14 weeks and mid and high dose groups at 27 weeks. At 52 weeks, these differences were not statistically significant.

Also in the mid and high dose groups, Breckenridge et al. (1984) noted a significant increase in absolute liver weight. In the high dose group, this was accompanied by increases in relative kidney and heart weights. No changes at any dose level, however, were observed in SGPT, SGOT, or alkaline phosphatase - all indicators of effects on the liver - and signs of histopathologic damage were not apparent. Assays of cytochrome P-450 levels or liver mixed-function oxidases

were not conducted. Adrenal weights were significantly reduced in low dose males. This effect, however, was not seen in higher dose males or any females and is probably incidental.

3.1.4. Reproductive and Teratogenic Effects. As detailed in appendix 1, two gavage teratogenicity studies have been conducted in rabbits and two dietary reproduction studies have been conducted in rats. Other than a decrease in maternal body weight, which is consistent with the information on the subchronic and chronic toxicity of clopyralid, these studies report few signs of toxicity in dams or offspring. At doses that cause no signs of maternal toxicity - i.e., doses below about 100 mg/kg/day - no reproductive or teratogenic effects are apparent.

3.1.5. Carcinogenicity and Mutagenicity. Several chronic bioassays have been conducted on clopyralid in both mice (West and Willigan 1976; Young et al. 1986) and rats (Barna-Lloyd et al. 1986; Dow AgroSciences 1998) and no evidence of carcinogenic activity has been detected. In addition, clopyralid is inactive in several different standard bioassays of mutagenicity (Dow AgroSciences 1998).

Technical grade clopyralid, however, is contaminated with hexachlorobenzene (Lade 1998), a compound classified as a potential carcinogen by the U.S. EPA (1997b). A recent review of the extensive toxicity data on hexachlorobenzene is available from ATSDR (1998). As discussed further in section 3.1.9.1, the risk of cancer from this contaminant is considered both qualitatively and quantitatively in this risk assessment.

3.1.6. Effects on the Skin and Eyes. After direct instillation into the eyes, both penta and electrochemical process clopyralid can cause persistent damage to the eyes. The damage is characterized as slight to marked redness, swelling of the conjunctiva, and discharge with reddening of the iris and moderate to marked opacity of the cornea. Details of these studies are presented in appendix 1.

Other than signs of transient dermal redness shortly after application (appendix 1), there is no evidence to suggest that clopyralid is a potent skin irritant. Dow AgroSciences (1998) indicates that neither penta process clopyralid nor electrochemical process clopyralid causes skin sensitization. As detailed in Appendix 1, this statement is consistent with and appears to be based on the studies by Jeffery (1987c), presumably using penta process clopyralid and Gilbert (1995d), presumably using electrochemical process clopyralid.

3.1.7. Systemic Toxic Effects from Dermal Exposure. The available toxicity studies summarized in appendix 1 suggest that dermal exposure to 2000 mg/kg clopyralid was not associated with any signs of systemic toxicity in rabbits based on standard acute/single application bioassays with 14-day observation periods. Although there are no data concerning the dermal absorption kinetics of clopyralid, dermal absorption is typically less rapid than absorption after oral exposure and dermal LD_{50}s are typically higher than oral LD_{50}'s (e.g., Gaines 1969). Since the reported acute oral LD_{50}'s of clopyralid are all more than 2000 mg/kg, the lack of apparent toxicity at dermal doses of up to 2000 mg/kg/day is to be expected and these studies add little to the assessment of risk for clopyralid.

Nonetheless, the dermal exposure route is important to this and other similar risk assessments. Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared with an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies. Thus, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which clopyralid is likely to be absorbed from the surface of the skin.

As discussed in Durkin et al. (1995), dermal exposure scenarios involving immersion or prolonged contact with chemical solutions use Fick's first law and require an estimate of the permeability coefficient, K_p, expressed in cm/hour. Because no kinetic data are available on the dermal absorption of clopyralid, the method for estimating a zero-order absorption rate (U.S. EPA 1992) is used in this risk assessment. Using this method, a dermal permeability coefficient for clopyralid is estimated at 0.0000017 cm/hour with a 95% confidence interval of 0.00000044-0.0000065 cm/hour. These estimates are used in all exposure assessments that are based on Fick's first law. The calculations for these estimates are presented in worksheet B05.

For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the skin's surface, dermal absorption rates (proportion of the deposited dose per unit time) rather than dermal permeability rates are used in the exposure assessment. Using the methods detailed in Durkin et al. (1998), the estimated first-order dermal absorption coefficient is 0.00063 $hour^{-1}$ with 95% confidence intervals of 0.00013-0.0031 $hour^{-1}$. The calculations for these estimates are presented in worksheet B04.

3.1.8. Inhalation Exposure. Compared with oral exposure data, data regarding the inhalation toxicity of clopyralid are extremely limited. As detailed in appendix 1, two relatively detailed inhalation studies have been submitted to the U.S. EPA in support of registration of clopyralid (Hoffman 1995; Streeter et al. 1987). At nominal concentrations of 1 mg/L or greater over 4-hour exposure periods, the only effects noted during were labored breathing and red stains around the nares. After a two week recovery period, Hoffman (1995) noted discoloration of the lungs in rats exposed to nominal concentrations of 1.2 mg/L but not in rats exposed to nominal concentrations of 5.5 mg/L. As noted by Hoffman (1995), both of these nominal concentrations were comparable in terms of respirable particles - i.e., $\leq$1.0 microns.

Although Hoffman (1995) did not attribute the changes in the lungs to clopyralid exposure, these changes are consistent with effects noted in a one-year dietary study in dogs - i.e., Breckenridge et al. (1984) detailed in section 3.1.3. In this study, three low-dose (100 mg/kg/day) animals, three mid-dose (320 mg/kg/day) animals, and five high-dose (1000 mg/kg/day) animals evidenced atypical foci or nodules in the lungs. These lung changes were not noted in any control animals. The study authors attributed these findings to the inhalation of food particles containing clopyralid with subsequent irritation of the lungs from direct clopyralid contact.

No occupational exposure criteria have been found for clopyralid. While any effects on the lungs are of substantial concern, such effects have not been seen at lower dietary dose levels in other

species. As noted in section 3.3.2, the current RfD for clopyralid is based on a NOAEL of 5 mg/kg/day from a two-year rats feeding study. This NOAEL (5 mg/kg/day) is a factor of 20 below the lowest dose associated with lung effects in dogs (100 mg/kg/day).

3.1.9. Impurities, Adjuvants, and Metabolites.

3.1.9.1. Impurities -- Virtually no chemical synthesis yields a totally pure product. Technical grade clopyralid, as with other technical grade products, undoubtedly contains some impurities. To some extent, concern for impurities in technical grade clopyralid is reduced by the fact that the existing toxicity studies on clopyralid were conducted with the technical grade product. Thus, if toxic impurities are present in the technical grade product, they are likely to be encompassed by the available toxicity studies on the technical grade product.

An exception to this general rule involves carcinogens, most of which are presumed to act by non-threshold mechanisms. Because of the non-threshold assumption, any amount of a carcinogen in an otherwise non-carcinogenic mixture may pose a carcinogenic risk. This is the situation with clopyralid. As indicated in Section 2, technical grade clopyralid contains hexachlorobenzene and pentachlorobenzene as contaminants. Nominal or average concentrations of hexachlorobenzene are less than 2.5 ppm. Nominal or average concentrations of pentachlorobenzene are less than 0.3 ppm (Lade 1998). The U.S. EPA has classified hexachlorobenzene as a probable human carcinogen for which the data are adequate to consider risk quantitatively (U.S. EPA 1997b). While a detailed review of hexachlorobenzene is beyond the scope of this risk assessment, adequate information is available on hexachlorobenzene to quantify the carcinogenic risk associated with the use of clopyralid (section 3.3).

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

This general uncertainty, however, has little impact on the risk assessment for clopyralid. Although the metabolism of clopyralid has been studied only in one mammalian species (Bosch 1991), this study suggests that rats do not metabolize clopyralid in detectable amounts and that 79-96% of the administered dose is excreted unchanged in the urine during the first 24 hours. This is similar to the pattern seen in plants that generally suggests that clopyralid is not extensively metabolized (Guo 1996), although it may be conjugated to form a methyl ester (Biehn 1990).

3.1.9.3. Adjuvants -- As indicated in section 2, the commercial formulation of clopyralid used by the Forest Service is Transline, which contains clopyralid as the monoethanolamine salt and also contains isopropyl alcohol. Both monoethanolamine and isopropyl alcohol are approved food additives (Clydesdale 1997) and there is no reason to assert that these compounds will materially impact the risks associated with the use of clopyralid.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. No occupational exposure studies are available in the literature that involve the application of clopyralid. Consequently, worker exposure rates are estimated from an empirical relationship between absorbed dose per kilogram of body weight and the amount of chemical handled in worker exposure studies on nine different pesticides (Rubin et al. 1998). Separate exposure assessments are given for backpack and boom spray ground applications. For these two groups, the central estimates and also the lower and upper estimates of exposure are similar: 0.0013 (0.000005 to 0.08) mg/kg/day for backpack workers and 0.0022 (0.000007 to 0.15) mg/kg/day for boom spray applicators. Although some clopyralid formulations are labeled for aerial application, the Forest Service is not using and does not plan to use that application method. Consequently, aerial applications are not considered in this risk assessment.

For the general public, all of the chronic or longer term exposure scenarios lead to levels of exposure that are below those for workers. The highest dose associated with any of the longer term exposure scenarios for the general public involves the consumption of contaminated fruit with exposure estimates of 0.0005 (0.00004 to 0.059) mg/kg/day. The accidental exposure scenario involving the consumption of contaminated water results in a central estimate of exposure of up to 0.023 mg/kg/day with an upper range of 0.51 mg/kg/day. The other accidental exposure scenarios for the general public result in central estimates of dose from 0.00009 to 0.0033 mg/kg/day with estimates of the upper ranges of exposure between 0.0068 and 0.067 mg/kg/day. All of the accidental exposure scenarios involve relatively brief periods of exposure and most should be regarded as extreme, some to the extent of limited plausibility.

Because of the potential carcinogenicity of hexachlorobenzene a separate exposure assessment for this compound is provided. General and incidental worker exposure scenarios as well as acute exposure scenarios for the general public follow the same general methods used for clopyralid. Chronic exposure scenarios for the general public are based on modeling the runoff of hexachlorobenzene from a treated site to nearby vegetation or water.

Hexachlorobenzene is a persistent ubiquitous environmental pollutant. Estimates of hexachlorobenzene release to the environment exceed 240,000 kg/year. Based on the amount of clopyralid currently used in Forest Service programs and the proportion of hexachlorobenzene in clopyralid, the amount of hexachlorobenzene released each year in Forest Service programs is about 0.0034 kg. Thus, Forest Service programs contribute very little to the background levels of hexachlorobenzene in the environment - i.e., about one part in one-hundred million (100,000,000) parts.

ATSDR (1998) reports that general background contamination of the environment with hexachlorobenzene results in long-term daily national average doses of about 0.000001 mg/kg/day for the general public. The exposure assessments based on the use of clopyralid by the Forest Service result in long-term dose estimates for the general public that are below this amount by factors of about 25,000 to several million. In the normal application of clopyralid, workers will be exposed to greater amount of hexachlorobenzene than members of the general public. Nonetheless, the central estimates of worker exposure under normal conditions to

hexachlorobenzene are below the background levels of exposure by factors of about one thousand. Upper ranges of worker exposure are below background levels of exposure by factors of about 3 to 5. Thus, there is no basis for asserting that the use of clopyralid by the Forest Service will result in substantial increases in the general exposure of either workers or members of the general public to hexachlorobenzene.

Accidental exposure scenarios for both workers and members of the general public do result in short term exposures that are above the background dose of 0.000001 mg/kg/day. The highest dose estimate is about 0.002 mg/kg, the upper range of exposure for a worker wearing contaminated gloves for one-hour. For members of the general public, the highest dose estimate is about 0.001 mg/kg and is associated with the short term consumption of contaminated fish. As with the exposure scenarios for clopyralid, all of the accidental exposure scenarios for hexachlorobenzene involve relatively brief periods of exposure and most should be regarded as extreme.

3.2.2. Workers. A summary of the exposure assessments for workers is presented in Table 3-1. Two types of exposure assessments are considered: general and accidental/incidental. The term *general* exposure assessment is used to designate those exposures that involve estimates of absorbed dose based on the handling of a specified amount of a chemical during specific types of applications. The accidental/incidental exposure scenarios involve specific types of events that could occur during any type of application. Details regarding all of these exposure assessments are presented in the clopyralid worksheets that accompany this risk assessment, as indicated in Table 3-1. In Table 3-1 and other similar tables presented below, numbers greater than or equal to 0.000001 are expressed in standard decimal notation. Smaller numbers are expressed in scientific notations, such as 7e-07 which is equivalent to 7×10^{-7}. Details of the conversion of scientific to decimal notation are given on page ix of this report.

As discussed further in section 3.4, a separate set of exposure assessments and worksheets are provided for hexachlorobenzene.

3.2.2.1. General Exposures **--** As outlined in the program description (see chapter 2), this risk assessment is concerned primarily with backpack and boom spray ground applications. Although Transline is labeled for aerial applications (helicopter only), the Forest Service is not using and does not plan to use that application method for Transline. Consequently, aerial applications are not considered in this risk assessment.

The assumptions used in worker exposure assessments for both backpack and boom spray applications are detailed in worksheets C01 and C02. No worker exposure studies with clopyralid

Table 3-1: Clopyralid - Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.0013	0.000005	0.08	WSC01
Broadcast ground spray (Boom spray)	0.0022	0.000007	0.15	WSC02
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	1.36e-07	2.64e-09	0.000008	WSC03
Contaminated Gloves, 1 hour	0.000008	1.58e-07	0.00047	WSC03
Spill on hands, 1 hour	0.000024	3.74e-07	0.0018	WSC04
Spill on lower legs, 1 hour	0.00006	9.23e-07	0.0044	WSC04

were found in the literature. As described in Rubin et al. (1998), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. These exposure rates are based on worker exposure studies on nine different pesticides with molecular weights ranging from 221 to 416 and log K_{ow} values at pH 7 ranging from -0.75 to 6.50. The estimated exposure rates are based on estimated absorbed doses in workers as well as the amounts of the chemical handled by the workers (Rubin et al. 1998, Table 2). As summarized in Table 2-1 of this risk assessment on clopyralid, the molecular weight of clopyralid is 192 and the log K_{ow} at pH 7 is about -2.63 [$\log_{10}(0.0023) = -2.638$]. Thus, the molecular weight of clopyralid is somewhat below and the K_{ow} for clopyralid is substantially below the corresponding range of values in the analysis by Rubin et al. (1998). This adds uncertainty to the exposure assessment, as further discussed in Section 3.4.

As further described in Rubin et al. (1998), the ranges of estimated occupational exposure rates vary substantially among individuals and groups, (i.e., by a factor of 50 for backpack applicators and a factor of 100 for mechanical ground sprayers). It seems that much of the variability can be attributed to the hygienic measures taken by individual workers (i.e., how careful the workers are to avoid unnecessary exposure).

The estimated number of acres treated per hour is taken from previous USDA risk assessments (USDA 1989a,b,c). The number of hours worked per day is expressed as a range, the lower end

of which, 6 hours per day, is based on an 8-hour work day with 1 hour at each end of the work day spent in activities that do not involve herbicide exposure. The upper end of the range, 8 hours per day, is based on an extended (10-hour) work day, allowing for 1 hour at each end of the work day to be spent in activities that do not involve herbicide exposure.

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

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

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

The range of application rates and the typical application rate are taken directly from the program description (see section 2.4). The central estimate of 0.1 lb clopyralid/acre is about the 1997 average application rate of 0.11 lb/acre when clopyralid was used as the sole herbicide (see Table 2-2). The upper end of the range of application rates is above the maximum labeled application but is identical to the reported application rate of 1.0 lb/acre used by the Forest Service in nursery weed control in 1997 (see Table 2-2).

The central estimate of the amount handled per day is calculated as the product of the central estimate of the acres treated per day and the typical application rate. The ranges for the amounts handled per day are calculated as the product of the range of acres treated per day and the range of application rates.

Similarly, the central estimate of the daily absorbed dose is calculated as the product of the central estimate of the exposure rate and the central estimate of the amount handled per day. The ranges of the daily absorbed dose are calculated as the product of the range of exposure rates and the range for the amounts handled per day.

3.2.2.2. Accidental Exposures **--** Typical occupational exposures may involve multiple routes of exposure (i.e., oral, dermal, and inhalation); nonetheless, dermal exposure is generally the predominant route for herbicide applicators (van Hemmen 1992). Typical multi-route exposures

are encompassed by the methods used in section 3.2.2.1 on general exposures. Accidental exposures, on the other hand, are most likely to involve splashing a solution of herbicides into the eyes or a variety of dermal exposure scenarios.

Clopyralid can cause irritant effects in the eyes (see section 3.1.6). The available literature does not include quantitative methods for characterizing exposure or responses associated with splashing a solution of a chemical into the eyes; furthermore, reasonable approaches to modeling this type of exposure scenario quantitatively are not apparent. Consequently, accidental exposure scenarios of this type are considered qualitatively in the risk characterization (section 3.4).

There are various methods for estimating absorbed doses associated with accidental dermal exposure (U.S. EPA 1992, Durkin et al. 1995,1998). Two general types of exposure are modeled: those involving direct contact with a solution of the herbicide and those associated with accidental spills of the herbicide onto the surface of the skin. Any number of specific exposure scenarios could be developed for direct contact or accidental spills by varying the amount or concentration of the chemical on or in contact with the surface of the skin and by varying the surface area of the skin that is contaminated.

For this risk assessment, two exposure scenarios are developed for each of the two types of dermal exposure and the estimated absorbed dose for each scenario is expressed in units of mg chemical/kg body weight. Details of these exposure estimates are presented in the worksheets appended to this risk assessment as specified in Table 3-1.

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

For both scenarios (the hand immersion and the contaminated glove), the assumption of zero-order absorption kinetics is appropriate. Following the general recommendations of U.S. EPA (1992), Fick's first law is used to estimate dermal exposure.

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

assumed that the contaminated skin is effectively cleaned after 1 hour. As with the exposure assessments based on Fick's first law, this product (mg of absorbed dose) is divided by body weight (kg) to yield an estimated dose in units of mg chemical/kg body weight. The specific equation used in these exposure assessments is taken from Durkin et al. (1998).

Confidence in these exposure assessments is diminished by the lack of experimental data on the dermal absorption of clopyralid. Nonetheless, the exposure scenario in which contaminated gloves are worn for 1 hour is very similar to the exposure scenario in which a chemical solution is spilled on to the skin surface of the hands and cleaned after 1 hour. As indicated in Table 3-1, the central estimates as well as the upper and lower ranges of exposure for these two scenarios are within a factor of 4 of each other. This consistency between these two scenarios based on different methods and data sets enhances, at least somewhat, confidence in the exposure assessments. In addition, as detailed in section 3.4 (risk characterization), the dose estimates for all of the accidental scenarios are far below the level of concern so that even very large errors in the estimates would have little impact on the characterization of risk.

3.2.3. General Public.

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

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

The exposure scenarios developed for the general public are summarized in Table 3-2. As with the worker exposure scenarios, details of the assumptions and calculations involved in these exposure assessments are given in the worksheets that accompany this risk assessment (worksheets D01-D09). The remainder of this section focuses on a qualitative description of the rationale for and quality of the data supporting each of the assessments.

3.2.3.2. Direct Spray **--** Direct sprays involving ground applications are modeled in a manner similar to accidental spills for workers (see section 3.2.2.2.). In other words, it is assumed that the individual is sprayed with a solution containing the compound and that an amount of the compound remains on the skin and is absorbed by first-order kinetics. As with the similar worker exposure scenarios, the first-order absorption kinetics are estimated from the empirical

Table 3-2: Clopyralid - Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00091	0.00001	0.067	WSD01
Direct spray, lower legs	Woman	0.00009	0.0000014	0.0068	WSD02
Dermal, contaminated vegetation	Woman	0.00159	0.000027	0.0963	WSD03
Contaminated fruit, acute exposure	Woman	0.0011	0.00011	0.05	WSD04
Contaminated water, acute exposure	Child	0.023	0.0011	0.51	WSD06
Consumption of fish, general public	Man	0.0007	0.00005	0.0102	WSD08
Consumption of fish, subsistence populations	Man	0.0033	0.00022	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0005	0.00004	0.059	WSD05
Consumption of water	Man	0.00001	1.10e-07	0.0003	WSD07
Consumption of fish, general public	Man	3.00e-08	1.00e-09	0.00002	WSD09
Consumption of fish, subsistence populations	Man	2.00e-07	1.00e-08	0.0001	WSD09

relationship of first-order absorption rate coefficients to molecular weight and octanol-water partition coefficients (Durkin et al. 1998), as defined in worksheet A07a.

For these exposure scenarios, it is assumed that during a ground application, a naked child is sprayed directly with clopyralid. These scenarios also assume that the child is completely covered (that is, 100% of the surface area of the body is exposed). These are extremely conservative exposure scenarios and are likely to represent upper limits of plausible exposure. An additional set of scenarios are included involving a young woman who is accidentally sprayed over the feet and legs. For each of these scenarios, some assumptions are made regarding the surface area of the skin and body weight, as detailed in worksheet A04.

3.2.3.3. Dermal Exposure from Contaminated Vegetation **--** In this exposure scenario, it is assumed that the herbicide is sprayed at a given application rate and that an individual comes in

contact with sprayed vegetation or other contaminated surfaces at some period after the spray operation.

For these exposure scenarios, some estimates of dislodgeable residue and the rate of transfer from the contaminated vegetation to the surface of the skin must be available. No such data are directly available for clopyralid, and the estimation methods of Durkin et al. (1995) are used as defined in worksheet D03. Other estimates used in this exposure scenario involve estimates of body weight, skin surface area, and first-order dermal absorption rates, as discussed in the previous section.

3.2.3.4. Contaminated Water **--** Water can be contaminated from runoff, as a result of leaching from contaminated soil, from a direct spill, or from unintentional contamination from aerial applications. Clopyralid is stable in water over a range of pH from 5 to 9 (Woodburn 1987) and the rate of hydrolysis in water is extremely slow - i.e., $t_{½}$=261 days (Concha and Shepler 1994). In addition, clopyralid is extremely stable in anaerobic sediments, with no significant decay noted over a one year period (Hawes and Erhardt-Zabik 1995). Concern for water contamination is increased because clopyralid is not tightly bound to most soils and thus may have a tendency to leach from soil into ground water (e.g., Cox et al. 1996; Cox et al. 1997; Pik et al. 1977; Woodburn and French., 1987).

For this risk assessment, the two types of estimates made for the concentration of clopyralid in ambient water are acute/accidental exposure and longer-term exposure. The accidental exposure scenario is based on a spill of a fixed amount of clopyralid into a body of water of a fixed size assuming instantaneous mixing. The longer-term exposure scenario is based on monitoring data that can be used to associate the application rate of clopyralid with clopyralid concentrations in ambient water.

3.2.3.4.1. ACUTE EXPOSURE -- As detailed in worksheet D06, the acute exposure scenario assumes that a young child (2- to 3-years old) consumes 1 L of contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation of clopyralid is considered.

This is an extremely conservative scenario dominated by arbitrary variability. The actual concentrations in the water would depend heavily on the amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs relative to the time of the spill, and the amount of contaminated water that is consumed. As indicated in Table 3-2, there is about a 500-fold difference in the upper and lower limits of the exposure assessment - i.e., 0.0011 mg/kg/day to 0.51 mg/kg/day. As detailed in worksheet D06, this wide range is attributable almost completely to the differences in field concentrations (a factor of 200) which is in turn attributable to the range in application rates (a factor of about 100 as detailed in worksheet D05). Differences in the estimated amounts of water that might be consumed (a factor of only about 2.5) have relatively little impact on the exposure estimate.

3.2.3.4.2. LONGER-TERM EXPOSURE -- The scenario for chronic exposure to clopyralid from contaminated water is detailed in worksheet D07. This scenario assumes that an adult (70 kg male) consumes contaminated ambient water for a lifetime. The levels of compound in the water are estimated from monitoring data. Thus, environmental processes such as dissipation and degradation are implicit in the assessment.

The most relevant monitoring data for this exposure scenario is the study by Leitch and Fagg (1985) in which clopyralid (LONTREL L) was aerially applied at a rate of about 2.5 lb a.i./acre over 56 hectares - i.e., about 140 acres [56 ha × 2.471 acres/ha = 138.376 acres]. As detailed in worksheet B07, this application rate is equivalent to an application rate of about 1.90 lb a.e./acre. Clopyralid was monitored in stream water during application and subsequently for 72 hours after application at a site 0.5 kilometers downstream from the application site (see Leitch and Fagg 1985, Figure 2, p. 203). The limit of detection in this study was 0.001 mg/L. During and immediately after application, only trace levels of clopyralid were detected in the stream water, suggesting that direct spray of the stream was negligible. The highest levels of clopyralid occurred during or shortly after storm events - i.e., rainfall at hourly rates of about 1 to 20 mm/hour. The maximum level in the stream water was 0.017 mg/L. This occurred shortly after the initial rainfall event during which the highest rainfall rate was about 4 mm/hour. Heavy rainfalls during the following 24 hours resulted in much lower levels of clopyralid in the water. Generally, the monitored concentrations of clopyralid were near the limit of detection of 0.001 mg/L. While Leitch and Fagg (1985) do not provide a tabular summary of the data, visual inspection of Figure 2 (p. 203) in the publication suggests that 0.004 mg/L, the geometric mean of the range from 0.001 mg/L to 0.017 mg/L [$(0.017 \times 0.001)^{0.5}$], is a reasonable estimate of a central value for the concentration of clopyralid in stream water.

For this risk assessment, the monitoring data from Leitch and Fagg (1985) are used to estimate the concentrations in ambient water that could be associated with the application of clopyralid. As detailed in worksheet B07, the central estimate is 0.0021 mg/L per lb a.e. clopyralid that is applied per acre - i.e., units of (mg/L) ÷ (lb a.e./acre). The range for this estimate is from 0.00053 to 0.0089 (mg/L) ÷ (lb a.e./acre).

This approach is clearly extremely conservative. The study by Leitch and Fagg (1985) involved the application of about 266 lbs a.e.. This is about the total amount of clopyralid used by the Forest Service during all of 1997 when clopyralid was applied as the sole herbicide - i.e., 303.43 lbs from Table 2-2. In addition, the monitoring data are from only a relatively brief period after application but are used to estimate longer term exposures for humans. For the characterization of potential human health effects (section 3.4), nonetheless, this extremely conservative approach makes no difference because the exposure levels are far below those of toxicological concern.

3.2.3.5. Oral Exposure from Contaminated Fish -- Many chemicals may be concentrated or partitioned from water into the tissues of animals or plants in the water. This process is referred to as bioconcentration. Generally, bioconcentration is measured as the ratio of the concentration in the organism to the concentration in the water. For example, if the concentration in the organism is 5 mg/kg and the concentration in the water is 1 mg/L, the bioconcentration factor

(BCF) is 5 L/kg [5 mg/kg ÷ 1 mg/L]. As with most absorption processes, bioconcentration depends initially on the duration of exposure but eventually reaches steady state. Details regarding the relationship of bioconcentration factor to standard pharmacokinetic principles are provided in Calabrese and Baldwin (1993).

One study regarding the bioconcentration of clopyralid has been encountered. Bidlack (1982) exposed bluegill sunfish to ^{14}C-labeled clopyralid for 28 days and found no indication of bioconcentration. For exposure assessments based on the consumption of contaminated fish, a BCF of 1 is used (i.e., the concentration in the fish will be equal to the concentration in the water).

For both the acute and longer-term exposure scenarios involving the consumption of contaminated fish, the water concentrations of clopyralid used are identical to the concentrations used in the contaminated water scenarios (see section 3.2.3.4). The acute exposure scenario is based on the assumption that an adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. No dissipation or degradation is considered. Because of the available and well-documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations (U.S. EPA 1996), separate exposure estimates are made for these two groups, as illustrated in worksheet D08. The chronic exposure scenario is constructed in a similar way, as detailed in worksheet D09, except that estimates of clopyralid concentrations in ambient water are based on the monitoring data by Leitch and Fagg (1985).

3.2.3.6. Oral Exposure from Contaminated Vegetation -- None of the Forest Service applications of clopyralid will involve the treatment of crops. Thus, under normal circumstances and in most types of applications conducted as part of Forest Service programs, the consumption of vegetation contaminated with clopyralid is unlikely. Nonetheless, any number of scenarios could be developed involving either accidental spraying of crops or the spraying of edible wild vegetation, like berries. Again, in most instances and particularly for longer-term scenarios, treated vegetation would probably show signs of damage from exposure to clopyralid (section 4.3.2.4), thereby reducing the likelihood of consumption that would lead to significant levels of human exposure.

Notwithstanding that assertion, it is conceivable that individuals could consume contaminated vegetation. One of the more plausible scenarios involves the consumption of contaminated berries after treatment of a right-of-way or some other area in which wild berries grow. The two accidental exposure scenarios developed for this exposure assessment include one scenario for acute exposure, as defined in worksheet D04 and one scenario for longer-term exposure, as defined in worksheet D05. In both scenarios, the concentration of clopyralid on contaminated vegetation is estimated using the empirical relationships between application rate and concentration on vegetation developed by Hoerger and Kenaga (1972). These relationships are defined in worksheet A05a. For the acute exposure scenario, the estimated residue level is taken as the product of the application rate and the residue rate given in worksheet A05a.

For the longer-term exposure scenario, a duration of 90 days is used - i.e., a fruit bearing plant is treated on day 0 and consumed by an individual over a 90-day post-treatment period. For this exposure scenario, an estimate is needed of the residues on the day of treatment as well as the rate of decrease in the residues over time. A large number of studies have been submitted to the U.S. EPA on clopyralid residues in plants (e.g., Biehn 1990; Biehn 1991a,b; Biehn 1995a,b; Markle 1991; McKellar 1995; Nugent and Schotts 1991; Teasdale and Coombe 1991; Yackovich and Lardie 1990).

The most relevant study, however, appears to be that of McMurray et al. (1996), which has recently been published in the open literature and is summarized in Table 3-3. In this study, pre-bloom strawberries (6- to 8-leaf stage) were treated at application rates ranging from 0.07 to 0.28 kg a.i./ha using a backpack sprayer. While McMurray et al. (1996) report the application rate as a.i. rather than a.e., they do not specify which formulation or salt of clopyralid was applied. This has no impact on this exposure assessment because the McMurray et al. (1996) study is used in this risk assessment only to estimate the foliar half-time. After application, these investigators measured clopyralid residues in the strawberry fruit on days 30, 59, and 87 after treatment.

The results of this study are summarized in Table 3-3. As summarized in worksheet B03, these data are well fit (r^2) by an exponential model using application rate and duration after treatment as the explanatory variables for the natural log of the residues on the strawberries as the dependent variable. Using this relationship, the central estimate of the half-time of clopyralid concentrations on strawberries can be estimated at 28.3 days with 95% confidence intervals of 21.2 days to 42.8 days. Again, details of these calculations are provided in worksheet B03.

As is also indicated in worksheet B03, the time zero estimate for residues on strawberries at an application rate of 1 lb/acre is 0.12 mg/kg based on the study by McMurray et al. (1996). This is a factor of about 12 less than the 1.5 mg/kg estimate given by Hoerger and Kenaga (1972). However, these studies are not comparable because the McMurray et al. (1996) study involved the application of clopyralid prior to the formation of the fruit. The Hoerger and Kenaga (1972) estimates are derived from studies in which a number of different herbicides were applied directly to vegetation and residues were monitored over time. For the longer-term exposure assessment detailed in worksheet D05, the estimates from Hoerger and Kenaga (1972) are used because the exposure scenario assumes that the fruit is sprayed directly. As with the drinking water exposure scenarios, this very conservative approach has little impact on the characterization of risk because the levels of projected exposure are far below the levels of concern (section 3.4).

Table 3-3: Clopyralid residue levels in strawberries. (McMurray et al. 1996)

Application rate (kg a.i./ha)	Residues (ppm or mk/kg) at different days after treatment		
	30	59	87
0.07	0.00054	0.00025	0
0.14	0.00083	0.00048	0.00027
0.28	0.00193	0.00079	0.00033

For the acute exposure scenario, it is assumed that a woman consumes 1 lb (0.4536 kg) of contaminated fruit. Based on statistics summarized in U.S. EPA (1996) and presented in worksheet D04, this consumption rate is approximately the mid-range between the mean and upper 95% confidence interval for the total vegetable intake for a 64 kg woman. The range of exposures presented in Table 3-2 is based on the range of concentrations on vegetation from Hoerger and Kenaga (1972) and the range of application rates for clopyralid. The longer-term exposure scenario is constructed in a similar way, except that the estimated exposures include the range of vegetable consumption (U.S. EPA 1996) as well as the range of concentrations on vegetation, the range of application rates for clopyralid, and the range of the confidence limits on foliar half-time.

3.2.4. Hexachlorobenzene.

As mentioned in section 2.2, technical grade clopyralid is contaminated with both hexachlorobenzene ($\leq$2.5 ppm) and pentachlorobenzene ($\leq$0.3 ppm). In terms of the potential for systemic toxic effects , the consequences of this contamination have a minimal impact on this risk assessment, as detailed in section 3.3.3.1, because of the very low levels of the chlorinated benzenes in technical grade clopyralid. However, hexachlorobenzene is classified as a carcinogen (section 3.1.5) and the U.S. EPA has recommended and derived a cancer potency factor for this compound (section 3.3.3.2).

In order to quantitatively consider the potential cancer risk posed by the use of technical grade clopyralid in Forest Service programs, separate exposure assessments are required for hexachlorobenzene. Summaries of the exposure assessments for workers and members of the general public are given in Tables 3-4 and 3-5, respectively. Details of these exposure assessments are presented in the hexachlorobenzene worksheets: worksheets C01 to C04 for workers and D01 to D10 for members of the general public. The following discussion of the exposure assessments for hexachlorobenzene focuses on aspects of the exposure assessments that differ substantially from those used for clopyralid.

3.2.4.1. Acute Exposures **--** For all of the worker exposure assessments as well as the acute exposure assessments for members of the general public, the exposure estimates follow the same general methods used for the clopyralid exposure assessments, as detailed in sections 3.2.2 and 3.2.3. The calculations for hexachlorobenzene are summarized in the hexachlorobenzene worksheets appended to this risk assessment. The major differences in these exposure assessments for clopyralid and hexachlorobenzene involve lipophilicity and water solubility. Clopyralid is highly water soluble ($\geq$1000mg/L, Table 2-2). Consequently, clopyralid does not have a tendency to partition into fatty tissue ($K_{o/w}$ at pH 7 of about 0.0023) and thus its dermal absorption, binding to soil, and bioconcentration are relatively low.

Hexachlorobenzene, on the other hand, is highly lipophilic. The $K_{o/w}$ of hexachlorobenzene is about 1,500,000 and the water solubility of hexachlorobenzene is only about 0.006 mg/L. Thus, hexachlorobenzene may be readily absorbed across the skin, will bind tightly to most soils, and will bioconcentrate in fish (ATSDR 1998). Although the amount of hexachlorobenzene in

Table 3-4: Summary of Worker Exposures to Hexachlorobenzene.

Scenario	Dose (mg/kg/day or event)			Hexachloro-benzene Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	3.28e-09	1.13e-11	2.00e-07	WSC01
Broadcast ground spray (Boom spray)	5.60e-09	1.65e-11	3.78e-07	WSC02
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	1.56e-07	3.65e-09	3.02e-05	WSC03
Contaminated Gloves, 1 hour	9.38e-06	2.19e-07	1.81e-03	WSC03
Spill on hands, 1 hour	2.09e-09	3.36e-11	5.86e-07	WSC04
Spill on lower legs, 1 hour	5.15e-09	8.28e-11	1.44e-06	WSC04

technical grade clopyralid is relatively low, the potential for human exposure, in terms of the proportion of the exposure dose that might be absorbed, is higher than that for clopyralid itself.

As with clopyralid, no studies have been encountered on the dermal absorption rate of hexachlorobenzene in humans and empirical relationships based on human data are used to estimate both zero-order (hexachlorobenzene worksheet B05) and first-order (hexachlorobenzene worksheet B04) dermal absorption rate coefficients. The central estimate of first-order rate coefficient is 0.021 $hour^{-1}$ with a range of about 0.005 to 0.1 $hour^{-1}$. This estimate is substantially higher than first-order rate coefficient of 0.0014 $hour^{-1}$ measured in rats over a 72 hour period (Koizumi 1991). For this risk assessment, the more conservative estimates based on human data are used.

Because of the extremely high lipophilicity and low water solubility of hexachlorobenzene, one adjustment is made in the acute exposure assessments that are impacted by water solubility: the dermal spill scenarios. As detailed in hexachlorobenzene worksheets B01 and B02, the calculation of the concentration of a compound, either a herbicide or contaminant, in a solution that is applied in the field is dependent on the concentration of the compound in the formulation

Table 3-5: Hexachlorobenzene - Summary of Exposure Assessments for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	7.90e-08	1.27e-09	2.21e-05	WSD01
Direct spray, lower legs	Woman	7.93e-09	1.28e-10	2.22e-06	WSD02
Dermal, contaminated vegetation	Woman	4.31e-08	7.52e-10	2.48e-06	WSD03
Contaminated fruit, acute exposure	Woman	2.66e-09	2.66e-10	1.24e-07	WSD04
Contaminated water, acute exposure	Child	5.68e-08	2.60e-09	1.28e-05	WSD06
Consumption of fish, general public	Man	1.71e-05	1.28e-06	2.56e-04	WSD07
Consumption of fish, subsistence populations	Man	8.31e-05	6.23e-06	1.25e-03	WSD07
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	3.83e-11	7.66e-13	8.91e-10	WSD05
Consumption of water	Man	8.57e-14	0.00e+00	6.86e-12	WSD08
Consumption of fish, general public	Man	4.29e-12	0.00e+00	4.51e-09	WSD09
Consumption of fish, subsistence populations	Man	3.47e-11	0.00e+00	2.20e-08	WSD09

as well as the dilution rates for the formulation recommended by the manufacturer. For hexachlorobenzene, the maximum concentration in a field solution based on these rates can be calculated as 0.015 mg/L (hexachlorobenzene worksheets, page WS-13). This exceeds the water solubility of hexachlorobenzene, 0.006 mg/L, by a factor of 2.5. Thus, for the dermal exposure assessments, the maximum water concentration is taken as 0.006 mg/L. This is consistent with the dermal exposure guidelines proposed by U.S. EPA (1992).

For acute exposure scenarios involving contaminated water (hexachlorobenzene worksheets D06 and D07), the nominal maximum concentration of hexachlorobenzene in field solutions, 0.015 mg/L, is used. Even though this concentration exceeds the solubility of hexachlorobenzene in water, these scenarios involve a spill of an amount of a contaminant into the water and the

assumption of instantaneous mixing. Thus, the estimates of the concentrations of hexachlorobenzene in the ambient water are well below of solubility of hexachlorobenzene in water.

As with clopyralid, both the acute and chronic scenarios for the consumption of fish contaminated with hexachlorobenzene (hexachlorobenzene worksheets D07 and D10) require estimates of a bioconcentration factor - i.e., the concentration in fish divided by the concentration in water. As reviewed in ATSDR (1998), reported bioconcentration factors in fish range from about 2,000 to 20,000. For this risk assessment, a bioconcentration factor 10,000 is used in the exposure assessment.

The application of a bioconcentration factor of 10,000 to the acute exposure scenario for contaminated fish (hexachlorobenzene D07) is clearly and perhaps grossly conservative. All of the bioconcentration factors reported in ATSDR (1998) involved exposure periods of at least one month. As detailed by Calabrese and Baldwin (1993, pp. 12-22), the kinetics of bioconcentration in fish are essentially identical to standard pharmacokinetic first-order absorption and first-order elimination models (e.g. Goldstein et al. 1974). Consequently, for compounds that are extensively bioconcentrated, such as hexachlorobenzene, the levels in fish after one day will reflect bioconcentration factors that are typically much less than those seen after long-term exposures. The impact of this conservative assumption on this risk assessment is discussed further in section 3.4.

3.2.4.2. General Considerations for Chronic Exposures -- The major source of exposure for the general public to hexachlorobenzene involves the consumption of contaminated food. The total amount of hexachlorobenzene released to the environment each year is approximately 334,174 kg. Of this amount, the presence of hexachlorobenzene as a contaminant in pesticides accounts for about 5% of this release (17,366 kg/year) (ATSDR 1998). Based on current concentrations of hexachlorobenzene in environmental media and food, daily doses of hexachlorobenzene - i.e., background levels of exposure - are in the range of 0.000001 mg/kg/day mg/kg/day (ATSDR 1998).

The use of clopyralid by the Forest Service is currently about 3000 lbs/year or about 1360 kg/year (section 2). Given a level of 2.5 ppm hexachlorobenzene in technical grade clopyralid, the amount of hexachlorobenzene released to the environment as a result of Forest Service programs is about 0.0034 kg:

$$1360 \text{ kg} \times 0.0000025 = 0.0034 \text{ kg}.$$

Thus, of the total amount of hexachlorobenzene released per year (334,174 kg), the proportion associated with the use of clopyralid by the Forest Service is about 0.00000001,

$$0.0034 \text{ kg} \div 334{,}174 \text{ kg} = 0.00000001$$

or one in one-hundred million.

This leads to the obvious conclusion that the use of clopyralid by the Forest Service will not substantially contribute to any wide-spread increase of ambient levels of hexachlorobenzene.

Notwithstanding the above assessment, localized increases in hexachlorobenzene contamination could occur in the use of clopyralid in Forest Service programs. In other words, while the use of clopyralid by the Forest Service will not result in any general increase in environmental levels of hexachlorobenzene, this does not demonstrate that localized contamination would be insignificant. In order to better assess the potential impact or local contamination, three chronic exposure scenarios are considered quantitatively: contaminated vegetation, contaminated water, and contaminated fish.

3.2.4.2. Chronic Exposures Involving Contaminated Vegetation -- Immediately after direct foliar application to vegetation, hexachlorobenzene will volatilize relatively rapidly from the surface of the vegetation and relatively little will be absorbed and available for longer-term exposures. Once hexachlorobenzene is absorbed into the soil column, however, it is relatively persistent, with reported half times in soil ranging from 3 to 6 years (ATSDR 1998). Thus, the primary concern for chronic exposures to contaminated vegetation is soil contamination with subsequent uptake by plants. This type of scenario requires estimates of long-term levels in soil as well as bioconcentration factors for terrestrial plants.

The highest bioconcentration factor for the uptake of hexachlorobenzene from soil into plants is 19 (ATSDR 1998). This BCF was measured in the edible portion of carrots and will be used directly for this exposure assessment (hexachlorobenzene worksheet D05).

The study by Beall (1976) is the most relevant and detailed study for estimating longer-term concentrations of hexachlorobenzene in soil after directed foliar applications. In this study, hexachlorobenzene was applied using a mechanical sprayer at a rate equivalent to 10 ppm (mg/kg) in the top 5 cm of soil in a simulated pasture maintained for 19 months in a greenhouse. Although Beall (1976) does not specify an application rate in units of quantity per unit area, such as lb/acre, the approximate application rate can be calculated. A 1 cm^2 soil surface that is 5 cm deep has a volume of 5 $cm^{3:}$

$$5 \text{ cm} \times 1 \text{ cm}^2 = 5 \text{ cm}^{3.}$$

The soil type used in the Beall (1976) study is specified as sandy loam but detailed soil characteristics are not provided in the publication. Taking a bulk density of 1.6 g/cm^3 for sandy loam soil (Knisel et al. 1992), a 5 cm^3 volume of soil would weigh 0.008 kg:

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

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

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

Thus, the application rate can be calculated as 80 µg/cm^2 or about 7.1 lbs/acre [1.0 lb/acre = 11.21 µg/cm^2]:

$$80\ \mu g/cm^2 \div (11.21\ \mu g/cm^2 \div 1\ lb/acre) = 7.136\ lbs/acre.$$

Over the 19 month duration of this study, the concentration of hexachlorobenzene in the 2-4 cm soil layer was initially 0.1124 mg/kg decreased linearly to 0.0876 mg/kg after one year. This decrease is equivalent to a dissipation coefficient of 0.25 year^{-1}:

$$0.0876 \div 0.1124 = e^{-kt}$$
$$k = -\ln(0.0876 \div 0.1124)/1\ year = 0.25\ year^{-1}$$

which is equivalent to a half time of 2.8 years:

$$\ln(2) \div 0.25\ year^{-1} = 2.78\ years$$

This is reasonably consistent with other reported half times in soil of 3 to 6 years (ATSDR 1998).

For this risk assessment, the approximate average concentration of hexachlorobenzene in soil over the 1 year period, 0.1 ppm (mg/kg), will be used as the basis for estimating soil levels that could be associated with the application of hexachlorobenzene to vegetation. As detailed in worksheet B01, a deposition rate for hexachlorobenzene can be calculated at 0.00000025 lb a.i./acre based on the typical clopyralid application rate of 0.1 lb a.e./acre. Thus, for the 2-4 cm layer of soil, the average concentration of hexachlorobenzene in soil over a one year period after the deposition of 0.00000025 lb a.i./acre can be estimated at 0.000000003 or 3×10^{-9} ppm (mg/kg soil):

$$0.1\ ppm \times 0.00000025\ lb\ HCB/acre \div 7.1\ lbs\ HCB/acre = 0.000000003\ ppm$$

Because of the relatively long half time of hexachlorobenzene, the potential impact of repeated applications must also be considered. Based on the plateau principle (e.g., Goldstein et al. 1974; O'Flaherty 1981), the concentration at infinite time (C_∞) relative to the concentration after the first treatment (C_0) may be calculated as:

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

where, k is the dissipation rate in units of reciprocal time and Δt is the time interval between treatments. The reported half times of 3 to 6 years, correspond to dissipation rates of 0.11 to 0.23 years [$k = \ln(2) \div t_{1/2}$]. Assuming treatments every year, the maximum build up would be a factor of about 5 to 10:

$$1 \div (1 - e^{-0.11\ to\ 0.23\ \times\ 1\ year}) = 4.9\ to\ 9.6.$$

Thus, in hexachlorobenzene worksheet D05, the concentration of hexachlorobenzene in soil of 3×10^{-9} ppm is multiplied by 10 and a concentration of 3×10^{-8} ppm is used for the typical application rate of 0.1 lb a.e. clopyralid/acre. As indicated in section 2, the lower and upper ranges are based on application rates that vary by a factor of 10 from the typical rate.

3.2.4.3. Chronic Exposures Involving Contaminated Water -- Immediately after application of a pesticide that is contaminated with hexachlorobenzene to soil or plants, there is not likely to be any immediate contamination of water attributable to the hexachlorobenzene in the contaminated pesticide. Nonetheless, because of the persistence of hexachlorobenzene, it will remain in the soil and could be transferred to surface waters where most of the hexachlorobenzene will be bound to sediments or bioconcentrated in aquatic organisms (ATSDR 1998).

No monitoring studies have been encountered that permit a direct estimate of the amount of hexachlorobenzene that would be found in ambient water as a result of applying a herbicide contaminated with hexachlorobenzene. Nonetheless, there is ample monitoring data to indicate that hexachlorobenzene can, over time, be transported to water either by runoff or by volatilization with subsequent redeposition in rainwater. Because hexachlorobenzene binds tightly to and is relatively immobile in soils, hexachlorobenzene is not likely to percolate through soils and directly contaminate ground water (ATSDR 1998). While volatilization may be an important route of environmental transport, volatilized hexachlorobenzene will be rapidly dispersed and transported over a relatively wide area. Although this will contribute to general background levels of hexachlorobenzene, the amounts of hexachlorobenzene released in Forest Service programs will not substantially contribute to background levels of hexachlorobenzene (section 3.2.4.2). Consequently, for this risk assessment, the contamination of ambient water is based on estimates of hexachlorobenzene runoff from contaminated soil.

In the absence of an appropriate monitoring study, the runoff of hexachlorobenzene to ambient water is estimated using the GLEAMS model (Knisel et al. 1992). Details of the application of this model to estimating hexachlorobenzene runoff are provided in Appendix 7. The basic exposure scenario assumes that hexachlorobenzene, as a contaminant in clopyralid, is applied along a ten acre right-of-way that is 50 feet wide and 8712 feet long. For estimating runoff to water, it is assumed that a body of water runs along the length of the right-of-way and that the slope toward the water is 20 percent. Two types of soils are modeled: clay (high runoff potential) and sand (low runoff potential). Annual rainfall rates ranging from 5 to 250 inches are used to reflect the variability of regional rainfall rates based on statistics from the U.S. Weather Service (1998) covering the period from 1961 to 1990.

For both clay and sand, the specific model parameters are selected to yield high estimates of pesticide runoff for each soil type. The model parameter having the greatest impact on runoff is the runoff curve number, a parameter that is used to estimate runoff based on soil texture and other physical characteristics of the soil. For both clay and sand, the runoff curve numbers are based on fallow straight row plots or hard packed surfaces.

As detailed in Appendix 7, runoff of hexachlorobenzene into surface water is not likely in relatively arid areas - i.e., annual rainfall of less than 10 inches. Because of the general rather than site-specific nature of the GLEAMS modeling, however, some runoff could occur in arid areas during unusually severe rainfalls, at least at sites with high runoff potential. In areas of extremely high rainfall - i.e., approaching 200 to 250 inches per year - annual runoff could range from about 5% of the applied amount in sandy soils to about 10% of the applied amount in clay soils.

All of these runoff estimates from GLEAMS apply to the edge of the field. In other words, for clay at rainfall rate of 100 inches per year, GLEAMS estimates that about 5% of the applied hexachlorobenzene will be transported off of the right-of-way. The GLEAMS model runs, however, do not provide any information on the transport of hexachlorobenzene beyond of the borders of the right-of-way. In the absence of a buffer zone, all of the hexachlorobenzene could be projected to go directly into the water. In the application of clopyralid, however, the Forest Service uses a 100 foot buffer around surface water.

Any attempt to realistically model the impact of a buffer zone on water contamination would be highly site-specific. A simplifying assumption could be that all of the annual runoff occurs on the first day of each year, is evenly dispersed on the first 50 foot strip adjacent to the right-of-way, and thus available for runoff toward the body of water. Similarly, all of the runoff on this first section of buffer be assumed to occur on the first day of each year, be evenly dispersed on the second 50 foot strip adjacent to the body of water, and thus available for runoff into the body of water. Thus, 12% of the applied hexachlorobenzene would runoff the right-of-way to the first section of buffer, 12% of this runoff will runoff to the second section of buffer, and 12% of this runoff will be discharged into the water. Under this assumption, the proportion running into the water each year would be approximately 0.002 of the amount applied to the right-of-way:

$$0.12 \times 0.12 \times 0.12 = 0.001728$$

While this might appear to be a highly conservative and protective assumption, it could underestimate exposure for sites in which the runoff from the right-of-way enters a channel or is otherwise more directly transported to surface water. Such site-specific factors cannot be specifically addressed in any general exposure assessment. Thus, the impact of the buffer is not quantitatively considered in the exposure assessment.

The calculations for estimating the typical concentrations of hexachlorobenzene in ambient water that could be expected from the application of clopyralid at a rate of 0.1 lb a.e./acre along a right-of-way are detailed in appendix 7. These calculations essentially involve the application of clopyralid along a 10 acre right-of-way adjacent to a 10 acre pond with an average depth of 1 meter. This scenario assumes that the hexachlorobenzene is bound to soil and mixed in the bottom 1 cm of the pond sediment. This assumption is intentionally conservative. Increasing the mixing depth will increase the amount of hexachlorobenzene bound to the sediment and hence decrease the amount of hexachlorobenzene in water. The amount of hexachlorobenzene in sediment relative to the amount in water is calculated from the soil sorption coefficient of hexachlorobenzene of 100,000 (U.S. EPA 1998) (appendix 7). Because of the persistence of

hexachlorobenzene in the environment, modeled scenarios assumed the annual application of clopyralid over a 20 year period.

The resulting estimates of concentration of hexachlorobenzene in surface water vary substantially with rainfall rates and the number of years over which clopyralid is applied. At an annual rainfall rate of 25 inches, about the national average, the estimated concentration of hexachlorobenzene in water associated with runoff from clay after one year is about 5×10^{-13} mg/L. After 20 years of annual applications, the modeled concentration is about 3×10^{-12} mg/L. At this rainfall rate (25 inches/year), no runoff from sand is anticipated. Higher levels of water contamination are estimated in areas with higher rainfall rates. For example, at an annual rainfall rate of 150 inches, concentrations of hexachlorobenzene in water of about 7×10^{-11} mg/L to 1×10^{-10} mg/L are estimated as a result of runoff from sand and clay soils, respectively. At atypically high rainfall rates of 250 inches per year, concentrations increase to about 1×10^{-10} mg/L to 2×10^{-10} mg/L over a 20 year period.

For this risk assessment, the central estimate of the concentration of hexachlorobenzene in water is taken as 3×10^{-12} mg/L - runoff from clay after a 20 year period with an annual rainfall rate close to the national average. The upper range of the concentration of hexachlorobenzene in water is taken as 2×10^{-10} mg/L - runoff from clay after a 20 year period with an annual rainfall rate of 250 inches, about 10 fold higher than the national average and substantially above upper range of rainfall rates in the United States - i.e., 172.2 inches for Yakutat, Alaska (U.S. Weather Service 1998). This may be viewed as and probably is an extremely conservative worst-case scenario. Nonetheless, given the persistence of hexachlorobenzene in water, the seriousness of the endpoint for hexachlorobenzene - i.e., cancer - and the need to encompass as wide a range of conditions as reasonably possible, this conservative approach seems justified. The lower range for water contamination is taken as zero. This simply reflects that fact that under may conditions of application - i.e., an arid region in an area relatively far removed from open water - contamination of surface water is implausible.

As summarized in ATSDR (1998), monitored levels of hexachlorobenzene in ambient water or drinking water in the Great Lakes region range from essentially zero (below the limits of detection) to about 0.2 nanograms/L or 2×10^{-10} mg/L. Thus, it appears that the use of clopyralid contaminated with hexachlorobenzene in Forest Service programs could lead to the localized contamination of ambient water that is in the same range as general background levels of contamination.

3.2.4.3. Chronic Exposures Involving the Consumption of Contaminated Fish -- Calculation of the doses of hexachlorobenzene that might be associated with the consumption of contaminated fish are detailed in hexachlorobenzene worksheet D09. These calculations are based on the same exposure scenario and estimates of hexachlorobenzene concentrations in ambient water that are detailed in the previous section as well as standard estimates of fish consumption data for the general public as well as subsistence populations (worksheet A04).

The most important variable unique to this scenario is the bioconcentration factor. This exposure assessment uses a bioconcentration factor in fish of 10,000. ATSDR (1998) reports bioconcentration factors that range from about 2000 to 20,000, depending on the species and experimental design. As with the acute exposure scenario for contaminated fish, a BCF of 10,000 is selected as a reasonably conservative estimate. The subsequent dose estimates vary linearly with the bioconcentration factor. As discussed further in section 3.4.7.2, this relatively modest variability in this factor has no substantial impact on the characterization of risk.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.5 mg/kg/day for clopyralid. This RfD is based on a chronic rat NOAEL of 50 mg/kg/day and an uncertainty factor of 100. The rat NOAEL is well-supported by chronic NOAELs in dogs and mice as well as additional chronic NOAEL in rats. The NOAELs for chronic toxic effects are below the NOAELs for reproductive effects. Thus, doses at or below the RfD will be at or below the level of concern for reproductive effects.

The only ambiguity in the dose-response assessment for clopyralid concerns the critical effect - i.e., the adverse effect which will occur at the lowest dose level. No specific adverse effect has been consistently observed in the available studies. Different studies in rats, mice, and dogs have noted general decreases in body weight, increases in liver and kidney weight, as well as a thickening in some epithelial tissue. Decreases in body weight and changes in organ weight are commonly observed in chronic toxicity studies and can indicate either an adaptive or toxic response. Changes in epithelial tissue are less commonly observed and the toxicologic significance of this effect is unclear.

The data on the toxicity of clopyralid are adequate for additional dose-response or dose-severity modeling. Because none of the anticipated exposures substantially exceed the RfD and the great majority of anticipated exposures are far below the RfD, such additional modeling is not necessary for the characterization of risk.

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

3.3.2. Existing Guidelines for Clopyralid. The U.S. EPA has not derived an agency-wide RfD for clopyralid (U.S. EPA 1997a). Nonetheless, the Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.5 mg/kg/day (U.S. EPA 1988a). This RfD is also discussed in Lade (1997). The RfD is based on a two-year rat feeding study in which groups of male and female rats were administered clopyralid in the diet for 2 years at concentrations that resulted in daily

doses of 0 (control), 5, 15, 50 or 150 mg/kg/day. No gross signs of toxicity, changes in organ or body weight, or histopathologic effects attributable to treatment were seen at doses of 50 mg/kg/day or lower. At 150 mg/kg/day, the only effect noted was a decrease in the body weight of the female rats (Humiston et al. 1977). Thus, the U.S. EPA (1988a) designated the dose of 50 mg/kg/day as a NOAEL and used an uncertainty factor of 100 (10 for species-to-species extrapolation and 10 for sensitive subgroups in the human population) to derive the RfD of 0.5 mg/kg/day [50 mg/kg/day ÷ 100 = 0.5 mg/kg/day]. Because the study by Humiston et al. (1977) entailed a 2-year exposure period which approximates the life span of rats, there is no need for an additional uncertainty factor to account for duration of exposure.

No other criteria for clopyralid have been found on INTERNET sites of any of the organizations responsible for setting environmental or occupational exposure recommendations, criteria or standards - i.e., WHO, OSHA, NIOSH, or ACGIH. No published recommendations from these agencies or organizations were encountered in the literature search, which included databases covering the Federal Register.

As detailed in Appendix 3, the Humiston et al. (1977) study is supported by a number of additional subchronic and chronic studies in rats, mice, and dogs. The selection by the EPA of 50 mg/kg/day as the NOEL on which to base the RfD is not contradicted by any of these other bioassays. The only elaboration that might be made to the U.S. EPA RfD is that hyperplasia and thickening of the gastric epithelium was noted at a daily dose of 150 mg/kg/day in another chronic rat feeding study (Barna-Lloyd et al. 1986). In the bioassay by Barna-Lloyd et al. (1986), decreased body weight was observed at 1500 mg/kg/day but not at 150 mg/kg/day. In dogs, daily doses of 150 mg/kg/day over a period of 18 months resulted in increased relative liver weight in females only at 150 mg/kg with no effects being noted at 50 mg/kg/day (Dow AgroSciences 1998).

Based on these data, the critical effect - i.e., the adverse effect which will occur at the lowest dose level - is somewhat ambiguous. At a factor of 3 above the chronic NOAEL effects have been reported on body weight (Humiston et al. 1977), liver weight (Dow AgroSciences 1998), and the gastric epithelium (Barna-Lloyd et al. 1986). Decreases in body weight and changes in organ weight are commonly observed in chronic toxicity studies and can indicate either an adaptive or toxic response. Changes in epithelial tissue are less commonly observed and the toxicologic significance of this effect is unclear.

The data in appendix 1 could be used to develop a more elaborate dose/response or dose/severity assessments with either explicit dose/response models or categorical regression analyses (e.g., Dourson et al. 1997). However, as detailed in section 3.2, none of the exposure scenarios for clopyralid result in doses that substantially exceed the RfD. Consequently, an elaboration of dose-response or dose-severity relationships is unnecessary.

3.3.3. Existing Guidelines for Hexachlorobenzene.

3.3.3.1. Systemic Toxicity -- Two contaminants are found in technical grade clopyralid: hexachlorobenzene (<2.5 ppm) and pentachlorobenzene (<0.3ppm) (section 3.1.9.1). No

guidelines, criteria, or standards have been encountered for pentachlorobenzene. The U.S. EPA has derived an RfD and a cancer potency factor for hexachlorobenzene (U.S. EPA 1997b) as well as an RfD for pentachlorobenzene (U.S. EPA 1988b). More recently, ATSDR (1998) has derived acute, intermediate, and chronic MRLs for hexachlorobenzene.

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

The U.S. EPA RfD for pentachlorobenzene is also 0.0008 mg/kg/day, identical to the RfD for hexachlorobenzene. This RfD is based on a subchronic feeding study in male and female rats in which hyaline droplets were seen in proximal kidney tubules at 8.3 mg/kg/day, the lowest dose tested. Thus, this study did not identify a NOAEL. The RfD is thus based on the LOAEL of 8.3 mg/kg/day divided by an uncertainty factor of 10,000. The uncertainty factor of 10,000 is based on four factors of 10 for interspecies variability, variability in the human population, the use of a subchronic rather than chronic study, and the use of a LOAEL rather than a NOAEL (U.S. EPA 1988b).

ATSDR (1998) has derived an MRL for hexachlorobenzene of 0.00002 mg/kg/day, a factor of 40 below the corresponding U.S. EPA RfD of 0.0008 mg/kg/day. This RfD is based on a LOAEL of 0.016 mg/kg/day from a study in which Sprague-Dawley rats were administered hexachlorobenzene in the diet for 130 weeks. The LOAEL is characterized as changes in liver histology - i.e., peribiliary lymphocytosis and fibrosis. These changes were also seen in a large number of control animals but the effects were significantly increased ($p<0.05$) in animals exposed to hexachlorobenzene and the magnitude of the increase was dose-related. In deriving the MRL, ATSDR applied an uncertainty factor of 1000, three factors of 10 for interspecies variability, variability in the human population, and the use of a LOAEL rather than a NOAEL.

Based on the U.S. EPA RfDs for clopyralid, pentachlorobenzene, and hexachlorobenzene as well as the available information on the levels of these chlorinated benzenes in technical grade clopyralid, the toxicologic significance of the contamination of clopyralid with pentachlorobenzene and hexachlorobenzene can be assessed. RfDs can be treated as estimates of toxicologically equivalent or equitoxic doses - i.e., all RfDs are doses that should cause no adverse effects. The ratio of equitoxic doses is one of the standard definitions of relative potency (e.g., Finney 1971). Using this definition, both pentachlorobenzene and hexachlorobenzene may be regarded as about 600 times more potent than clopyralid:

$$0.5 \text{ mg/kg/day} \div 0.0008 \text{ mg/kg/day} = 625.$$

One common approach to assessing the hazards of chemical mixtures and the relative contribution that each component makes to the mixture is the concept of *potency weighted dose* (e.g. Mumtaz et al. 1994). This can be defined as the sum of the products of the relative potencies (β) and amounts or proportions (π) of each of the components in the mixture:

$$D_{mix} = \sum_{i=1}^{n} B_i \pi_i$$

where the subscript, *i*, designates the i^{th} component in the mixture. For technical grade clopyralid, estimates are available of the proportions of both hexachlorobenzene (2.5 ppm or 0.0000025) as well as pentachlorobenzene (0.3 ppm or 0.0000003) [1 ppm = 0.000001]. The proportion of clopyralid may be calculated by subtracting the proportions of each of these two contaminants:

$$1 - (0.0000025 + 0.0000003) = 0.9999972.$$

Since the toxicity of clopyralid relative to itself is unity (1) by definition, the potency weighted relative toxicity of technical grade clopyralid can be calculated as:

clopyralid:	0.9999972 × 1	=	0.9999972
hexachlorobenzene:	0.0000025 × 625	=	0.0015625
pentachlorobenzene:	0.0000003 × 625	=	0.0001875
Total:			1.0017472

Thus, in terms of the toxicologic contribution of each component, clopyralid contributed approximately 99.8 % [0.9999972 ÷ 1.0017472 = 0.998253] of the toxicity and the two chlorinated benzenes contribute approximately 0.2% of the toxicity.

The same type of calculation can be conducted using the MRL for hexachlorobenzene derived by ATSDR (1998). Using this MRL, the potency of hexachlorobenzene relative to clopyralid is 25,000:

$$0.5 \text{ mg/kg/day} \div 0.00002 \text{ mg/kg/day} = 25000.$$

Thus, the potency weighted relative toxicity of technical grade clopyralid can be calculated as:

clopyralid:	0.9999972 × 1	=	0.9999972
hexachlorobenzene:	0.0000025 × 25000	=	0.0625
pentachlorobenzene:	0.0000003 × 25000	=	0.015
Total:			1.0774972

Based on this more conservative estimate of the chronic toxic potency of hexachlorobenzene, clopyralid still accounts for approximately 93% [0.9999972÷1.0774972 = 0.9281] of the chronic toxic potency of the technical grade product. Thus, although the two chlorinated benzenes should be regarded as much more potent toxicologically than clopyralid, the chlorinated benzenes do not appear to be present in a significant quantity with respect to systemic toxicity. In addition, all of

the toxicity studies on clopyralid used the technical grade clopyralid and thus encompass the likely toxic contribution of the chlorinated benzene contaminants.

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

3.3.3.2. Carcinogenic Potency -- In addition to systemic toxicity, hexachlorobenzene has been shown to cause tumors of the liver, thyroid and kidney in three species of rodents - mice, rats, and hamsters (EXTOXNET 1996; U.S. EPA 1997b). Based on a two-year feeding study in rats, the U.S. EPA (1997b) derived a cancer slope factor for lifetime exposures of 1.6 $(mg/kg/day)^{-1}$. In other words, cancer risk over a lifetime is calculated as the product of the daily dose over a lifetime and the potency parameter:

$$P = d\,\beta$$

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

$$d = P \div \beta$$

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

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

As noted in section 3.1.5, clopyralid is not classified as a carcinogen. While it can be argued that the technical grade clopyralid used in the standard bioassays encompasses any toxicologic effects that could be caused by hexachlorobenzene, this argument is less compelling for carcinogenic effects because, for most cancer causing agents, the cancer risk is conservatively viewed as a non-threshold phenomenon - i.e., zero risk is achieved only at zero dose.

The potency factor of 1.6 $(mg/kg/day)^{-1}$ is intended to be applied to lifetime daily doses. As summarized in section 3.2, many of the exposure assessments used in this risk assessment involve much shorter periods of time. Following the approach recommended by U.S. EPA (1997b, p. 35), this risk assessment assumes that the average daily dose over a lifetime is the appropriate measure for the estimation of cancer risk. Thus, the lifetime potency of 1.6 $(mg/kg/day)^{-1}$ is scaled linearly when applied to shorter periods of exposure. For example, taking 70 years [70 years × 365 days/year = 25,550 days] as a reference life span, the potency parameter for a one-day exposure is calculated as 0.000063 $(mg/kg/day)^{-1}$:

$$1.6\ (mg/kg/day)^{-1} \times (1\ day \div 25{,}550\ days) = 0.000062622\ (mg/kg/day)^{-1}.$$

For example, taking a dose of 0.001 mg/kg/day, the lifetime risk associated with a one-day exposure at this dose would be calculated as 0.000000063:

$$0.000063\ (\text{mg/kg/day})^{-1} \times 0.001\ \text{mg/kg/day} = 0.000000063.$$

This method of estimating risk is used in the worksheets for hexachlorobenzene that are appended to this document.

No explicit dose response assessment is made for the potential carcinogenic effects of pentachlorobenzene. This is consistent with the approach taken by U.S. EPA (1988b) and reflects the fact the available data on pentachlorobenzene are inadequate to classify this compound as a carcinogen or to estimate carcinogenic potency. This is not the most conservative approach that could be taken. For example, because pentachlorobenzene and hexachlorobenzene are structurally and toxicologically similar and because the chronic RfD for pentachlorobenzene is identical to the RfD for hexachlorobenzene, a more conservative approach would be to assume that pentachlorobenzene is a carcinogen and that the carcinogenic potency of pentachlorobenzene is identical to that of hexachlorobenzene. If such an approach were taken, the cancer risks taken in this risk assessment would increase by 10 percent. In other words, pentachlorobenzene has the same potency as hexachlorobenzene but it present at a ten-fold lower concentration relative to hexachlorobenzene. As detailed in the following section, this relatively modest difference has little impact on the characterization of cancer risk.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. The risk characterization for potential human health effects associated with the use of clopyralid in Forest Service programs is relatively unambiguous. Based on the estimated levels of exposure and the criteria for chronic exposure developed by the U.S. EPA, there is no evidence that typical or accidental exposures will lead to dose levels that exceed the level of concern. In other words, all of the anticipated exposures - most of which involve highly conservative assumptions - are at or below the RfD. The use of the RfD - which is designed to be protective of chronic or lifetime exposures - is itself a very conservative component of this risk characterization because the duration of any plausible and substantial exposures is far less than lifetime.

Irritation and damage to the skin and eyes can result from exposure to relatively high levels of clopyralid - i.e., placement of clopyralid directly onto the eye or skin. From a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling clopyralid. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of clopyralid.

The only reservation attached to this assessment of clopyralid is that associated with any risk assessment: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated.*** No chemical, including clopyralid, has been studied for all possible effects and the use of data from laboratory animals to estimate hazard or the lack of hazard to humans is a process that is fraught with uncertainty. Prudence dictates that normal and reasonable care should

be taken in the handling of this or any other chemical. Notwithstanding these reservations, the use of clopyralid does not appear to pose any identifiable hazard to workers or the general public in Forest Service programs.

The contamination of clopyralid with hexachlorobenzene does not appear to present any substantial cancer risk. Administratively, the Forest Service has adopted a cancer risk level of one in one-million (1÷1,000,000) as a trigger that would require special steps to mitigate exposure or restrict and possibly eliminate use. Based on relatively conservative exposure assumptions, the risk levels estimated for members of the general public are below this trigger level. The highest risk level is estimated at about 8 in 100 million (7.82e-08 or about 0.00000008), about a factor of 12 below the level of concern. The exposure scenario associated with this risk level involves the consumption of contaminated fish by subsistence populations - i.e., groups that consume relatively large amounts of contaminated fish. The consumption of fish contaminated with hexachlorobenzene is a primary exposure scenario of concern because of the tendency of hexachlorobenzene to bioconcentrate from water into fish. This is also consistent with the general observation that exposure to hexachlorobenzene occurs primarily through the consumption of contaminated food.

For workers, the only cancer risk level that approaches a level of concern involves workers wearing contaminated gloves for one-hour. In this instance, the risk level is about one in ten-million [1.13e-07], about a factor of 10 below the Forest Service trigger level of one in one-million. As with the fish consumption scenario for members of the general public, the contaminated glove scenario for workers leads to relatively high risks because of the tendency of hexachlorobenzene to partition into fatty tissue.

Both of these relatively high risk scenarios are based on upper ranges of plausible exposures. Based on central estimates of exposure, the cancer risk levels are below the trigger level by factors of about one-thousand (1000) to ten-million (10,000,000). In other words, the cancer risk estimates based on central or most likely estimates of exposure are in the range of about 1 in one-billion (1÷1,000,000,000) to less than 1 in one-trillion (1÷1,000,000,000,000).

In terms of potential toxic effects, the only scenarios of marginal concern with hexachlorobenzene are the scenarios that approach the level of concern for cancer risk: consumption of contaminated fish by members of the general public and workers wearing contaminated gloves. In all cases, however, projected exposures are below the RfD by at least a factor of five.

3.4.2. Workers. A quantitative summary of the risk characterization for workers associated with exposure to clopyralid is presented in Table 3-6. The quantitative risk characterization is expressed as the hazard quotient, which is the ratio of the estimated exposure doses from Table 3-1 to the RfD of 0.5 mg/kg/day, as derived in section 3.3.2. As in previous tables, numbers greater than or equal to 0.000001 are expressed in standard decimal notation and smaller numbers

Table 3-6: Summary of risk characterization for workers associated with exposure to clopyralid[1]

RfD	0.5	mg/kg/day	Sect. 3.3.2.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.003	0.000009	0.2	WSC01
Broadcast ground spray (Boom spray)	0.004	0.00001	0.3	WSC02
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	3e-07	1e-08	0.00002	WSC03
Contaminated Gloves, 1 hour	0.00002	3e-07	0.0009	WSC03
Spill on hands, 1 hour	0.00005	7e-07	0.004	WSC04
Spill on lower legs, 1 hour	0.0001	0.000002	0.009	WSC04

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Table 3-1 for a summary of exposure assessments.

are expressed in scientific notations - e.g., 7e-07 equivalent to 7×10^{-7} or 0.0000007. Details of the conversion of scientific to decimal notation are given on page ix of this report.

Given the very low hazard quotients for both general occupational exposures as well as accidental exposures, the risk characterization for workers is unambiguous. None of the exposure scenarios approach a level of concern.

While the accidental exposure scenarios are not the most severe one might imagine (e.g., complete immersion of the worker or contamination of the entire body surface for a prolonged period of time) they are representative of reasonable accidental exposures. Given that the highest hazard quotient for any of the accidental exposures is a factor of about 111 below the level of concern (i.e., a hazard quotient of 0.009 as the upper limit for a spill on to the lower legs for 1 hour), far more severe and less plausible scenarios would be required to suggest a potential for systemic toxic effects. As discussed in section 3.2, however, confidence in this assessment is diminished by the lack of information regarding the dermal absorption kinetics of clopyralid in humans. Nonetheless, the statistical uncertainties in the estimated dermal absorption rates, both zero-order and first-order, are incorporated into the exposure assessment and risk

characterization. Again, these estimates would have to be in error by a factor of over 100 in order for the basic characterization of risk to change. In addition, the hazard quotients for these acute occupational exposure are based on a chronic RfD. This adds and additional level of conservatism and, given the very low hazard quotients for these scenarios, reenforces the conclusion that there is no basis for asserting that systemic toxic effects are plausible.

The hazard quotients for general occupational exposure scenarios are somewhat higher than those for the accidental exposure scenarios. Nonetheless, the upper limit of the hazard quotients for both backpack and boom spray applications are below the level of concern - i..e., a hazard index of 1. As discussed in section 3.2 and detailed in worksheets C01 and C02, these upper limits of exposure are constructed using the highest anticipated application rate, the highest anticipated number of acres treated per day, and the upper limit of the occupational exposure rate. If any of these conservative assumptions are modified (e.g., the compound is applied at the typical rather than the maximum application rate) the hazard quotients would drop substantially. For example, the upper end of the range for the hazard quotient involving broadcast application is 0.3. This is based on an application of 1 lb a.e./acre. At the typical application rate of 0.1 lb a.e./acre, the hazard quotient would be 0.03, a factor of about 30 below the level of concern.

The simple verbal interpretation of this quantitative characterization of risk is that even under the most conservative set of exposure assumptions, workers would not be exposed to levels of clopyralid that are regarded as unacceptable. Under typical application conditions, levels of exposure will be far below levels of concern.

As discussed in section 3.1.6, clopyralid can cause irritation and damage to the skin and eyes. Quantitative risk assessments for irritation are not derived; however, from a practical perspective, eye or skin irritation is likely to be the only overt effect as a consequence of mishandling clopyralid. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of clopyralid.

3.4.3. General Public. The quantitative hazard characterization for the general public associated with exposure to clopyralid is summarized in Table 3-7. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the RfD of 0.5 mg/kg/day.

None of the longer-term exposure scenarios approach a level of concern and none of the acute/accidental scenarios exceed a level of concern, based on central estimates of exposure, although the upper limit of the hazard quotient for the consumption of water after an accidental spill reaches the level of concern.

Although there are several uncertainties in the longer-term exposure assessments for the general public, as discussed in section 3.2, the upper limits for hazard quotients are sufficiently far below a level of concern that the risk characterization is relatively unambiguous: based on the available information and under the foreseeable conditions of application, there is no route of exposure or

Table 3-7: Summary of risk characterization for the general public associated with exposure to clopyralid [1].

RfD		0.5	mg/kg/day	Sect. 3.3.2	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.002	0.00003	0.1	WSD01
Direct spray, lower legs	Woman	0.0002	3e-06	0.01	WSD02
Dermal, contaminated vegetation	Woman	0.003	0.00005	0.2	WSD03
Contaminated fruit, acute exposure	Woman	0.002	0.0002	0.1	WSD04
Contaminated water, acute exposure	Child	0.05	0.002	1	WSD06
Consumption of fish, general public	Man	0.001	0.0001	0.02	WSD08
Consumption of fish, subsistence populations	Man	0.007	0.0004	0.1	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.001	0.00009	0.1	WSD05
Consumption of water	Man	0.00002	2e-07	0.0006	WSD07
Consumption of fish, general public	Man	1e-07	2e-09	0.00004	WSD09
Consumption of fish, subsistence populations	Man	4e-07	2e-08	0.0002	WSD09

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Worksheet E02 for summary of exposure assessments.

scenario suggesting that the general public will be at any substantial risk from longer-term exposure to clopyralid.

For the acute/accidental scenarios, the exposure resulting from the consumption of contaminated water by a child is the only scenario that reaches or even approaches a level of concern. As discussed in some detail in section 3.2.3.4.1, the exposure scenario for the consumption of contaminated water is an arbitrary scenario: scenarios that are more or less severe, all of which may be equally probable or improbable, easily could be constructed. All of the specific assumptions used to develop this scenario have a simple linear relationship to the resulting hazard

quotient. Thus, if the accidental spill were to involve 20 rather than 200 gallons of a field solution of clopyralid, all of the hazard quotients would be a factor of 10 less. Nonetheless, this and other acute scenarios help to identify the types of scenarios that are of greatest concern and may warrant the greatest steps to mitigate. For clopyralid, such scenarios involve oral (contaminated water) rather than dermal (spills or accidental spray) exposure. As with the acute exposure scenarios for workers, the hazard quotients for the general public that involve acute exposure scenarios are inherently conservative in that they are based on the chronic RfD.

3.4.4. Sensitive Subgroups. There is no information to suggest that specific groups or individuals may be especially sensitive to the systemic effects of clopyralid. As discussed in sections 3.1.3 and 3.3.2, the likely critical effect of clopyralid in humans cannot be identified clearly. Clopyralid can cause decreased body weight, increases in kidney and liver weight, deceased red blood cell counts, as well as hyperplasia in gastric epithelial tissue. These effects, however, are not consistent among species or even between different studies in the same species. Thus, it is unclear if individuals with pre-existing diseases of the kidney, liver, or blood would be particularly sensitive to clopyralid exposures, although individuals with any severe disease condition could be considered more sensitive to many toxic agents.

In addition, some individuals may suffer from multiple chemical sensitivity (e.g., ATSDR 1995). Such individuals may respond adversely to extremely low levels of chemicals and in a manner that is atypical of the general population. There are no data or case reports, however, on idiosyncratic responses to clopyralid.

3.4.5. Connected Actions. As indicated in section 3.1.10, clopyralid may be applied in combination with other herbicides, particularly in combination with 2,4-D or 2,4-D and picloram. There are no data in the literature suggesting that clopyralid will interact, either synergistically or antagonistically with these or other compounds.

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

3.4.7. Hexachlorobenzene.

3.4.7.1. Workers -- Summaries of the exposure assessments and risk characterization for workers are given in the hexachlorobenzene worksheets that accompany this risk assessment. Worksheet E01 summarizes the exposure assessment for workers and is analogous to the corresponding worksheet for clopyralid. Worksheets E02a, E02b, and E02c summarize the risk characterization for workers.

Worksheet E02a presents the hazard quotients for workers. For acute exposures, the hazard quotient is the level of exposure divided by the acute MRL from ATSDR of 0.008 mg/kg/day. For chronic exposures, the hazard quotient is the level of exposure divided by the chronic RfD.

from U.S. EPA of 0.0008 mg/kg/day. For general worker exposures, the hazard quotients are approximately three orders of magnitude below the corresponding hazard quotients for clopyralid (see Table 3-6). Even using the much more conservative chronic MRL for hexachlorobenzene of 0.00002 mg/kg/day, none of the dose estimates approach a level of concern. Similarly, hazard quotients associated with spill scenarios are generally lower for hexachlorobenzene than the corresponding scenarios for clopyralid. These comparisons are consistent with the general assertion from section 3.3.3.1 that the amount of hexachlorobenzene in technical grade clopyralid it not toxicologically significant. Immersion scenarios for hexachlorobenzene, however, results in higher estimated hazard quotients than the corresponding values for clopyralid. For the scenario in which contaminated gloves are worn for 1 hour, the upper range of the estimated dose is below the acute MRL by a factor of 5. Thus, under reasonable work practices, none of the anticipated accidental or incidental exposures to hexachlorobenzene exceed the acute MRL.

Worksheet E02b presents the cancer risks - i.e., the levels of exposure from E01 multiplied by the cancer potency factor. In worksheet 02b, the cancer potency factor is adjusted to estimate daily risks by dividing the lifetime cancer potency factor of 1.6 $(mg/kg/day)^{-1}$ by 25,500 days as detailed in section 3.3.3.2. The last worksheet for workers, worksheet 02c, presents the cancer risk relative to a risk level of one in one-million - i.e., each risk level from worksheet 02b is divided by one million. A risk level of one in one-million or less has been administratively selected by the Forest Service as a reference level for risk assessments. Thus, in worksheet 02c, any value greater than unity represents a risk that is considered unacceptable by the Forest Service.

For the general exposure scenarios, the upper limits of cancer risk are about 1×10^{-11} to 2×10^{-11} - i.e., one or two in one-hundred billion - for each day of exposure. Thus, using the upper levels of exposure, a worker would have to handle clopyralid for 50000 to100000 days ($1\times10^{-6} \div 1\times10^{-11}$ to 2×10^{-11}) to reach a risk level of one in one-million (1×10^{-6}). This is equivalent to about 140 to 270 years. Based on daily risks associated with central estimates of exposure (i.e., risks of 3.5×10^{-13}), a worker would have to handle clopyralid for 3×10^{6} days [$1\times10^{-6} \div 3.5\times10^{-13}$]. This is equivalent to 3,000,000 days or about 8000 years. For the accidental exposure scenarios, the highest risk level is about 1×10^{-7}.

While there are substantial uncertainties involved in any cancer risk assessment, the verbal interpretation of this numeric risk characterization is relatively simple. There is no plausible basis for asserting that the contamination of clopyralid with hexachlorobenzene will result in any substantial risk of cancer in workers applying clopyralid under normal circumstances.

For the accidental scenarios, however, the cancer risk associated with the upper range of exposures for workers wearing contaminated gloves for one-hour yields a risk estimate of about 1×10^{-7}, a factor of only 10 below the level of concern. This relatively high risk reflects the likely tendency of hexachlorobenzene to partition from an aqueous solution into the skin.

3.4.7.2. General Public -- Summaries of the acute exposure assessments and risk characterization for the general public are given in the hexachlorobenzene worksheets that accompany this risk assessment and parallel those for the risk characterization for workers discussed in the previous

section: worksheet E03 summarizes the exposure assessments and worksheets E04a, E04b, and E04c summarize the risk characterizations.

Worksheet E04a presents the hazard quotients for the general public associated with the acute exposure scenarios. As with the corresponding worksheet for workers, the hazard quotients for acute exposures are based on the acute ATSDR MRL of 0.008 mg/kg/day and the hazard quotients for chronic exposures are based on the U.S. EPA RfD of 0.0008 mg/kg/day. All exposure scenarios result in hazard quotients that are below unity - i.e., the level of exposure is below the RfD. In addition, almost all of the exposure scenarios result in hazard quotients that are substantially below the corresponding hazard quotient for clopyralid (Table 3-7). This is consistent with the analysis presented in section 3.3.3.1, indicating that amount of hexachlorobenzene in clopyralid is toxicologically insignificant. The only exceptions are the acute scenarios based on the consumption of contaminated fish. For these scenarios, the hazard quotients for hexachlorobenzene and clopyralid are comparable because hexachlorobenzene is likely to bioconcentrate in fish while clopyralid will not. In any event, the highest hazard quotient for hexachlorobenzene is about 0.2, the upper range of the hazard quotient associated with the acute scenario for the consumption of contaminated fish by subsistence populations.

The cancer risk assessment for acute exposure scenarios involving the general public is given in worksheet E04b. As with the corresponding worksheets for workers, the last worksheet for the general public, worksheet 04c, presents the cancer risk relative to a risk level of one in one-million. All scenarios, including the consumption of fish by subsistence populations, are below the reference risk level of one in one-million by factors of about 10 [acute scenario for the consumption of contaminated fish] to several thousand. As with the hazard quotients, the highest cancer risks associated with acute exposures involve the consumption of contaminated fish by subsistence populations.

As with the acute exposure scenarios, the consumption of contaminated fish leads to the highest risk estimates for the longer-term scenarios involving the general public,. Based on typical fish consumption values for members of the general public, the estimated lifetime cancer risks are below the reference risk level of one in one-million by factors of over 100 to nearly 150,000. For subsistence populations, the upper limit of risk is about a factor of 30 below the level of concern. Given the very conservative nature of the exposure assessment for this scenario, there does not appear to be a substantial cause for concern. This scenario, however, is based on the typical application rate for clopyralid of 0.1 lb a.e./acre. At a ten fold higher application rate - i.e., 1 lb clopyralid a.e./acre, the cancer risk be only about a factor of three below the reference cancer risk level of one in one-million..

This risk characterization must be interpreted in terms of the underlying assumptions. As detailed in appendix 7, the upper limits for all of the exposure scenarios involving contaminated water and fish are based on relatively conservative estimates of runoff at an annual rainfall rate of 250 inches. This rainfall rate is implausible in most areas of the country. In addition, all of the modeling scenarios are based on assumptions that tend to maximize runoff and subsequent water contamination. In relatively arid areas of the country or in areas with average rainfall rates, water

contamination would be substantially less. Furthermore, even at relatively high rates of rainfall, runoff may be insignificant under site-specific conditions that do not favor runoff or in cases in which the clopyralid is applied at sites far from surface water. This types of situational or site-specific variability cannot be well-encompassed or well-represented in generic exposure assessments.

As discussed in section 3.3.3.2., no explicit dose response assessment is made for the potential carcinogenic effects of pentachlorobenzene, another impurity in clopyralid Based on the comparison of apparent toxic potencies and the relative amounts of both hexachlorobenzene and pentachlorobenzene in clopyralid, a case could be made for suggesting that presence of pentachlorobenzene in technical grade clopyralid could increase the cancer risk by 10%. Given the extremely low levels of estimated cancer risk, this has essentially no impact on the risk characterization.

The simple verbal interpretation of this risk characterization is that, in general, the contamination of clopyralid with hexachlorobenzene does not appear to pose a risk to the general public. The prolonged use of clopyralid at the highest plausible application rate, 1 lb a.e./acre, could approach a level of concern in areas with small ponds or lakes used for fishing and in areas with local conditions that favor runoff. In such cases, site-specific exposure assessments and/or monitoring of hexachlorobenzene concentrations in water could be considered.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. The toxicity of clopyralid is relatively well characterized in experimental mammals but few wildlife species have been assayed relative to the large number of non-target species that might be potentially affected by the use of clopyralid. Within this admittedly substantial reservation, clopyralid appears to be relatively non-toxic to terrestrial or aquatic animals, is highly selective in its toxicity to terrestrial plants, and relatively non-toxic to aquatic plants. Thus, the potential for substantial effects on non-target species appears to be remote. Consistent with this assessment of toxicity to non-target species, one long-term (8-year) field study has been conducted that indicates no substantial or significant effects on species diversity (Rice et al. 1997).

The toxicity to non-target terrestrial animals is based almost exclusively on toxicity studies using experimental mammals - i.e., the same studies used in the human health risk assessment. Some additional studies are available on birds, bees, and earthworms that generally support the characterization of clopyralid as relatively non-toxic. An additional study of the toxicity of clopyralid to non-target invertebrates also suggests that clopyralid has a low potential for risk (Hassan et al. 1994). A caveat in the interpretation of this study is the limited detail in which the experimental data are reported. As with terrestrial species, the available data on aquatic species, both plants and animals, suggest that clopyralid is relatively non-toxic.

The toxicity of clopyralid to terrestrial plants has been examined in substantial detail in studies that have been published in the open literature as well as studies that have been submitted to the U.S. EPA to support the registration of clopyralid. Clopyralid is a plant growth regulator and acts as a synthetic auxin or hormone, altering the plant's metabolism and growth characteristics, causing a proliferation of abnormal growth that interferes with the transport of nutrients throughout the plant. This, in turn, can result in gross signs of damage and the death of the affected plant. The phytotoxicity of clopyralid is relatively specific to broadleaf plants because clopyralid is rapidly absorbed across leaf surfaces but much less readily absorbed by the roots of plants. For the same reason, clopyralid is much more toxic/effective in post-emergent treatments (i.e., foliar application) rather than pre-emergent treatment (i.e., application to soil).

Clopyralid does not bind tightly to soil and thus would seem to have a high potential for leaching. While there is little doubt that clopyralid will leach under conditions that favor leaching - i..e., sandy soil, a sparse microbial population, and high rainfall - the potential for leaching or runoff is functionally reduced by the relatively rapid degradation of clopyralid in soil. A number of field lysimeter studies and the long-term field study by Rice et al. (1997) indicate that leaching and subsequent contamination of ground water are likely to be minimal. This conclusion is also consistent with a short-term monitoring study of clopyralid in surface water after aerial application (Leitch and Fagg 1985).

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals– As summarized in the human health risk assessment (see section 3), there are several toxicity studies in experimental mammals, specifically rats, mice, rabbits, and dogs, exposed to clopyralid. The acute toxicity of clopyralid is relatively low: about 3000 mg/kg for clopyralid produced by electrochemical process and >5000 mg/kg for clopyralid produced by the penta process (LD_{50}s).

Clopyralid is a plant toxin and its mode of action in plants is well understood; however its mode of action for causing toxicity in mammals is not determined and there is no consistent effect or set of effects that can be attributed to clopyralid. While the U.S. EPA (1997a) RfD uses decreased body weight in rats as a critical effect - i.e., the adverse effect occurring at the lowest dose level - effects on liver and kidney weight as well as changes in gastric epithelial tissue have been noted at comparable dose levels.

4.1.2.2. Birds– As summarized in appendix 2, the acute toxicity of clopyralid has been assayed using Mallard ducks and Bobwhite quail, both standard test species required by the U.S. EPA in the registration of pesticides. Most of the acute studies involve dietary administration over short periods of time - i.e., 5 days. The LD_{50} data on experimental mammals, however, involve gavage administration - i.e., placing the compound directly into the stomach by intubation. One gavage study in birds (Dow Chemical 1980) is available on the acute toxicity of clopyralid to Mallard ducks. As indicated in appendix 2, the LD_{50} by gavage to this species was 1465 mg/kg bw. Since this study was conducted in the early 1980's, clopyralid from the older penta process was probably used. Thus, this LD_{50} in birds is most directly comparable to the reported LD_{50} in rats of >5000 mg/kg (Jeffrey et al. 1987b). As summarized in appendix 1, the study in rats by Jeffrey et al. (1987b) noted no mortality and no signs of toxicity after single gavage doses of 5000 mg/kg bw to 9 week old male and female Fischer rats. The lower LD_{50} of 1465 mg/kg bw in ducks (Dow Chemical 1980) suggests that clopyralid could be somewhat more toxic to birds than mammals.

This apparent difference, however, is based on the comparison of only two studies. As discussed in Section 3.1.2 with respect to the comparison of the acute toxicity of penta process and electrochemical process clopyralid to rats, substantial random variation is found in the conduct of acute toxicity studies on the same material in the same species. Thus, it is possible that this apparent difference between birds and rats is attributable to chance rather than any underlying consistent difference in sensitivity among species or groups of species.

The dietary bioassay studies on birds can also be used to assess the potential contribution of the monoethanolamine moiety to the toxicity of Transline, the formulation used by the Forest Service that contains the monoethanolamine salt of clopyralid as the active ingredient. Acute dietary studies can be used, albeit with substantial limitations, to compare the toxicity of clopyralid to the toxicity of the monoethanolamine salt of clopyralid in Mallard ducks (Dow Chemical USA 1980; Dow AgroSciences 1998) and Bobwhite quail (Dow Chemical 1980; Dow AgroSciences 1998). The primary problem with all of these studies, however, is that none of the exposures resulted in adequate mortality for the estimation of an LC_{50} or LD_{50} (appendix 2). Nonetheless, these studies

suggest that the dietary LC_{50} values for both clopyralid and the monoethanolamine salt of clopyralid are above the range of 2000 ppm to about 6000 ppm.

In addition to the standard acute toxicity studies, Dabbert et al. (1997) have found that direct spray of bobwhite quail eggs at up to 0.56 kg a.e./ha caused no gross effects - i.e., viability, hatchability, body weight - and no effects on immune function in chicks.

4.1.2.3. Terrestrial Invertebrates– Several studies (Cole 1974; Dow Chemical 1980;Dow Chemical 1980; Hinken et al. 1986) have been conducted on the toxicity of clopyralid to bees - a test required by the U.S. EPA in the registration of pesticides - using both oral and direct contact exposures (appendix 3). In both cases, the LD_{50} to bees was greater than 0.1 mg/bee. Taking an average weight of 110 mg/bee from Hinken et al. (1986), the LD_{50} of 0.1 mg/bee corresponds to an LD_{50} of greater than 9090 mg/kg bw [0.1 mg/bee ÷ 110 mg/bee = 0.1 mg/bee ÷ 0.11 g/bee = 0.1 mg/bee ÷ 0.00011 kg/bee = 909 mg/kg bw]. This order of toxicity is comparable to the LD_{50} values reported in experimental mammals (appendix 1) and birds (appendix 2).

Based on the results of a static bioassay on earthworms summarized in Dow AgroSciences (1998), the soil LC_{50} of clopyralid to earthworms is greater than 1000 ppm soil.

In addition to these standard bioassays, Hassan et al. (1994) have provided a summary of an apparently large series of bioassays and field trials on clopyralid as well as a number of other pesticides using a variety of terrestrial invertebrates. The form of clopyralid used in this study was Lontrel 100, a formulation of clopyralid that is no longer marketed commercially. While this publication does not provide detailed dose, exposure, or response data, it does indicate that clopyralid was classified by the study authors as *harmless* - a category that is defined by these investigators as exposures which result in less than 30% mortality - to several insect parasites and predatory mites in contact bioassays. Mortality rates of 25-50% were seen in *Semiadalia 11-notata* (Coccinellidae) and *Anthocoris nemoralis* (Anthocoridae).

4.1.2.4. Terrestrial Plants (Macrophytes)– Clopyralid is a plant growth regulator and acts as a synthetic auxin or hormone, altering the plant's metabolism and growth characteristics and often causing a proliferation of abnormal growth that interferes with the transport of nutrients throughout the plant. This, in turn, can result in gross signs of damage and the death of the affected plant (Crosswhite et al. 1995). At the biochemical level, clopyralid has been shown to inhibit glutamine synthetase and NADPH reductase in pea and oat chloroplasts (Levchenko et al. 1990). In the honey mesquite, clopyralid interferes with normal carbohydrate balance and the decline and recovery of total nonstructural carbohydrates in stems and roots is similar to that seen after hand cutting (Cralle and Bovey 1996).

Although clopyralid can be absorbed from both the leaves and the roots, foliar absorption predominates. In the sunflower and rapeseed, 97% foliar absorption occurs within 24 hours after foliar application (Hall and Vanden Born 1988). Thus, clopyralid is preferentially toxic to broad-leaf weeds and relatively non-toxic to grasses (Bachman et al. 1995; Crosswhite et al. 1995). Nonetheless, at sufficiently high soil concentrations, clopyralid can cause significant

damage by root absorption, particularly in seedlings (Clay et al. 1996). Root absorption appears to occur by non-facilitated diffusion. The rate of uptake is greater at low pH, suggesting that the undissociated form is more readily absorbed than the anionic form (Devine et al. 1987).

A great deal of information is available on the toxicity of clopyralid to terrestrial plants. A large number of studies have been conducted on efficacy to target species, particularly honey mesquite (Bovey and Whisenant 1991; Bovey et al. 1988a,b; Bovey et al. 1990a,b; Bovey et al. 1991, Bovey et al. 1994; Cralle and Bovey 1996; Whisenant and Bovey 1993; Whisenant et al. 1993). Additional efficacy studies have been conducted on Canada thistle (Devine and VandenBorn 1985; Devine and Vandenborn 1985), the field pansy *Viola arvensis* (Grundy et al. 1995), wild buckwheat (Kloppenburg and Hall 1990a,b,c), hemp dogbane (Orfanedes and Wax 1991; Orfanedes et al. 1993), wild carrot (Stachler and Kells 1997) and spotted knapweed (Rice et al. 1997). With the exception of the study by Rice et al. (1997), these studies are not directly useful for assessing potential effects on non-target species. Other than to acknowledge the efficacy of this compound and suggest the types of vegetation on which clopyralid might be most often applied, these efficacy studies are not detailed further.

A large number of studies are also available on the toxicity of clopyralid to non-target vegetation. The studies that can be used to identify sensitive as well as resistant species are summarized in appendix 4. These studies support the generalization that clopyralid can be highly toxic to broadleaf plants but is relatively non-toxic to grasses or grains. For example, at application rates that approach or exceed the upper range of 1 lb a.e./acre that might be used by the Forest Service, little damage is likely to be apparent in barley or wheat (O'Sullivan and Kossatz 1984a,b). A more quantitative consideration of the dose-response relationships and species differences in sensitivity to clopyralid is given in section 4.3.

While many of the toxicity studies on terrestrial plants are relatively short-term, some longer-term field studies have been conducted. Rice et al. (1997) conducted an 8 year follow-up study of plots treated with clopyralid at a rate of 0.28 kg a.e./ha by backpack sprayer for the control of spotted knapweed (*Centaurea maculosa*). The formulation of clopyralid used was Stinger which, like Transline, contains the monoethanolamine salt of clopyralid. Four sites were examined, two characterized as fescue grassland and two as seral stage forest habitat. All sites were in west-central Montana and were initially treated in 1989, with two of the sites (one of each type) being re-treated in 1993. Over the 8-year period, clopyralid had no substantial or statistically significant effect on species diversity or species richness. Clopyralid was not detected in soil below 25cm. This is consistent with a number of field lysimeter studies that suggest that clopyralid is not likely to leach deeply into soil layers and thus is not likely to contaminate ground water. Although clopyralid has an apparently high potential mobility because it does not bind tightly to soil, the functionally low leaching potential is apparently due to rapid microbial metabolism (Baloch-Haq et al. 1993; Bergstrom et al. 1991; Bovey and Richardson 1991), as discussed further in section 4.2.2.4.

4.1.2.5. Terrestrial Microorganisms– Relatively little information is available on the toxicity of clopyralid to terrestrial microorganisms. At concentrations of 1-10 ppm soil, clopyralid had no

effect on nitrification, nitrogen fixation or degradation of carbonaceaus material (Dow AgroSciences 1998). Applications of Lontrel EC, an emulsifiable concentrate of clopyralid, at 0.3 kg a.i./ha had no substantial effect on spore germination in *Colletotrichum gloeosporioides*, a bioherbicide for round-leaved mallow (Grant et al. 1990). Dodd and Jeffries (1989) report that Harrier, a formulation of clopyralid with mecoprop (2-(4-chloro-2-methylphenoxy)-propanoic acid) and ioxynil (4-hydroxy-3,5-duodobezonitrile) inhibited the growth of a fungi - *Glomus geosporum* - that is associated with winter wheat. This effect, however, was probably attributable to mecoprop, not clopyralid, because the same effect was seen with other herbicide mixtures containing mecoprop. Clopyralid alone, however, was not tested.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish– Standard toxicity bioassays to assess the effects of clopyralid on fish and other aquatic species are summarized in appendix 5. For fish, only standard 96-hour acute toxicity bioassays are available. The lowest reported LC_{50} for clopyralid is 103 mg a.e./L in trout (Dow Chemical 1980). At least for aquatic species, the monoethanolamine salt of clopyralid appears to be substantially less toxic than technical clopyralid. As indicated in appendix 5, 96-hour LC_{50} values for the monoethanolamine salt of clopyralid are in the range of 2900 mg a.i./L to 4700 mg a.i./L, which is equivalent to 700-1645 mg a.e./L. Since clopyralid has a pK_a of about 2 (Table 2-1), it is reasonable to speculate that the apparently lower toxicity of the monoethanolamine salt of clopyralid is attributable to buffering of the water pH by the monoethanolamine moiety.

No longer-term toxicity studies are available on the toxicity of clopyralid to fish eggs or fry.

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

4.1.3.3. Aquatic Invertebrates– The only species of aquatic invertebrate on which toxicity data are available is *Daphnia magna*, a test species required by the U.S. EPA for the registration of pesticides (appendix 5). The lowest reported LC_{50} for technical clopyralid to *Daphnia* is 232 mg/L (Dow AgroSciences 1998), about a factor of 2 higher than the lowest reported LC_{50} in fish of 103.5 mg/L (Dow Chemical 1980) Unlike the case with fish, the monoethanolamine salt appears to only marginally reduce the toxicity of clopyralid - i.e., an LC_{50} of 350 mg a.e./L for the salt and 232 mg a.e./L for the acid (appendix 5).

A standard chronic reproduction bioassay has been conducted in *Daphnia magna* using the monoethanolamine salt of clopyralid. The no observed effect concentration was 66 mg a.i./L, which is equivalent to 23.1 mg a.e./L (Dow AgroSciences 1998).

4.1.3.4. Aquatic Plants– Aquatic plants are more sensitive to clopyralid than fish or aquatic invertebrates. The EC_{50} for growth inhibition in duckweed, an aquatic macrophyte, is 89 mg/L (Dow AgroSciences 1998). At lower concentrations, however, in the range of 0.01 to 0.1 mg/L, growth of other aquatic macrophytes is stimulated (Forsyth et al. 1997). The lowest report EC_{50} for growth inhibition of green algae is 6.9 mg/L.

4.1.3.5. Other Aquatic Microorganisms– There are no published or unpublished data regarding the toxicity of clopyralid to aquatic bacteria or fungi.

4.2. EXPOSURE ASSESSMENT

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

In this exposure assessment, estimates of oral exposure are expressed in the same units as the available toxicity data (i.e., oral LD_{50} and similar values). As in the human health risk assessment, these units are usually expressed as mg of agent per kg of body weight and abbreviated as mg/kg body weight. For dermal exposure, the units of measure usually are expressed in mg of agent per cm of surface area of the organism and abbreviated as mg/cm^2. In estimating dose, however, a distinction is made between the exposure dose and the absorbed dose. The *exposure dose* is the amount of material on the organism (i.e., the product of the residue level in mg/cm^2 and the amount of surface area exposed), which can be expressed either as mg/organism or mg/kg body weight. The *absorbed dose* is the proportion of the exposure dose that is actually taken in or absorbed by the animal.

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), small animals will receive a higher dose, in terms of mg/kg body weight, than large animals will receive.

For many compounds, allometric relationships for interspecies sensitivity to toxicants indicate that for exposure levels expressed as mg toxicant per kg body weight (mg/kg body weight), large animals, compared with small animals, are more sensitive. For clopyralid, the available information is not adequate to quantify species differences in sensitivity to clopyralid. As with the dose-response relationship, 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 (1989), unless otherwise specified.

The exposure assessments for terrestrial animals are summarized in Table 4-1. As with the human health exposure assessment, the computational details for each exposure assessment presented in this section are provided in the attached worksheets (worksheets F01 through F06).

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

For this risk assessment, three groups of direct spray exposure assessments are conducted. The first, which is defined in worksheet F01, involves a 20 g mammal that is sprayed directly over one half of the body surface as the chemical is being applied. The range of application rates as well as the typical application rate is used to define the amount deposited on the organism. The absorbed dose over the first day (i.e., a 24-hour period) is estimated using the assumption of first-order dermal absorption. In the absence of any data regarding dermal absorption in a small mammal, the estimated absorption rate for humans is used (see section 3.1.7). An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal. The estimates of absorbed doses in this scenario may bracket plausible levels of exposure for small mammals based on uncertainties in the dermal absorption rate of clopyralid.

Other, perhaps more substantial, uncertainties affect the estimates for absorbed dose. For example, the estimate based on first-order dermal absorption does not consider fugitive losses from the surface of the animal and may overestimate the absorbed dose. Conversely, some animals, particularly birds and mammals, groom frequently, and grooming may contribute to the total absorbed dose by direct ingestion of the compound residing on fur or feathers. Furthermore, other vertebrates, particularly amphibians, may have skin that is far more permeable than the skin of most mammals (Moore 1964).

Quantitative methods for considering the effects of grooming or increased dermal permeability are not available. As a conservative upper limit, the second exposure scenario, detailed in worksheet F02, is developed in which complete absorption over day 1 of exposure is assumed.

Because of the relationship of body size to surface area, very small organisms, like bees and other terrestrial insects, might be exposed to much greater amounts of clopyralid per unit body weight, compared with small mammals. Consequently, a third exposure assessment is developed using a

Table 4-1: Summary of exposure scenarios for terrestrial animals

Scenario	Dose (mg/kg/day)			Worksheet
	Typical	Lower	Upper	
Acute/Accidental Exposures				
Direct spray, small mammal, first-order absorption	0.037	0.00076	1.75	F01
Direct spray, small animal, 100% absorption	2.4	0.24	24.4	F02
Direct spray, bee, 100% absorption	16	1.6	163	F03
Consumption of contaminated vegetation, acute exposure	0.53	0.05	18.8	F04
Consumption of contaminated water, acute exposure	0.075	0.006	1.14	F06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.18	0.025	4.3	F05
Consumption of contaminated water, chronic exposure	0.0001	0.000001	0.002	F07

body weight of 0.093 g for the honey bee (USDA 1993) and the equation above for body surface area proposed by Boxenbaum and D'Souza (1990). Because there is no information regarding the dermal absorption rate of clopyralid by bees or other invertebrates, this exposure scenario, detailed in worksheet F03, also assumes complete absorption over the first day of exposure.

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) (worksheet A04) is used to estimate that the dislodgeable residue will be approximately 10 times less than the nominal application rate.

Unlike the human health risk assessment in which transfer rates for humans are available, there are no transfer rates available for wildlife species. As discussed in Durkin et al. (1995), the transfer rates for humans are based on brief (e.g., 0.5- to 1-hour) exposures that measure the transfer from

contaminated soil to uncontaminated skin. Wildlife, compared with humans, are likely to spend longer periods of time in contact with contaminated vegetation.

It is reasonable to assume that for prolonged exposures an equilibrium may be reached between levels on the skin, rates of absorption, and levels on contaminated vegetation, although there are no data regarding the kinetics of such a process. The bioconcentration data on clopyralid (section 3.2.3.5) suggest that clopyralid is not likely to partition from the surface of contaminated vegetation to the surface of skin, feathers, or fur. Thus, a plausible partition coefficient is unity (i.e., the concentration of the chemical on the surface of the animal will be equal to the dislodgeable residue on the vegetation).

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

4.2.1.3. Ingestion of Contaminated Vegetation or Prey – For this component of the exposure assessment, the estimated amounts of residue on food are based on the relationship between application rate and residue rates on leaves and leafy vegetables. For the lower and central estimates of absorbed dose, the 'typical' value given in worksheet A05a is used because Hoerger and Kenaga (1972) do not provide estimates of the lower range of expected residues.

Allometric relationships and species specific data (U.S. EPA 1989) suggest that the amount of food consumed per day by a small mammal (i.e., an animal weighing approximately 20 g) is equal to about 15% of the mammal's total body weight. All of the estimates of ingested dose 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. Details regarding the calculations for these acute exposure scenarios are given in worksheet F04.

As discussed in section 4.4, the exposure estimates discussed above are of minimal concern for acute exposure. For estimating the effects of longer-term exposures, time-weighted average concentrations are used, which is similar to the approach taken in the human health risk assessment and using the same estimates of halftime of fruit (McMurray et al. 1996 detailed in worksheet B03) as were used in the corresponding human health risk assessment. Also, the longer-term exposure scenario is based on a 90-day post-spray period and uses the geometric mean over this period as the central estimate of the exposed dose, as in the human health risk assessment. Like the acute exposure scenario, this exposure scenario assumes that 100% of the diet is contaminated. Details regarding the calculations for these chronic exposure scenarios are given in worksheet F05.

4.2.1.4. Ingestion of Contaminated Water -- Estimated concentrations of clopyralid in water are identical to those used in the human health risk assessment (worksheet B07). The only major differences involve the weight of the animal and the amount of water consumed. There are

well-established relationships between body weight and water consumption across a wide range of mammalian species [e.g., U.S. EPA (1989)]. Mice, weighing about 0.02 kg, consume approximately 0.005 L of water/day (i.e., 0.25 L/kg body weight/day). These values are used in the exposure assessment for the small (20g) mammal. Unlike the human health risk assessment, estimates of the variability of water consumption are not available. Thus, for the acute scenario, the only factors affecting the variability of the ingested dose estimates include the field dilution rates (i.e., the concentration of the chemical in the solution that is spilled) and the amount of solution that is spilled. As in the acute exposure scenario for the human health risk assessment, the amount of the spilled solution is taken as 200 gallons. In the chronic exposure scenario, the factors that affect the variability are the water contamination rate, (see section 3.2.3.4.2) and the application rate. Details regarding these calculations are summarized in worksheet F06 (acute exposure) and worksheet F07 (chronic exposure).

4.2.2. Terrestrial Plants. In general, the primary hazard to non-target terrestrial plants associated with the application of most herbicides is unintended direct deposition or spray drift, particularly in aerial applications (e.g., Bird 1995).

4.2.2.1. Direct Spray – Unintended direct spray will result in an exposure level equivalent to the application rate. Many broadleaf plants that are sprayed directly with clopyralid at and, in some cases substantially below, the recommended application rate will be damaged (section 4.3.2.4).

4.2.2.2. Off-Site Drift – Data regarding the drift of clopyralid during ground or aerial applications were not found in the literature. Because off-site drift is more or less a physical process that depends on droplet size and meteorological conditions rather than the specific properties of the herbicide, estimates of off-site drift can be made based on data for other compounds. The potential for spray drift was investigated in numerous field studies reviewed recently by Bird (1995), as summarized in worksheet A06. The monitoring studies involved low-flight agricultural applications of pesticides and employed various types of nozzles under a wide range of meteorological conditions. The central estimates of off-site drift for single swath applications, expressed as a proportion of the nominal application rate, were approximately 0.03 at 100 feet, 0.002 at 500 feet, 0.0006 at 1000 feet, and 0.0002 at 2500 feet (Bird 1995, Figure 2, p. 204). Although multiple swath applications lead to higher rates of off-site deposition, they are less suitable for estimating drift from ground spray applications of clopyralid.

Another approach to estimating drift involves the use of Stoke's law, which describes the viscous drag on a moving sphere. According to Stoke's law:

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

or

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

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

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

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

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

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

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

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

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

4.2.2.4. Soil Contamination by Runoff – Other mechanisms of transport for herbicides involve movement in the soil either by runoff or percolation. Clopyralid should have a substantial tendency to leach or percolate through soil because clopyralid is not tightly bound to most types of soil. Conversely, because clopyralid is not readily bound to soil, the potential for clopyralid runoff from the washing of soil particles containing bound clopyralid is relatively low (Woodburn and French. 1987).

Another factor that will reduce the possibility of either leaching or runoff is relatively rapid degradation of clopyralid in soil. Baloch and Grant (1991a) studied the fate of 2,6-^{14}C-pyridine labeled clopyralid under laboratory conditions at a soil concentration of 0.3 mg/kg. This concentration is referred to as the field rate. Five types of agricultural soils were used: sand, sandy loam, silt loam, sandy clay loam, and organic sandy loam. In addition, degradation was assayed at 2 different temperatures (10°C and 20°C) and three soil moisture levels: 10%, 40%, and 60% of moisture holding capacity. Other than $C0_2$ and clopyralid, no soil metabolites were identified.

The results of this study are summarized in Table 4-2. In addition to these data, Baloch and Grant (1991a) also assayed the mineralization of clopyralid at different initial soil concentrations, 1 mg/kg and 0.05 mg/kg, as well as the field concentration of 0.3 mg/kg. There was a clear trend for increasing rates of mineralization as the initial soil concentration decreased. It is unclear if this relationship is attributable to changes in microbial acclimation or toxicity at higher initial soil concentrations of clopyralid. As detailed in Baloch and Grant (1991b), the rates of disappearance of clopyralid from soil correspond generally to the microbial biomass of the soil ($r^2 \approx 0.5$ to 0.7). This pattern is similar to the less detailed studies by Smith and Aubin (1989) that reported half times of 10 to 47 days depending on temperature and soil composition. These results are also similar to those in the study by Pik et al. (1977), in which clopyralid was applied at 0.95 or 1.9 kg/ha in three different soil types: Loam, sandy loam, and luvisol. Fastest degradation ($t_{1/2}$ of 2 months) occurred in moist soil with high organic carbon content and the extent of leaching was inversely related to organic carbon content.

The most relevant study for quantitatively assessing runoff and leaching potential appears to be the publication by Elliott et al. (1998). This study was designed as a worst case scenario for clopyralid mobility. A clopyralid formulation, Lontrel, was applied using ground equipment at a rate of 0.2 kg a.i./ha to a 4.6 ha field. In addition to natural rainfall, irrigation was started on day 3 and totaled 300 mm (about 0.1 inch) of water in a 21 day period. The maximum concentration in soil water was monitored at 187.3 µg/L and the maximum concentration in drainage water was monitored at 6.4 µg/L on day 26. In the period between day 9 and 35, only 1.5% of the applied amount was washed off. Again, these results are consistent with field lysimeter studies that suggest that the rapid degradation of clopyralid in soil is the predominant factor in the functionally low rate of both leaching and runoff. (Baloch-Haq et al. 1993; Bergstrom et al. 1991).

4.2.3. Aquatic Organisms. For aquatic organisms, the estimated amount of clopyralid in ambient water and in water bodies associated with an accidental spill (see section 3.2.3.4) may be used as a very conservative estimate of exposure. As summarized in worksheet B07, the estimated rate of contamination of ambient water is 0.0021 (0.00053 to 0.0089) mg a.e./L at an application rate of 1 lb a.e./acre. This is the highest application rate considered in this risk assessment. As detailed in the dose-response assessment (section 4.3.3.1.), these concentrations are far below those that might be associated with any chronic adverse effects in aquatic species.

For acute exposure scenarios (worksheet D06), the highest estimated concentration of clopyralid in water is 4.54 mg a.e./L. This is about a factor of 50 below the lowest reported LC_{50} for any aquatic animal (232 mg a.e./L for *Daphnia magna*) and about a factor of two below the lowest reported EC_{50} in any aquatic plant (6.9 mg/L for *Selenastrum capricornutum*).

Given the relatively low level of toxicity of clopyralid to aquatic species, further elaboration of the exposure assessment for these species is unnecessary. For the characterization of risk, an exposure level of 0.0089 mg a.e./L (the upper limit from worksheet B07) is used to characterize the risks associated with chronic exposure scenarios and 4.54 mg a.e./L (the upper limit from worksheet D06) is used to characterize the risks associated with acute exposure scenarios.

Table 4-2: Summary of the degradation times and apparent first-order rates [1] for clopyralid at a concentration of 0.3 mg/kg soil in different soils under different conditions (from Baloch and Grant 1991a).

Soil Type	DT_{50}	k_e from DT_{50}	DT_{90}	k_e from DT_{90}
20°C and 40% MCH				
silt loam	25	0.0277	82	0.0281
sandy clay loam	14	0.0495	46	0.0501
organic sandy loam	16	0.0433	54	0.0426
sand	29	0.0239	90	0.0256
loamy sand	13	0.0533	66	0.0349
10°C and 40% MCH				
silt loam	177	0.0039	>200	<0.0115
sandy clay loam	69	0.0100	>200	<0.0115
organic sandy loam	66	0.0105	>200	<0.0115
20°C and 10% MCH				
silt loam	>200	<0.0035	>200	<0.0035
sandy clay loam	>200	<0.0035	>200	<0.0035
organic sandy loam	>200	<0.0035	>200	<0.0035
20°C and 60% MCH				
silt loam	24	0.0289	79	0.0291
sandy clay loam	14	0.0495	46	0.0501
organic sandy loam	1	0.6931	15	0.1535

[1] k_es calculated as $-\ln(1-x)/t_x$ where x is 0.5 for DT_{50} and 0.1 for DT_{90}.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview. For terrestrial mammals, the dose-response assessment is based on the same data as the human health risk assessment (i.e., a NOAEL of 50 mg/kg/day from a 2-year rat feeding study). None of the exposure scenarios, acute or longer-term, result in exposure estimates that exceed this NOAEL. The very limited data on toxicity to birds suggest that birds

may be somewhat more sensitive than mammals. The data on birds, however, are not as extensive or of the same detail as the data on experimental mammals. The available data on terrestrial invertebrate are also less complete than the data on mammals. Nonetheless, there is no indication that clopyralid is highly toxic to birds or terrestrial invertebrates.

The toxicity of clopyralid to terrestrial plants can be characterized relatively well and with little ambiguity. Clopyralid is more toxic to broadleaf plants than grains or grasses and is more toxic in post-emergence applications - i.e., foliar spray - than pre-emergence applications - i.e., soil treatment. Many non-target species - especially grains, grasses, and several types of trees - are not likely to be affected by clopyralid even if the plants are sprayed at application rates of 0.1 lb a.e./acre or greater. When applications are made prior to emergence - i.e., directly to the soil before the germination of the plant seeds - NOAELs for sensitive species such as soybeans, snap beans, tomatoes, and sunflowers are in the range of 0.028 to 0.056 kg/ha. When applied directly to the foliage - i.e., post-emergence - the NOAELs are about 0.00056 kg/ha. This difference is attributable to the very rapid absorption of clopyralid after direct foliar application.

Based on the results of acute bioassays, fish and aquatic invertebrates are equally sensitive to clopyralid. While there are no chronic studies available in fish, a chronic reproductive NOAEL of about 20 mg/L has been determined in *Daphnia magna*, a common aquatic invertebrate test species. Given the low levels of plausible exposure to clopyralid in water, this NOAEL can be used to characterize risk to both fish and aquatic invertebrates. Aquatic plants are somewhat more sensitive than aquatic animals to clopyralid. The lowest reported LC_{50} for aquatic algae is 6.9 mg/L, about a factor of 3 below the chronic NOAEL in *Daphnia*.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals– As summarized in the dose-response assessment for the human health risk assessment (section 3.3.3), the Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.5 mg/kg/day for clopyralid based on a two-year rat feeding study in which the NOAEL was 50 mg/kg/day. All of the estimated mammalian exposures (Table 4-1) are below the NOEL of 50 mg/kg/day and all of the central estimates of mammalian exposures are below the NOEL of 50 mg/kg/day by a factor of over 40. Consequently, the dose of 50 mg/kg/day is used directly and without elaboration to assess the consequences of all exposures, acute and chronic.

4.3.2.2. Birds – As noted in section 4.1.2.2, one acute gavage LD_{50} values in Mallard ducks is about a factor of 3 below a gavage dose in rats that resulted in no apparent signs of toxicity. This suggests that birds may be somewhat more sensitive to clopyralid than mammals but the data supporting this suggestion are extremely limited. Given the normal variability in animal bioassays, the differences between feral and laboratory populations of animals, and the large number of species that might be exposed to clopyralid, this relatively modest difference in the results of the acute oral bioassays adds relatively little to the inherent uncertainties of using the available data to characterize the risks that could be associated with the use of clopyralid to birds or any other species. Consequently, a separate criteria for bird is not developed in this risk assessment - i.e., the chronic of NOAEL of 50 mg/kg/day is used. Again, given the very large differences between this NOAEL and any of the exposure assessments, birds would have to be much more sensitive to

clopyralid than mammals to alter the characterization of risk. Based on the admittedly limited experimental data, such large differences in toxicity are not apparent.

4.3.2.3. Terrestrial Invertebrates– As discussed in section 4.1.2.3, several studies indicate that the toxicity of clopyralid to bees is on the same order of magnitude and perhaps somewhat less than the toxicity of clopyralid to mammals - i.e., acute oral or contact LD_{50} values >9000 mg/kg bw. Based on a single study, the acute toxicity of clopyralid to earthworms also appears to be low - i.e., soil LC_{50} >1000 ppm soil. While these data can be used to assess acute hazard, no quantitative consideration can be given to other potential subchronic or non-lethal effects.

The report by Hassan et al. (1994) on both laboratory bioassays and field trials with clopyralid does not suggest that clopyralid is likely to be remarkably hazardous to terrestrial invertebrates. However, this publication provides only a very brief summary of what appears to be a large and complex study on many invertebrates species. Consequently, it cannot be used quantitatively to develop species specific dose/response relationships.

4.3.2.4. Terrestrial Plants (Macrophytes)-- As discussed in section 4.1.2.4, clopyralid is relatively ineffective against grasses and grains but can be highly toxic to broadleaf plants, both target and non-target. A summary of the dose-severity relationships for terrestrial plants is given in Table 4-3. This table is based on the data presented in appendix 4. The first column of this table gives the range of application rates. The next four columns represent four severity categories: no effect, slight effect, moderate effect, and severe effect as defined in the key to Table 4-3. The definitions of these levels of severity are intended to broadly encompass the various types of observations specified in appendix 4.

Listings of the same plant group in multiple columns indicates species differences within the group. For example, at application rates of 0.2 to 0.5 lb a.i./acre, the responses of different species of cacti are highly variable. Some species of cacti will evidence no effects, some will suffer high levels of mortality, and other species will show intermediate responses (Crosswhite et al. 1995). Thus, in Table 4-3 cactus species are listed in each of the four severity columns in the row associated with application rates of >0.2 - 0.5 lb/acre. Table 4-3 does not attempt to capture temporal relationships. For example, at an application rate of 0.28 kg a.i./ha, red maple evidenced significant visual injury at 60 to 150 days after treatment but these effects were transient and over the longer term there was no effect on growth (Smith and Skroch 1995). In Table 4-3, red maple is simply put into the severe response category for the appropriate range of application rates.

Several studies are available on a variety of different plant species in which clopyralid was applied at rates that are in the range of the typical (0.1 lb a.e./acre) to the highest application rate (1.0 lb a.e./acre). While these studies generally support the specificity of clopyralid to broadleaf plants, the likelihood of observing damage will vary within groups of plants depending on the species. For example, damage to grasses or grass-like grains at or near the upper range of the application rate may be minimal in some species of grains such as Glenlea wheat but apparent in other species such as Meepawa wheat (O'Sullivan and Kossatz 1984a,b). Simiarly, near the typical application

Table 4-3: Summary of dose-severity relationships in terrestrial plants[1].

Application Rate (lb a.e./acre)	Severity[2] None	Slight	Moderate	Severe
> 0.5	barley, canola, soybean, sweet corn, raddish, wheat sp.	wheat sp.	strawberries	onion, soybeans, snap bean, tomato, sunflowers
>0.2 - 0.5	ash, beech, birch, cacti sp., cherry, *Juniperus*, oak, pear, sycamore willows,	alder, asparagus, cacti, *Contoneaster*, eastern redbud, strawberries, spruce	cacti, *Lagerstroemia*, poplar,	cacti, cranberries, red maple
>0.05-0.2	ash, beech, birch, cherry, forbes, grasses, oak, onion, snapbean, sycamore	alder, cotton, forbes, grasses, spruce, strawberries		potatoes
>0.01 - 0.05	cotton, tomato, soybean, sunflower [pre-emergence]		kumara, tomatoes	potatoes
>0.001 - 0.01			potatoes	
>0.0001 - 0.001	soybean, snap bean, tomato, sunflower [post-emergence]			

[1] See Appendix 4 for data and citations.
[2] KEY: Slight - No or minimal visual damage. Detectable decrease in growth.
Moderate - Some visual damage. Mortality unlikely.
Severe - Obvious visual damage and substantial (>10%) mortality.

rate of 0.1 lb a.e./acre, some forbes or trees may evidence damage while others will not (e.g., Bachman et al. 1995; Pywell et al. 1996; Smith and Skroch 1995).

The extent to which these differences within various groups of plants can be attributed to simple physical differences among the various plant groups as opposed to intrinsic differences in sensitivity or persistence is unclear. In some case, such as the differential sensitivities of willow (less sensitive) and poplar (more sensitive), the differences may be due simply to greater retention of clopyralid by the more sensitive species (Clay 1991). In other cases, such as the effects seen in red maple but not in pear, myrtle and redbud, the basis for the differing effects is unclear (Smith and Skroch 1995).

In addition, a substantial difference in the sensitivity of plants is seen depending on the stage at which clopyralid is applied - i.e., pre-emergence or post-emergence. This is best illustrated in the study by Weseloh (1987), who estimated NOAELs for various species after both pre-emergent

and post-emergent applications. When applications were made prior to emergence - i.e., directly to the soil before the germination of the plant seeds - NOAELs for sensitive species such as soybeans, snap beans, tomatoes, and sunflowers was in the range of 0.028 to 0.056 kg/ha. When applied directly to the foliage - i.e., post-emergence - the NOAELs were much lower, in the range of 0.00056 kg/ha. As discussed in section 4.1.2.4, this difference is attributable to the very rapid absorption of clopyralid after direct foliar application.

Because of the substantial differences in sensitivity among different groups of plants as well as the differences that are apparent within groups of plants, such as the cacti, general dose-response or dose-severity modeling combining all of the available data is not appropriate. Nonetheless, the data summarized in Table 4-3 and detailed in appendix 4 cover the range of application that might be used by the Forest Service as well as much lower rates of application. These data are used directly in characterizing risks to non-target terrestrial plants (section 4.4).

4.3.2.5. Terrestrial Microorganisms– The available data on clopyralid are not sufficient for any quantitative dose-response modeling for terrestrial microorganisms other than the apparent NOAEL of 1-10 mg/kg soil reported by Dow AgroSciences (1998).

4.3.3. Aquatic Organisms.

4.3.3.1. Animals– As indicated in sections 4.1.3.1 through 4.1.3.3, fish and aquatic invertebrates appear to be equally sensitive to clopyralid. Although no chronic data are available on fish, there is one chronic invertebrate study in *Daphnia magna* in which the NOAEL is 23.1 mg a.e./L. Thus, for this risk assessment, 23.1 mg a.e./L will be used as the benchmark concentration for both fish and aquatic invertebrates - i.e., at this concentration, no adverse effects are anticipated even over prolonged periods of time.

For acute exposures, higher estimates of acutely toxic or non-toxic doses could be made. However, as discussed in section 4.2.3, the highest anticipated concentration of clopyralid in water even after an accidental spill is 4.54 mg a.e./L. Since this is below the chronic NOAEL, no additional elaboration of the dose-response relationship for aquatic animals seems justified.

4.3.3.2. Aquatic Plants– The relevant data on the toxicity of clopyralid to aquatic plants is summarized in appendix 5. The most sensitive aquatic plant species appears to be *Selenastrum capricornutum*, with a 96-hour EC_{50} of 6.9 mg a.e./L base on a reduction in cell count relative to controls (Dill and Milazzo 1985). EC_{50} values for other freshwater algal species are generally greater than 50 mg/L (Dow AgroSciences 1998). The more recent study by Forsyth et al. (1997), which reports NOAELs at 0.1 mg/L for two aquatic macrophytes, adds relatively little to the dose-response assessment because, based on the other earlier studies, no effects would be anticipated at clopyralid concentrations of 0.1 mg/L.

4.3.3.3. Aquatic Microorganisms– There is no information that would permit a quantitative dose-response assessment for aquatic microorganisms.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. Clopyralid is a herbicide and the most likely damage to non-target species will involve terrestrial plants. As is the case with any herbicide, the likelihood of damage to non-target plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential non-target species. In this respect, the apparent selectively of clopyralid substantially narrows the number of non-target plants that might be affected. With clopyralid, some sensitive post-emergent plants could be adversely effected by off-site drift over a relatively narrow band. Most species of trees, grains, or grasses, however, are not likely to be affected by off-site drift or even direct spray. This risk characterization is conservative in that the off-site drift estimates are derived from studies involving aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no substantial or detectable impact on off-site plant species outside of a very narrow range - i.e., less than and perhaps much less than 25 feet.

Soil contamination by runoff, which could potentially harm off-site plant species, does not appear to be a major concern with clopyralid. Rains are most likely to cause clopyralid to leach into the soil column rather than wash-off. The best available estimate of runoff is on the order of 0.015 (1½%) of the applied amount. Because clopyralid is less effectively absorbed from roots than from leaf surfaces, the consequences of runoff are likely to be less severe than those of drift. In addition, once in the soil column, clopyralid will be rapidly degraded except in arid soils with low microbial populations. Thus, while damage to off-site plants from runoff cannot be ruled-out under conditions that would be highly favorable to runoff, this is not likely to be a major problem with clopyralid.

The potential for adverse effects on other non-target species appears to be remote. The weight of evidence suggests that no adverse effects in terrestrial or aquatic animals are plausible using typical or even very conservative worst case exposure assumptions. Some inhibition of growth in aquatic plants would be possible in cases involving accidental spills. Such effects, however, would be transient.

As with the human health risk assessment, this characterization of risk must be qualified by the general reservation for any risk assessment: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated.*** Clopyralid has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging non-target animals or some populations of non-target plants. Notwithstanding this limitation, the available data do not indicate that adverse effects are likely in terrestrial or aquatic animals from the use of this compound in Forest Service programs. Under normal and proper conditions of application, effects on non-target vegetation would likely be confined to sensitive plant species in or very near to the treatment area.

4.4.2. Terrestrial Organisms.

4.4.2.1. Terrestrial Animals– The quantitative risk characterization for terrestrial animals is summarized in Table 4-4. Except for the direct spray scenario for the bee, all of the quantitative risk characterizations apply to a 20 g mammal. In Table 4-4, the hazard quotient for each scenario, except that for the honey bee, is calculated as the exposure estimate presented in Table 4-1 divided by the chronic NOAEL for rats of 50 mg/kg/day, discussed in section 4.3.2.1. In some respects, this approach may be regarded as extremely conservative, particularly in the application of the chronic NOAEL to acute exposure scenarios. For the honey bee, the hazard quotient is based on the non-lethal acute dose level of 1000 mg/kg from the study by Hinken et al. (1986).

As specified in Table 4-4, both the central estimates as well as the upper range of the hazard quotients associated with the longer-term exposure scenarios are below unity, indicating that toxic effects are not likely to occur.

For acute exposures of small mammals, none of the central values for the hazard quotient approach a level of concern. With regard to the upper limit of the estimated hazard quotients, the direct spray with 100% absorption and the consumption of contaminated vegetation, both of which are acute exposure scenarios, approach a level of concern based on the chronic NOAEL. As indicated in Table 4-1, these hazard quotients are associated with dose levels of about 20 mg/kg. This dose is a factor of 25 below the single gavage dose of 500 mg/kg that caused no overt signs of toxicity in rats (Gilbert and Crissman 1995) and a factor of over 100 below the lowest reported LD_{50} of 2675 mg/kg (Dow AgroSciences 1998).

The simple verbal interpretation of this quantitative risk characterization is similar to that of the human health risk assessment: the weight of evidence suggests that no adverse effects in mammals are plausible using typical or even very conservative worst case exposure assumptions. As with the human health risk assessment, this characterization of risk must be qualified. Clopyralid has been tested in only a limited number of species and under conditions that may not well-represent populations of free-ranging non-target animals. Notwithstanding this limitation, the available data are sufficient to assert that no adverse effects are anticipated in terrestrial animals from the use of this compound in Forest Service programs.

4.4.2.2. **Terrestrial Plants–** Clopyralid is an effective herbicide, at least for a number of different broadleaf weeds and adverse effects on some non-target plant species are plausible under certain application conditions and circumstances. As discussed in section 4.2.2, three kinds of exposure are considered in the assessment for non-target plants species: direct spray, drift, and water erosion.

As is the case with any herbicide, the likelihood of damage to non-target plant species is related directly to the difference between the sensitivity of target species—which dictates the application rate—and the sensitivity of the potential non-target species. In this respect, the apparent selectivity of clopyralid substantially narrows the number of non-target plants that might be affected. As summarized in Table 4-3, a number of different plant species - particularly grains,

Table 4-4: Summary of quantitative risk characterization for terrestrial animals[1]

Scenario	Hazard Quotient[2]		
	Typical	Lower	Upper
Acute/Accidental Exposures			
Direct spray, small mammal, first-order absorption	0.0007	0.00002	0.04
Direct spray, small animal, 100% absorption	0.05	0.005	0.5
Direct spray, bee, 100% absorption[3]	0.02	0.002	0.2
Consumption of contaminated vegetation, acute exposure	0.01	0.001	0.4
Consumption of contaminated water, acute exposure	0.002	0.0001	0.001
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.004	0.0005	0.1
Consumption of contaminated water, chronic exposure	0.000002	2e-08	0.00004
Toxicity value for mammal [2]		50	mg/kg/day
Toxicity value for bee [3]		1000	mg/kg

[1] See Worksheet F07 for details of exposure assessment.
[2] Except for the honey bee, the hazard quotient is calculated as the estimated exposure divided by the chronic rats NOAEL of 50 mg/kg/day and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on the marginally-lethal acute dose level of 1000 mg/kg from the study by (Hinken et al. 1986) .

grasses and several species of trees - are not likely to evidence any adverse effects from clopyralid if treated/accidently sprayed at the typical application rate of 0.1 lb a.e./acre and many of these species are not likely to evidence adverse effects even at substantially higher application rates. Other more sensitive species, such as beans, tomatoes, potatoes, and some trees, will be adversely affected if they are accidently sprayed.

Based on estimates using Stoke's Law (see section 4.2.2.2), it is plausible that droplets ranging in size from 100 µ to 400 µ might drift about 3-23 feet at a wind speed of 5 miles per hour and 9-69 feet at a wind speed of 15 miles per hour. Although this drift might cause damage to some sensitive species, the impact would be limited and damage to non-target species probably could be minimized or avoided during the application process.

4.2.2.2 suggest that 0.03 of the nominal application rate could drift 100 feet off-site. At an application rate of 0.1 lb a.e./acre, this would correspond to an effective off-site application of 0.003 lb a.e./acre. This rate is about a factor of 10 above the NOAELs for post-emergent foliar spray of sensitive species such as soybean, snap bean, tomato, and sunflower but well below the NOAELs for pre-emergent treatment. At 1000 feet off-site, the data summarized by Bird (1995) can be used to estimate an effective rate of 0.00006 lb a.e./acre [0.0006 ×0.1 lb a.e./acre], which is below the post-emergence NOAEL for sensitive species by a factor of about 10.

The simple verbal interpretation for this quantitative risk characterization is that some sensitive post-emergent plant species could be adversely affected by off-site drift over a relatively narrow band. Most species of trees, grains, or grasses, however, are not likely to be affected by off-site drift. This risk characterization is conservative in that the drift estimates from Bird (1995) are based on aerial application. Well-directed ground applications conducted under conditions that do not favor off-site drift will probably have no impact on off-site plant species.

Soil contamination by runoff does not appear to be a major concern with clopyralid. As detailed in section 4.2.2.4, rains are most likely to cause clopyralid to leach into the soil column rather than wash-off. Based on the study by Elliott et al. (1998), the extent of runoff - i.e., 0.015 of the applied amount. This is similar to the magnitude of off-site drift within 100 feet, 0.01 of the applied amount (Bird 1995). As discussed in section 4.1.2.4, however, clopyralid is less effectively absorbed from roots than from leaf surfaces. The lesser toxicity of clopyralid as a result of soil exposure relative to direct spray is also indicated in the study by Weseloh (1987). Thus, while damage from runoff cannot be ruled-out under conditions that would be highly favorable to runoff, this is not likely to be a major problem with clopyralid.

4.4.3. Aquatic Organisms. The risk assessment for aquatic organisms is relatively simple and unambiguous. Clopyralid appears to have a very low potential to cause any adverse effects in any aquatic species. As detailed in section 4.2.3, concentrations of clopyralid in ambient water over prolonged periods of time are estimated to be no greater than 0.0089 mg/L. This is a factor of about 775 [6.9÷0.0089] below the lowest reported EC_{50} in any aquatic plant (6.9 mg/L for *Selenastrum capricornutum*) and about a factor of 2500 [23.1÷0.0089] below the chronic NOAEL for reproductive effects in *Daphnia magna*. Thus, while the available monitoring data are limited and may not represent a wide range of environmental conditions, the exposure estimates would have to be in error by factors of 100 to over 1000 to substantially alter the characterization of risk.

In the accidental spill scenario used in this risk assessment (worksheet D06), the highest estimated concentration of clopyralid in water is 4.54 mg/L. Again, this is substantially below the lowest reported LC_{50} for any aquatic animal (232 mg a.e./L for *Daphnia magna*). Aquatic plants, however, could evidence at least transient effects. The concentration of 4.54 mg/L is less than a factor of two below the lowest reported EC_{50} in any aquatic plant (6.9 mg/L for *Selenastrum capricornutum*). It seems reasonable to suspect the this species and other perhaps more sensitive species of algae would evidence a transient decrease in population in the event of a severe spill.

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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 pharmacological or toxic agent effect of the active ingredient.

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.

Alkaline phosphatase – An enzyme that occurs in various normal and malignant tissues. The activity of the enzyme in blood is useful in diagnosing many illnesses.

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.

Amphibian – A cold-blooded vertebrate capable of operating on land and in water.

Arid – A terrestrial region lacking moisture, or a climate in which the rainfall is not sufficient to support the growth of trees or woody plants.

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

Bioconcentration factor (BCF) -- The concentration of a compound in an aquatic orgainism divided by the concentration in the ambient water of the organism.

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).

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 to control vegetation.

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.

Creatine – An organic acid composed of nitrogen. It supplies the energy required for muscle contraction.

Creatinine – The end product of the metabolism of creatine. It is found in muscle and blood and is excreted in the urine.

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.

Dams – A term used to designate females of some species such as rats.

Degraded -- Broken down or destroyed.

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.

Electrochemical process -- A newer manufacturing process for clopyralid. Details of the method are proprietary.

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.

Fetal anomaly – An abnormal condition in a fetus, which is usually the result of a congenital defect.

Forbes – a non-grass or broadleaf herb.

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.

Hymolytic anemia – A medical condition in which the number of red blood cells is decreased due to intravascular fragmentation or destruction.

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 of glyphosate that are not readily active with the other components of the mixture.

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.

LC_{50} (lethal concentration$_{50}$) -- 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.

LD_{50} (lethal dose$_{50}$) -- 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.

Lymphatic – Pertaining to lymph, a lymph vessel, or a lymph node.

Lymph – A clear water fluid containing white blood cells. Lymph circulates throughout the lymphatic system, removing bacteria and certain proteins from body tissue. It also is responsible for transporting fat from the small intestine and suppling mature lymphocytes to the blood.

Macrophyte – Terrestrial plant

Malignant -- Cancerous.

Margin of safety (MOS) -- The ratio between an effect or no effect level in an animal and the estimated human dose.

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.

Mitochondria -- Subcellular organelles involved in the conversion of food to stored chemical energy.

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.

Non-target -- 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.

Pathogen – A living organism that causes disease; for example, a fungus or bacteria.

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

Penta process -- The original manufacturing process for clopyralid. Details of the method are proprietary.

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

Permeability – The property or condition of being permeable. In this risk assessment, dermal permeability refers to the degree to which a chemical or herbicide in contact with the skin is able to penetrate the skin.

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

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

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

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.

Pup – The offspring or young of various animal species.

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

Relative weight -- The weight of an organ, such as the liver or kidney, divided by the total body weight of the animal.

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 = 1×10^3 g and 1 mg = 0.001 would be expressed as 1 mg = 1×10^{-3}.

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

Sensitization – A condition in which one is or becomes hypersensitive or reactive to an agent through repeated exposure.

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.

Terrestrial – Anything that lives on land as opposed to living in an aquatic environment.

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

Thymus – A small gland that is the site of T-cell production. The gland is composed largely of lymphatic tissue and is situated behind the breastbone. The gland play an important role in the human immune system.

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.

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.

7. INDEX

Note: Page number starting with *ClWS* and *HxWS* refer to the worksheets for clopyralid and hexachlorobenzene, respectively. Page numbers starting with *A* refer to the appendices.

D

E

F

G

H

I

K

L

M

N

O

P

R

S

T

U

V

W

APPENDICES

Appendix 1: Toxicity of clopyralid to mammals.
Appendix 2: Toxicity of clopyralid to birds after oral administration.
Appendix 3: Toxicity of clopyralid to terrestrial invertebrates.
Appendix 4: Toxicity of clopyralid to non-target terrestrial plants.
Appendix 5: Toxicity to fish, aquatic invertebrates, and aquatic plants.
Appendix 6: Field studies on the fate of clopyralid in soil.
Appendix 7: GLEAMS modeling of hexachlorobenzene runoff.

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
ORAL			
		Acute Oral Toxicity Studies	
Rats, Fischer, 9 week old male and female, 5 rats per sex. Gavage.	Gavage, 5000 mg/kg of Lontrel T. [95.4% clopyralid]. 14 day observation period.	No mortality, signs of toxicity, or changes in body weight. No gross tissue lesions.	Jeffrey et al. 1987b MRID 41641301
Rats, Fischer 344, 5 males and 5 females/dose group, Lontrel TE technical (Clopyralid, 3,5-dichloro-2-pyridinecarboxylic acid), 2-week observation period.	500, 2000, or 5000 mg/kg Lontrel TE (25% suspension in water) by single-dose oral gavage	at 500 mg/kg all rats survived and were grossly normal; clinical signs included fecal soiling in 1/5 male rats at 1-3 hours after dosing and urine soiling in 1/5 female rats at 7 hours to 2 days after dosing; at 2000 mg/kg 1/5 males and 1/5 females died on day 2 (excessive gas was observed in the GI tract of both animals, attributed to mouth breath and swallowing air); all other treated rats survived the 14-day observation period; clinical signs included fecal soiling in 1/5 males at 1-3 hours after dosing and urine soiling and chromorhinorrhea in 1/4 surviving males on day 2 after dosing; all surviving rats showed no signs of residual effects; at 5000 mg/kg 4/5 male rats and 5/5 female rats died by day 2; the surviving male rat was grossly normal; clinical signs at the high dose level included decreased activity, lacrimation, and lateral recumbence; gross findings in the non-surviving rats were non-specific and primarily in the stomach.	Gilbert and Crissman 1995 MRID 44114101S

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
		Acute Oral Toxicity Studies *(cont)*	
Rat, Fischer 344, males and females	Clopyralid, penta process	LD_{50} >5000 mg/kg	Dow AgroSciences 1998
Rat, Fischer 344, males	Clopyralid, electrochemical process	LD_{50} 3738 mg/kg	Dow AgroSciences 1998
Rat, Fischer 344, females	Clopyralid, electrochemical process	LD_{50} 2675 mg/kg	Dow AgroSciences 1998
		Reproduction/Teratology Studies, Oral	
Rabbits, New Zealand White, 6-7 months old, 3.5-4.5 kg. Two groups were tested. The first involved 16/group. A second group with 10-18 per group were added after 3 weeks because of the low number of litters with pups.	0, 50, 110, and 250 mg/kg bw by gavage on days 7-19 of gestation. Numbers of does at end of study were 19, 15, 17, and 15 - going from control to high dose. Cesarean section performed on Day 28.	50 and 110 mg/kg: No significant treatment related difference in maternal or fetal parameters. 250 mg/kg: labored breathing in about 1/3 of the does. No apparent or reportedly significant effects on maternal body weight over 28 day period [Tables 9 and 10]. Six does sacrificed early because of mortality or toxicity. Significant decrease in fetal body weights.	Hanley et al. 1990a MRID 41649801 Also summarized in Dow AgroSciences 1998.

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
	Reproduction/Teratology Studies, Oral *(cont)*		
Rabbits, New Zealand White, 3.5-4.5 kg. Two groups were tested. The first involved 16/group. A second group with 10-18 per group were added after 3 weeks because of the low number of litters with pups.	0, 110, 250, and 350 mg/kg bw by gavage in corn oil on days 7-19 of gestation. Cesarean section performed on Day 20.	110 mg/kg: No significant treatment related difference in maternal or fetal parameters. 250 mg/kg: Signs of maternal toxicity. 350 mg/kg: Authors report a decreased maternal body weight. This does not appear to be supported in Table 5 and 6. Death of three does before the end of study. No evidence of embryo toxicity at any dose level - i.e., no significant, substantial, or systematic differences in pregnancy rates, numbers of corpora lutea, implantations, litter size, or resorption rates.	Hanley et al. 1990b MRID 41649802
Rat, Fischer 344	Daily average doses of 15, 75, and 250 mg/kg/day on days 6-15 of gestation.	Decreased body weight in dams at 250 mg/kg dose group. No effects on offspring.	Dow AgroSciences 1998
Rats, Fischer 344	Dietary exposures adjusted to provided targeted doses of 0, 150, 500, and 1500 mg/kg/day over two successive generations.	Reduced pup weight and increased relative liver weight at 1500 mg/kg/day in F1a and F1b pups. No effects on growth or morphology, viability of pups ,or fertility or reproductive performance.	Dow AgroSciences 1998

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
	Subchronic Oral Studies		
Mice, B6C3F1	Dietary exposure to clopyralid resulting in doses of 0, 200, 750, 2000, and 5000 mg/kg/day for 90 days.	At 2000 mg/kg/day dose, decreased body weight in males and females. Increased liver weights and histologic changes in liver at 2000 and 5000 mg/kg in females and 5000 mg/kg in males.	Dow AgroSciences 1998
Rat, Fischer 344	Dietary exposures adjusted to provided doses of 0, 5, 15, 50, and 150 mg/kg/day for 90 days.	No effects attributable to treatment	Dow AgroSciences 1998
Rat, Fischer 344	Dietary exposures adjusted to provided doses of 0, 300, 1500, 2500 mg/kg/day for 90 days.	At 2500 mg/kg/day, decreased body weights associated with decreased food consumption. Increased kidney and liver weights at all dose levels in males and at the upper two dose levels in females.	Dow AgroSciences 1998
	Chronic Oral Studies		
Dogs, beagles	Doses of 100, 320, and 1000 mg/kg BW/day for 1 year	Reduced red blood cell parameters and serum proteins as well as increased relative liver weights at 320 and 1000 mg/kg/day.	Dow AgroScience 1998 [Appears to be identical to Breckenridge et al. 1984. See section 3.1.3. for a detailed description of this study.]
Dogs, beagles	Doses of 15, 50, and 150 mg/kg BW/day for 18 months. Two separate studies were conducted.	Increased relative liver weight in females only at 150 mg/kg in the second study.	Dow AgroScience 1998
Mice, Charles River, 50 males and 50 females in control group, 60 males and 60 females in low and mid dose group, 52 males and 50 females in high dose group.	Dietary exposure to 0, 35, 100, and 350 ppm to parents for 13 weeks and to progeny for 18 months.	No effects on body weight, survival, or pathology.	West and Willigan 1976 MRID 00061377

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
Mice, B6C3F1, 50 per sex per dose level.	Dietary exposures adjusted to provided doses of 0, 100, 500, and 2000 mg/kg BW/day for 24 months.	Decreased mean body weight (10-12%) in male mice at 2000 mg/kg BW/day. No other effects attributable to treatment based on standard clinical observations and pathology.	Young et al. 1986 MRID 00157783
Rats, Fischer-344, 70 per sex per dose level.	Dietary exposures adjusted to provided doses of 0, 15, 150, and 1500 mg/kg BW/day for 2 years.	At 1500 mg/kg/day, increased relative liver and kidney weights with changes in pathology or clinical chemistry relating to these endpoints. Also, decreased food consumption and body weight. At 150 mg/kg/day, hyperplasia and thickening of the epithelium of the anterior surface of the gastric limiting ridge (increased cells in the stratum spinosum). No treatment related effects at 15 mg/kg/day.	Barna-Lloyd et al. 1986 MRID 00162393 Also summarized in Dow AgroSciences 1998.
Rat, Sprauge-Dawley	Dietary exposures adjusted to provide doses of 0, 5, 15, 50, 150 mg/kg BW/day for two years.	Decrease BW in females at 150 mg/kg/day.	Humiston et al. 1977 MRID 00061376

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
DERMAL			
Guinea pigs, 10 albino, male	Three applications of 0.4 ml of 10% solution of clopyralid [purity not specified] on shaved and intact shoulder skin.	No erythema or edema.	Jeffery 1987c MRID 41641306
Guinea pigs, 10 Hartley males in 3-dose induction group and subsequent single-dose challenge group; 5 Hartley males in single-dose naive group; same number of controls for each group	Induction Phase: three weekly 6-hour applications of 0.4 g Lontrel TE technical (clopyralid) 96.2% pure to the left side, clipped free of hair (controls exposed by same protocol to 0.4 mL neat DER 331 epoxy resin)	There were no observations of erythema or body weight changes 48 hours after treatment in any of the animals exposed to Lontrel TE, which indicates that the compound did not cause delayed contact hypersensitivity in guinea pigs.	Gilbert 1995d MRID 44114106
	Challenge Phase: single 6-hour application of 0.4 g Lontrel TE technical to the right side, clipped free of hair (controls exposed by same protocol to 0.4 mL neat DER 331).	Slight to moderate erythema, suggesting a hypersensitivity response, was observed in 5/10 control animals 48 hours after exposure to 0.4 mL DER 331; none of the naive animals exposed to DER 331 showed signs of irritation; body weight effects were not observed in any of the animals exposed to DER 331	
Rabbits, New Zealand, male and female, 5 per sex, 2.8 to 3.1 kg.	2000 mg/kg of clopyralid [purity not specified] applied to the back. Plastic wraps used for first 24 hours to prevent ingestion. Observed for 14 days.	No mortality. Erythema and edema at application site that reversed after 3 days. Seen in all animals except one male that only displayed erythema. All animals recovered by end of study. No treatment related lesions on group pathology exam.	Jeffrey et al. 1987a MRID 40246301
Rabbits, New Zealand white, male and female, 2.6-3.3 kg, 3 per sex.	5000 mg of clopyralid [purity not specified] applied to intact skin of back.	No evidence of dermal irritation.	Jeffrey et al. 1987b MRID 41641305

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
DERMAL *(continued)*			
Rabbits, New Zealand White, Male and Female, 5 animals/sex/dose level	0, 100, 500, and 1000 mg/kg. 15 applications over a 21 day period. Applied as a powder under a moistened gauze to the shaved back of each animal.	Localized skin effects at the application site. Slight erythema in 2 males at both 500 and 1000 mg/kg/day and on female at 500 mg/kg/day. No signs of systemic toxicity.	Vedula et al. 1990 MRID 41790701
Rabbits, New Zealand, 2.04-2.4 kg, male and female, 7 males and 5 females.	Clopyralid (96.2%) 5000 mg/kg to the clipped but non-abraded back for 24 hours. Observed for 14 days.	No mortality. Erythema in six animals and edema in seven animals. Normal by day 10 of test.	Gilbert 1995a MRID 44114102
Rabbits, New Zealand white, weighing 2.24-2.69 kg, 2 males and 4 females	Clopyralid (96.2%) 0.5 g applied to the clipped but non-abraded back for 4 hours. Application sites graded for erythema and edema at 30 minutes and 24, 48, and 72 hours.	No dermal irritation was observed and there was no effect on body weight	Gilbert 1995c MRID 44114105
Guinea Pigs, Hartley albino	Penta and electrochemical processes, 10% solution	No skin sensitization.	Dow AgroSciences 1998
Rabbits, New Zealand	Penta process and electrochemical process	LD_{50} >2000 mg/kg.	Dow AgroSciences 1998

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
EYES			
Rabbits, adult male and female, New Zealand, albino, 3 per sex, 2.7-3.3 kg. Observations at 1 hour as well as 1, 2, 4, 7, 14, and 21 days after instillation.	0.1 g in right conjunctival sac without washing.	Slight to marked redness, chemosis, and discharge. Reddening of the iris with moderate to marked opacity of the cornea. Opacity persisted to 21 days post-treatment.	Jeffery 1987a MRID 41641304
Rabbits, adult male and female, New Zealand, albino, 3 per sex, 2.53-3.01 kg. Observations at 1 hour as well as 1, 2, 4, 7, 14, and 21 days after instillation.	100 mg of Lontrel TE (96.2% clopyralid) in right conjunctival sac without washing.	Slight to moderate conjunctival redness, diffuse to marked corneal opacity, and slight to marked chemosis in all six animals within 24 hours. In one rabbit, congestion of the iris was apparent on day 21.	Gilbert 1995b MRID 41641304
Rabbits, New Zealand	Penta and electrochemical processes	Slight to marked redness and chemosis. Reddening of the iris and corneal opacity in all animals. Signs of irritation were apparent at 21 days after treatment.	Dow AgroSciences 1998

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
INHALATION			
Rats, Albino Fischer 344 [CDF (F-344)/CrlBR (Inbred)], Group I: 10 rats (5/sex/group), 8-to 9-weeks old, weighing 165-193 g (males) and 123-136 g (females); 2-week observation period	Group I: nose only exposure to nominal concentration of 5.5 mg/L (gravimetric concentration of 1.0 mg/L) for 4 hours Group II: nose only exposure to nominal concentration of 1.2 mg/L (gravimetric concentration of 0.38 mg/L) for 4 hours	No mortality in either group; all rats had generally normal body weights during 14-day observation period; labored breathing was the only substantial effect observed during exposure period; 2-hours after exposure clinical signs included red or clear nasal discharge, chromodacryorrhea, dried red material on the face, and labored breathing; one day after exposure, most of the rats had recovered completely and remained normal during the remainder of the 14-day observation period; in Group I (1.0 mg/L), there were no abnormal macroscopic postmortem observations; in Group II (0.38 mg/L), 4/10 rats had discolored lungs. According to the investigators: "Although Group II exposure was at a lower exposure level (total mass) than Group I, the two exposures were comparable on the basis of concentration of particles most likely to provide alveolar deposition and inflammatory response ($\leq$1.0 micron in size). Therefore the observations only in the lungs of Group II animals were probably not treatment related."	Hoffman 1995 MRID 44114103

Appendix 1: Toxicity of clopyralid to mammals.

Animal	Dose	Response	Reference
INHALATION *(continued)*			
Rats, Fischer 344, 7-weeks old, male and female, 5/sex. Lontrel T [95.4% clopyralid]. Two week observation period.	TWA nominal concentration of 0.2 mg/L for 4 hours. Mass median aerodynamic diameter of 13.45 µ. Actual conc. was less because material settled in the glass works and chamber.	During exposure, a few animals had red stains around nares and one salivated. Red stains around nares also noted in all females and three males after exposure. By test day six, all animals appeared normal. No mortality, clinical effects, or gross pathology after exposure.	Streeter et al. 1987 MRID 41641303
Rats, Fischer 344	Penta process	4-hour nose-only LC_{50} 1 mg/L (highest attainable concentration)	Dow AgroSciences 1998
Rats, Fischer 344	Electrochemical process	4-hour nose-only LC_{50} 0.38 mg/L (highest attainable concentration)	Dow AgroSciences 1998

Appendix 2: Toxicity of clopyralid to birds after oral administration.

Animal	Dose/Endpoint	Response	Reference
Ducks, mallard, NOS	LD_{50} after single oral exposure to 3,6-dichloropicolinic acid (DOWCO 290)	1465 mg/kg	Dow Chemical 1980; 1981 MRID 00059968/ 00081594
Ducks, mallard, NOS	LC_{50} of 3,6-dichloropicolinic acid (DOWCO 290) for 5 days in the diet (plus 3 days on untreated food)	>4640 ppm	Dow Chemical 1980 MRID 00059968
Ducks, mallard, NOS	LD_{50} for clopyralid, monoethanolamine salt (35% a.e.)	>2000 mg/kg (> 700 mg a.e./kg)	Dow AgroSciences 1998
Ducks, mallard, NOS	5-day dietary LD_{50} for clopyralid, monoethanolamine salt (35% a.e.)	>5620 ppm a.i. [>1967 ppm a.e.]	Dow AgroSciences 1998
Quail, bobwhite, NOS	LC_{50} 3,6-dichloropicolinic acid (DOWCO 290) for 5 days in the diet (plus 3 days on untreated food)	>4640 ppm	Dow Chemical 1980; 1981 MRID 00059968/ 00081594
Quail, bobwhite	5-day dietary LD_{50} for clopyralid, monoethanolamine salt (35% a.e.)	>5620 ppm a.i. [>1967 ppm a.e.]	Dow AgroSciences 1998
Quail, bobwhite eggs	sprayed at 0 [control] or 0.56 kg a.e./ha. In a field environment.	No effect on viability, hatchability, body weight. Also no effect PHA-P wing-web r anti-SRBC antibody titer.	Dabbert et al. 1997

Appendix 3: Toxicity to terrestrial invertebrates.

Organism	Exposure	Response	Reference
DIRECT CONTACT			
Bee, NOS	>100 μg/bee 3,6-dichloro-picolinic acid for 48 hours	LD_{50}	Dow Chemical 1980; 1981 MRID 00059968/ 00081594
Worker honey bee (*Apis mollifera*), 10 replicates/dose, 10 bees/replicate	100 μg/bee DOWCO 290 in acetone applied to ventral thorax	LD_{50} = >100 μg/bee	Cole 1974 MRID 00059971/ 00081595
Honey bee (*Apis mellifera*), 1-to 7-days old, mean individual weight 110 mg, 4 replicates/dose, 50 bees/replicate	0, 13, 22, 36, 60, 100 μg/bee LONTREL 35A herbicide concentrate (3,6-dichloropicolinic acid, monoethanolamine salt, 35% a.e.) for 48 hours	48-hour mortality: control = 4/100 solvent control = 2/100 13 μg/ a.i. per bee = 5/100 22 μg/ a.i. per bee = 3/100 36 μg/ a.i. per bee = 5/100 60 μg/ a.i. per bee = 8/100 100 μg/ a.i. per bee = 6/100 48-hr LD_{50} = >100 μg/bee NOEL = 100 μg/bee	Hinken et al. 1986 MRID 40151612
ORAL			
Bee, NOS	>100 μg/bee 3,6-dichloro-picolinic acid for 48 hours	LD_{50}	Dow Chemical 1980; 1981 MRID 00059968/ 00081594
Worker honey bee (*Apis mellifera*), 10 replicates/dose, 10 bees/replicate	100 μg/bee DOWCO 290 via feeding tube	LD_{50} = >100 μg/bee	Cole 1974 MRID 00059971/ 00081595
SOIL			
Earthworm	14-day static LC_{50} using technical clopyralid	>1000 mg/kg soil	Dow AgroSciences 1998

Appendix 4: Toxicity to non-target plants (listed alphabetically by author).

Plant	Exposure	Response	Reference
Six species of landscape plants: 4 species of *Juniperus*, *Lagerstroemia indica*, and *Cotoneaster dammeri*	backpack applications at 0.14, 0.28, and 0.56 kg/ha [0.125, 0.25, 0.5 lb a.i./acre]	Visual damage [10-16 on a 100 point scale] to *Lagerstroemia* at 3 and 6 weeks after application. Extent of visual damage was not dose-related or progressive. Less severe damage [5-9 on a 100 point scale] to *Cotoneaster* at 3 weeks with apparent partial recovery at 6 weeks [0-3 on a 100 point scale]. No damage to Juniper species. No effects on growth rates of any species.	Bachman et al. 1995
Willows (two varieties) and poplar	track sprayer, 0.2 and 0.4 kg a.i./ha	no marked effect on willow varieties. About 50% growth inhibition in poplar. Difference probably due to greater amount of spray retained on poplar.	Clay 1991
Strawberries	backpack sprayer at 0.1 or 0.2 kg a.e./ha.	Some leaf distortion but no effect on yield when applied to established plants.	Clay and Andrews 1984

Appendix 4: Toxicity to non-target plants (listed alphabetically by author).

Plant	Exposure	Response	Reference
Cacti, five species, seed-groun nursery plants or grafts. All were related to but not classified as endangered species.	Hand sprayer, 0.25 and 0.5 lb a.i./acre	No effect on survival of *Echinocatus grusonii or Echinocereaus engelmannii* at either application rate. A modest but not strongly dose-related effect on vigor in *Echinocatus grusonii*. Increased vigor in *Echinocereaus engelmannii*. No dose-related effect on survival or vigor in *Mammillaria thornberi* In *Pediocatus papyracanthus*, mortalities of 60% and 80% and a dose/related reduction in vigor after six months at low and high rates, respectively. In *Corphantha hesteri*, 40% mortality as well as comparable decreases in vigor at both application rates.	Crosswhite et al. 1995
Cotton	0.01, 0.05, 0.1 and 0.25 lb a.i./acre	No effects at 0.01 lb a.i./acre. When applied to pre-bloom cotton plants, 0.05 lb/acre or higher reduced yeilds from 35-45%.	Jacoby et al. 1990
Variety of forestry trees: ash, beech, birch, cherry, Japanese larch, oak, red alder, Sitka spruce, sycamore; all as 2-year old pot grown plants.	0.1 and 0.3 kg a.i./ha by laboratory track sprayer	No visible signs of damage or effects on fresh weight. Transient and not clearly dose-related changes in shoot fresh weight in alder and Sitka spruce. Some transient distortion of Japanese larch needles.	Lawrie and Clay 1994

Appendix 4: Toxicity to non-target plants (listed alphabetically by author).

Plant	Exposure	Response	Reference
Potatoes	0.0001, 0.001, 0.01, 0.1 kg a.i./ha in year 1. Replanting done in years 2 and 3. Application by broadcast sprayer at 30% or 70% canopy crop cover. Soil type not specified.	In year 1, damage only at highest application rate. In year 2, there was severe damage - tuber malformation and reduced yield - at both 0.1 and 0.01 kg a.i./ha. No damage was apparent in year 3.	Lawson et al. 1992
Potatoes, kumara, and tomatoes, mature vegetative to early flowering stage	0.0001, 0.001, 0.01, 0.1, 0.5, and 1.0 kg a.i./ha. Broadcast spray.	In potatoes, reduced yield and severe foliar damage at 0.01 kg/ha and reduced yield at 0.001 kg/ha. In kumara, reduced yield at 0.01 kg/ha. In tomatoes, some foliar damage and reduced yield at 0.01 mg/kg.	Lucas and Lobb 1987
Sweet corn (*Zea mays*)	0.2, 0.3, 0.6 or 1.1 kg/ha by backpack sprayer	No substantial or dose/related effects on stalk curvature, stunting, or yield.	Masiunas and Orfanedes 1991
Glenlea and Neepawa Wheat; 3 and 6 leaf stages and boot stage.	0.1 to 0.9 kg a.e./ha using motorized plot sprayer	No effect on Glenlea wheat. Effects on Neepawa wheat at 0.6 kg/ha and above depending on plant stage at the time of application	O'Sullivan and Kossatz 1984a.
Galt and Klondike barley	0.1 to 0.9 kg a.e./ha using motorized plot sprayer	No effect at any application rates.	O'Sullivan and Kossatz 1984b.
Cranberries	0.21 or 0.42 kg a.i./ha by broadcast sprayer	At 0.21 kg/ha, moderate to severe damage only if applied to prebloom stage. At 0.42 kg/ha, damage to both prebloom and fruit set stages	Pattern et al. 1994
17 species of forbs and 4 species of grasses	0.2 kg a.i./ha by AZO pedestrian sprayer	Decrease rooted frequency and flowering in several species with visible signs of damage in several forbs.	Pywell et al. 1996
Landscape trees: Pear, myrtle, redbud, and red maple. Observations over a two year period.	0.28 kg a.i./ha. Directed backpack spray.	Significantly decreased trunk diameter and total weight in Eastern redbud. Significant visual injury to red maple of 60 to 150 days after treatment but no effect on tree diameter or weight by the end of the study.	Smith and Skroch 1995

Appendix 4: Toxicity to non-target plants (listed alphabetically by author).

Plant	Exposure	Response	Reference
Onion, corn, wheat, barley, soybean, snap bean, radish, tomato, canol, and sunflow. Assays on germinating seeds, emerging seedlings, and emerged plants.	Rates of 0.056, 0.112, 0.56, 5.6, 56, and 560 g/ha. [Equivalent to 0.000056, 0.000112, 0.00056, 0.0056, 0.056, and 0.560 kg/ha.] Clopyralid applied as the potassium salt - 75% weight percent acid equivalent. Applications by greenhouse track sprayer. Sandy loam soil.	At 0.56 kg/ha, adverse effects on sunflower germination [all determinations made 3-4 days after treatment]. When applied as a pre-emergence spray to soil at 0.56 kg/ha, toxic to onion, soybean, snap bean, tomato, and sunflower but not other species [observations made 10 and 14 days after treatment]. NOEL for emergence for onion of 0.14 kg/ha. NOEL for emergence for tomato and sunflower of 0.035 kg/ha. NOEL for emergence for soybean of 0.028 kg/ha. NOEL for emergence for snap bean of 0.056 kg/ha. Some signs of phytotoxicity were apparent as low as 0.007 kg/ha. As a post-emergent foliar spray, 0.00056 kg/ha was the NOAEL for soybean, snap bean, tomato, and sunflower [observations made up to 42 days post-spray]. Barley, corn, radish, and canola were unaffected at 0.56 kg/ha.	Weseloh 1987 MRID 400081401

Appendix 5: Toxicity to fish, aquatic invertebrates, and aquatic plants. [a.e. unless otherwise specified]

Organism	Exposure	Response	Reference
Fish			
Minnow, Fathead	monoethanolamine salt (a.i.) of clopyralid (35% a.e.)	96-hour LC_{50} >2900 mg a.i./L [>1015 mg a.e./L]	Dow AgroSciences 1998
Trout, Rainbow (*Salmo gairdneri* Richardson)	3,6-dichloro-picolinic acid (DOWCO 290) for 96 hours	96-hour LC_{50} = 103.5 mg/L	Dow Chemical 1980; 1981 MRID 00059968; 00081594
Trout, Rainbow	monoethanolamine salt (a.i.) of clopyralid (35% a.e.)	96-hour LC_{50} = 2000 mg a.i./L [700 mg a.e./L]	Dow AgroSciences 1998
Sunfish, Bluegill (*Lepomis macrochirus macrochirus* Rafinesque)	3,6-dichloro- picolinic acid (DOWCO 290) for 96 hours	96-hour LC_{50} 125.4 mg/L	Dow Chemical 1980; 1981 MRID 00059968; 00081594
Sunfish, Bluegill	formulation (NOS)	1000 mg/L	Dow AgroSciences 1998
Sunfish, Bluegill	monoethanolamine salt (a.i.) of clopyralid (35% a.e.)	96-hour LC_{50} 4700 mg a.i./L [1645 mg a.e./L]	Dow AgroSciences 1998
Aquatic Invertebrates			
Daphnia magna	technical grade clopyralid	48-hour LC_{50} = 232 mg/kg	Dow AgroSciences 1998
Daphnia magna	Formulation (NOS)	4700 mg/L	Dow AgroSciences 1998
Daphnia magna	monoethanolamine salt (a.i.) of clopyralid (35% a.e.)	96-hour LC_{50} 1000 mg a.i./L [350 mg a.e./L]	Dow AgroSciences 1998
Daphnia magna	monoethanolamine salt (a.i.) of clopyralid (35% a.e.)	NOEC for reproduction of 66 mg a.i./L [23.1 mg a.e./L]	Dow AgroSciences 1998

Appendix 5: Toxicity to fish, aquatic invertebrates, and aquatic plants. [a.e. unless otherwise specified]

Organism	Exposure	Response	Reference
Aquatic Macrophytes			
Duckweed	14-days	EC_{50} = 89 mg/L	Dow AgroSciences 1998
Potamogeton pectinatus and *Myriophyllum sibiricum*	12-ha pond. 1 m square enclosures in 50-70 cm deep water. Concentrations of 0.01 mg/L and 0.1 mg/L	No adverse effects. Growth and flowering of both species were stimulated at 0.01 mg/L. At both 0.01 and 0.1 mg/L, tuber production by *Potamogeton pectinatus* was also stimulated.	Forsyth et al. 1997
Unicellular Algae			
Selenastrum capricornutum	96 hour exposures	EC_{50} for growth inhibition was 6.9 mg/L based on cell count and 7.3 mg/L based on total volume.	Dill and Milazzo 1985 MRID 40081402
Green alga, NOS	5-days	EC_{50}= 6.9 mg/L	Dow AgroSciences 1998
Green alga, NOS	72 hours	EC_{50} = 449 mg/L	Dow AgroSciences 1998
Green alga, NOS	72 hours	EC_{50} = 61 mg/L	Dow AgroSciences 1998

Appendix 6: Field Studies on the Fate of Clopyralid in Soil

Treatment	Location	Results	Reference
Clopyralid, 0.5 lbs ae and picloram 0.5 lb ae/acre. Observations over a 4 month period.	Bremond TX, loamy fine sand to fine sand soil. Irrigation used to supplement rainfall. Average monthly rainfall/irrigation of 2.87 to 4.44 inches.	Rapid dissipation in soil: $t_{1/2}$ of 10 days. Dissipation $t_{1/2}$ on vegetation of about 8 days. Initial concentration on plants of about 40 ppm as read from Figure 6. [Table of plant residues is not provided.] No residues in ground water at limit of detection (1 ppb). Maximum level in soil on day 9 probably due to wash-off.	Oliver et al. 1988
Clopyralid, XRM-4703 (clopyralid 0.5 lb a.e./acre) and picloram at 0.5 lb a.e./acre.	Highly permeable loamy fine sand to fine sand soil in high rainfall region. Irrigation used to supplement rainfall.	Soil $t_{1/2}$ of about 10 days. Only trace levels by day 79. Residues largely in upper 36 inches of soil. No residues detected in ground water. No detectable levels at days 128 or 189.	Petty and Knuteson 1991 MRID 42415400
^{14}C-labeled clopyralid at 280 g/ha.	Applied to a small plots of soil.	After 312 days in field, 24% of radioactivity remained mostly associated with soil organic matter. No soil metabolites or degradation products were detected.	Yackovich et al. 1993 MRID 42815001
Clopyralid at 278 g a.e./ha (0.25 lb a.e./acre)	California, natural rainfall supplemented with irrigation.	Soil $t_{1/2}$ of 19 days. Field $t_{1/2}$ in grass/thatch of 48 days.	Roberts et al. 1996 MRID 44184701
	Cultivated soil and high humic acid soil	57 days in cultivated soil. 161 days in high humic acid soil.	Schutz et al. 1996

Appendix 7: GLEAMS modeling of hexachlorobenzene runoff.

GLEAMS is a root zone model that can be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions. As with many environmental fate and transport models, the input and output files for GLEAMS can be complex. The input files used for this analysis have been provided to the Forest Service. Only the most relevant information is detailed in the following paragraphs.

In terms of estimating runoff, the key chemical-specific parameters for hexachlorobenzene are water solubility, $K_{o/c}$, and soil halftime. The water solubility of hexachlorobenzene is 0.006 mg/L and reported $K_{o/c}$ values range from about 4,000 to 1,200,000 (ATSDR 1998). For the GLEAMS modeling, the $K_{o/c}$ was set at 100,000. This is the geometric mean of the range reported by ATSDR (1998), rounded to one significant figure.

The kinetics of hexachlorobenzene in the topmost soil layer are somewhat complex. When hexachlorobenzene is applied to the surface of soil, volatilization will be a major mechanism of dissipation for that portion of the compound that remains on or near the soil surface (ATSDR 1998). Typical reported halftimes for hexachlorobenzene in soil are in the range of 3 to 6 years (ATSDR 1998). As detailed in section 3.2.4.2, a halftime of 2.8 years for hexachlorobenzene in soil can be calculated for the 2-4 cm soil layer from relatively detailed data provided in Beall (1976). While these halftimes are appropriate for estimating uptake from vegetation associated with hexachlorobenzene residues below the soil surface, they are not appropriate for estimating runoff values using the GLEAMS model because they do not take into account the volatilization of hexachlorobenzene from the soil surface.

A more relevant soil halftime can be estimated from data on the top 0-2 cm soil layer reported in the study by Beall (1976) and illustrated in Figure A7-1. In this figure, the squares represent the actual measurements over the 19-month observation period (Table 1, p. 369 of Beall, 1976). The relatively rapid initial drop in soil residues followed by a more gradual decline suggests a bi-exponential kinetics,

$$C_t = Ae^{-\alpha t} \times Be^{-\beta t}$$

where C_t is the soil concentration at time *t*, α, and β are dissipation coefficients, and A and B, are model constants. These general types of models are detailed in most texts on kinetics (e.g., Goldstein et al. 1974). This model was fit to the data on the 0-2 cm soil layer (Beall 1976) using the SOLVER function in EXCEL (Middleton 1997).

As illustrated by the solid line in Figure A7-1, the bi-exponential model fits the observed data extremely well yielding coefficients of 0.0975 $days^{-1}$ (α) and 0.0054 $days^{-1}$ (β), corresponding to initial and terminal halftimes of 7.1 days (α) and 128 day (β) [$t_{1/2}=\ln(2)/k$]. Given the importance of volatilization in the dissipation of hexachlorobenzene from soil (ATSDR 1998), the fit of these data to a bi-exponential model seems reasonable.

The GLEAMS model, however, requires a simple first-order (mono-exponential) halftime in soil and does not accommodate bi-exponential dissipation. Fitting the data from Beall (1976) to a simple first-order model,

$$C_t = Ae^{-\alpha t},$$

yields a dissipation coefficient (α) of 0.0344 days^{-1} with a corresponding halftime of 20 days. In the first-order model, the *A* parameter is the concentration at time-zero and is estimated at 5.355 ppm. As illustrated in Figure 1 with the longer dashed lines, this model does not fit the data well and tends to underestimate the concentrations of hexachlorobenzene in soil over most of the observation period. This underestimation by the simple first-order model is important because, in estimating runoff over a prolonged period of time, the amount of runoff will be dependent on the estimated amount of the chemical remaining on or near the soil surface and thus subject to runoff.

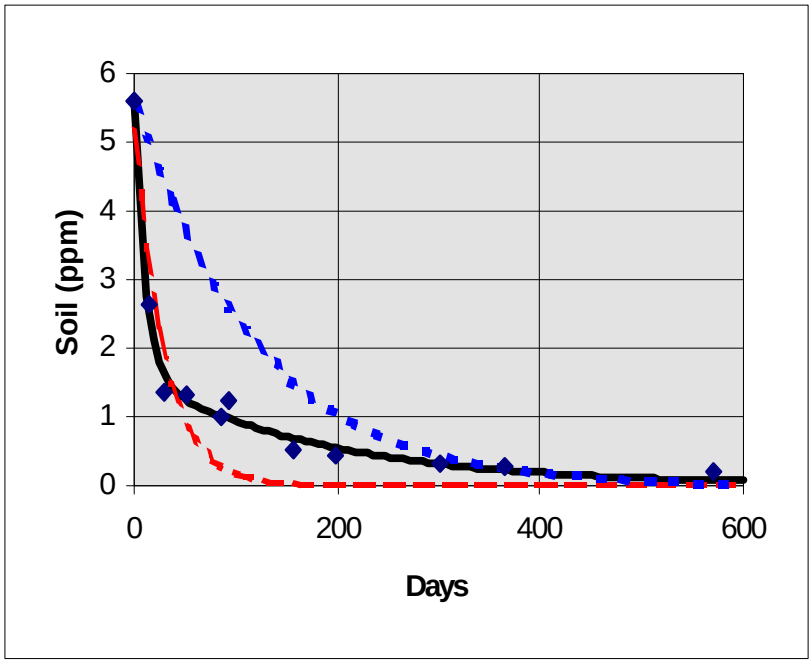

Figure A7-1: Residues of hexachlorobenzene in the 0-2 inch soil layer (data from Beall 1976. Solid line: bi-exponential dissipation, dashed line: first-order dissipation, dotted line: first-order approximation. See text for discussion).

The magnitude of the underestimate can be found by calculating the time-weighted average soil concentration based on each model - i.e., integrating with respect to time and dividing by the time interval. In this analysis, all integrations were performed using Mathematica (Wolfram Research 1997). Since repeated applications may be conducted each year in Forest Service programs, a one-year time interval is most relevant. The definite integral of the bi-exponential model between t_0 and t_{365} is approximately 300 ppm and the time-weighted average concentration is about 0.823 ppm [300 ppm ÷ 365 days]. The definite integral of the simple first-order model between t_0 and t_{365} is approximately 155 and the time-weighted average concentration is about 0.426 ppm [155 ppm ÷ 365 days]. Thus, the simple first-order model underestimates the average soil concentration over a one-year period by a factor of about 2 [0.823 ppm ÷ 0.426 ppm = 1.96].

As an alternative, a conservative first-order approximation of a dissipation rate coefficient (α) can be calculated from the concentrations in the 0-2 cm soil layer on day one and day 365. These

values are 5.5992 ppm and 0.2654 ppm, respectively (Table 1, p. 369 of Beall, 1976). The first-order approximation of the dissipation rate coefficient (α) is thus:

$$-\ln(0.2654 \div 5.5992)/365 \text{ -1 day} = 0.00837 \text{ days}^{-1}$$

which corresponds to a halftime of 82.7 days. This approximation is illustrated by the short dashed line in Figure 1 and is above either of the lines generated from the bi-exponential or simple first-order methods. Consequently, using this approximation will result in over-estimates of the amount of hexachlorobenzene available for runoff in the upper layer of soil. The definite integral of the first-order approximation between t_0 and t_{365} is 638 ppm and the time-weighted average concentration is about 1.75 ppm [638 ppm ÷ 365 days]. Thus, the magnitude of the overestimate relative to the bi-exponential model is about a factor of 2 [1.75 ppm ÷ 0.823 ppm = 2.126]. Because GLEAMS requires a simple first-order halftime, the first-order approximation of 83 days is used.

The only other noteworthy chemical-specific parameters required by GLEAMS involve foliar interception, foliar wash-off, and foliar half-time. For all GLEAMS models used in this exposure assessment, foliar interception is set to zero - i.e., the assumption is made that all of the applied hexachlorobenzene reaches the soil surface. Because of this assumption, foliar wash-off and foliar half-time do not impact the estimates. As will the use of soil halftimes, this will over-estimate the amount deposited on soil and hence the amount available for runoff.

No attempt is made to correct for these over-estimates because of the tendency of GLEAMS to under-estimate runoff. For example, Reyes et al. (1994) have noted that GLEAMS and various modifications to the GLEAMS model under-estimate runoff losses by factors of about 2 to 3. Thus, while some of the chemical-specific assumptions used in the GLEAMS modeling will tend to over-estimate runoff, these factors will be at least partially offset by the tendency of the GLEAMS model to underestimate runoff.

Two types of soils are modeled: clay (high runoff potential) and sand (low runoff potential). Two erosion parameter files and two hydrology parameter files are used, one each for clay and sand. Both sets of files specify a 10 acre (435,600 sq. ft.) area that is 50 feet wide and 8712 feet long - e.g., a right-of-way. For estimating runoff to water, it is assumed that a body of water runs along the length of the right-of-way and that the slope toward the water is 20 percent. Because of the general rather than site-specific nature of this exposure assessment, only a single overland profile is used. Additional parameters specified in this file are consistent with a clay or sand with little resistance to runoff. The most sensitive hydrological parameters affecting runoff are organic carbon and runoff curve numbers, both of which are directly related to runoff. As with the parameters used in the pesticide file, the parameters used in these files should lead to relatively high but reasonable estimates of pesticide runoff for each soil type. Specific parameter values were selected based on reference tables provided in the documentation for GLEAMS (Knisel et al. 1992) as well as texts dealing with runoff (Boulding 1995; Leng et al. 1995; Nix 1994; Winegardner 1996).

Rainfall also has a substantial influence on runoff and GLEAMS requires daily rainfall data files. National monthly rainfall statistics covering the period from 1961 to 1990 were obtained from the U.S. Weather Service (1998). Based on these files, national annual summary statistics were generated in a DBASE file. Average annual rainfall ranged from a low of 0.3 inches (lower range for Yuma, Arizona) to 172.2 inches (upper range for Yakutat, Alaska) with a mean average annual rainfall of 27.69 inches.. Based on these statistics, model runs for both clay and sandy soil were conducted using precipitation rates of 5, 10, 25, 50, 100, 150, 200, and 250 inches per year.

Each GLEAMS model run was conducted over a 20 year period, with applications of hexachlorobenzene contaminated herbicide on Julian day 002 of years 1 through 20. For each year, equal amounts of rainfall were generated every tenth day to yield the average annual rainfall. This approach was taken because most runoff as well as soil erosion will occur during periods of relatively intense rainfall. Combined with the pesticide, erosion, and hydrology parameters discussed above, this should yield relatively high but still plausible estimates of runoff.

As summarized in worksheet B01, the typical application rate for clopyralid is 0.1 lb a.e./acre and this corresponds to a functional application rate for hexachlorobenzene of 0.00000025 lb/acre - i.e., 2.5 ppm hexachlorobenzene in technical grade clopyralid. GLEAMS does not permit application rates in the range of 0.00000025 lb/acre. Thus, for the GLEAMS runs, an application rate of 1 lb/acre was used and the outputs were adjusted by a factor of 0.00000025.

Consistent with the information on hexachlorobenzene reviewed by ATSDR (1998), all off-site movement of hexachlorobenzene occurred in runoff and no losses occurred through percolation. Also consistent with general patterns of pesticide runoff (e.g., Knisel et al. 1992), the proportion of runoff was greater for clay than sandy soil and directly proportional to rainfall. For clay, no runoff occurred at annual rainfall rates of 5 or 10 inches. For sand, no runoff occurred at annual rainfall rates of 5, 10, or 50 inches.

The runoff rates provided by GLEAMS are in units of g/ha (output field 601). Based on a 50 foot wide ROW, one hectare (10,760 ft2) is about 215 feet long [10,760 ft2÷50 ft =215.2 feet]. Using a 50 foot wide standing body of water adjacent to the ROW, the volume of water can be calculated from the dimensions - 215 ft (65.532 meters) by 50 ft (15.24 meters) by 1 meter deep - as 1,000,000 liters:

$$65.532\ m \times 15.24\ m \times 1\ m = 998.70\ m3 \approx 1000\ m3 \times 1000\ L/m3 = 1{,}000{,}000\ L.$$

For any time, t, amount of hexachlorobenzene in water A_t in units of g/ha is calculated as:

$$A_t = A_{t-1} - (A_{t-1} * k_e) + \delta$$

where δ is the amount added at time *t* by runoff read from the GLEAM output files.

ATSDR (1998) gives reported halftimes for hexachlorobenzene in surface water ranging from 2.7 to 5.7 years, corresponding to dissipation rates of 0.122 $year^{-1}$ to 0.256 $year^{-1}$ or 0.00031 day^{-1} to

0.00070 day^{-1}. Thus, the value of k_e used in the above equation is taken at 0.19 $year^{-1}$ or 0.0005 $day^{-1,}$ the mid-range of k_e's based on halftimes in surface water.

The amount added at time *t* by runoff, δ, is adjusted using two factors. The first factor of 0.00000025 adjusts to an application rate of 0.00000025 lb hexachlorobenzene/acre which, as discussed above, is associated with an application rate of 0.1 lb clopyralid a.e./acre.

The second factor is 0.000999 [1÷1001], which is used to account for the partitioning of hexachlorobenzene to sediment. This factor is derived from the soil-water partition coefficient of 100000 from U.S. EPA (1998). This value is defined as the ratio of the concentration of hexachlorobenzene in soil (mg/kg soil) to the concentration of hexachlorobenzene in water (mg/L water). Assuming a 1 cm (0.01 meter) mixing depth for sediment and a 1 meter water depth, the amount of hexachlorobenzene in water relative to the amount in sediment is thus 1000:

$$100{,}000 \times 0.01 \div 1 = 1000.$$

Thus, of the total amount of hexachlorobenzene transported to water, a proportion of 0.000999 [1÷1001] will be in the aqueous phase.

Using these factors, the amount of runoff each day that is added to water, δ, was calculated as:

$$\delta = R \times 0.00000025 \times 0.000999$$

where R is the amount read from the GLEAMS output file.

The concentration in water at time *t* (C_t) in units of picograms/L is then calculated as:

$$C_t \text{ (pg/L)} = A_t \text{ (g/ha)} \times 1{,}000{,}000{,}000 \text{ pg/g} \div 1{,}000{,}000 \text{ L/ha}.$$

Units of picograms per liter (pg/L), which is equivalent to 10^{-12} g/L or 10^{-9} mg/L, were used because of the extremely low concentrations of hexachlorobenzene in water.

Based on the GLEAMS model runs and the above calculations, the estimated concentrations of hexachlorobenzene in water associated with a clopyralid application rate of 0.1 lb a.e./acre in areas with clay and sand soil are illustrated in Figures A7-2 and A7-3, respectively. At an annual rainfall rate of 25 inches, about the national average, the estimated concentration of hexachlorobenzene in water associated with runoff from clay is 0.000526 picograms/L or about 5×10^{-13}mg/L. After 20 years of annual applications, the modeled concentration is 0.003169 picograms/L or about 3×10^{-12}mg/L. At this rainfall rate (25 inches/year), no runoff from sand is anticipated. As illustrated in Figures A-2 and A-3, higher levels of water contamination are estimated in areas with higher rainfall rates. For example, at an annual rainfall rate of 150 inches, water concentrations of about 0.07 to 0.1 picograms/L or 7×10^{-11} mg/L to 1×10^{-10} mg/L are estimated for sand and clay soils, respectively. At atypically high rainfall rates of 250 inches per

year, concentrations increase to about 0.1 to 0.2 picograms/L or 1×10^{-10} mg/L to 2×10^{-10} mg/L over a 20 year period.

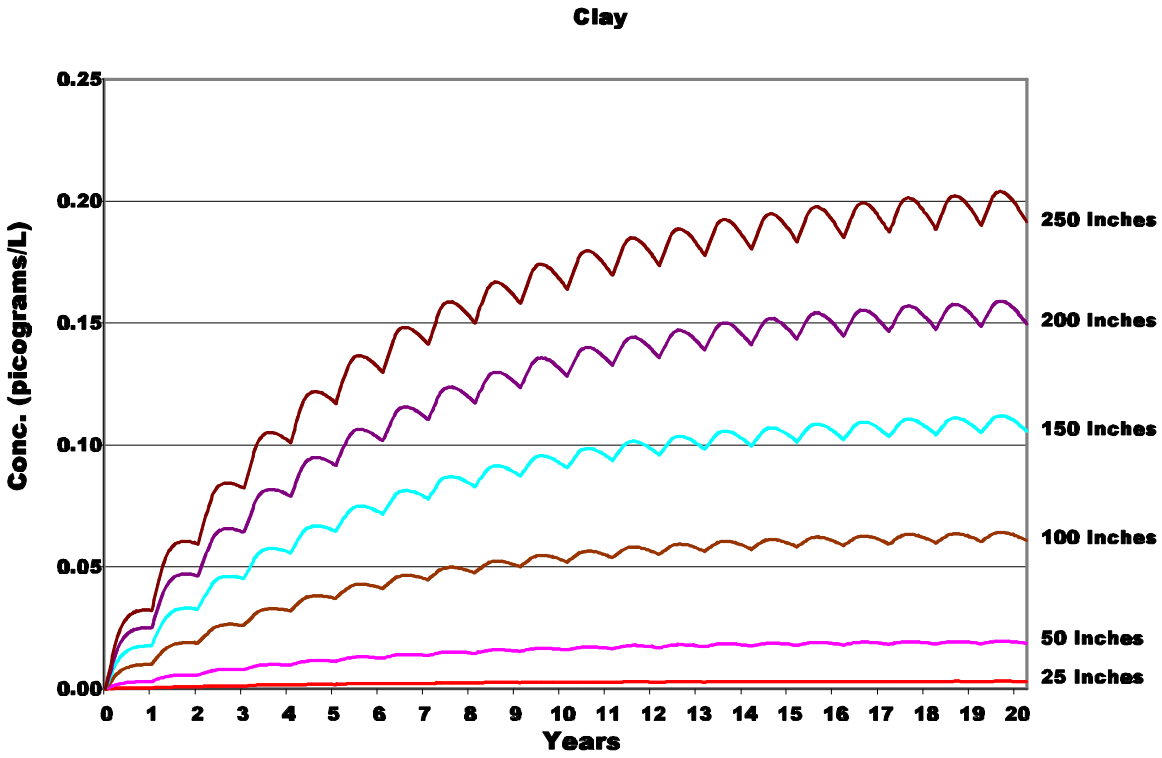

Figure A7-2: Estimated concentrations of hexachlorobenzene in water (in units of picograms/L or 10^{-9} mg/L) associated with runoff from clay at rainfall rates of 25 inches to 250 inches per year.

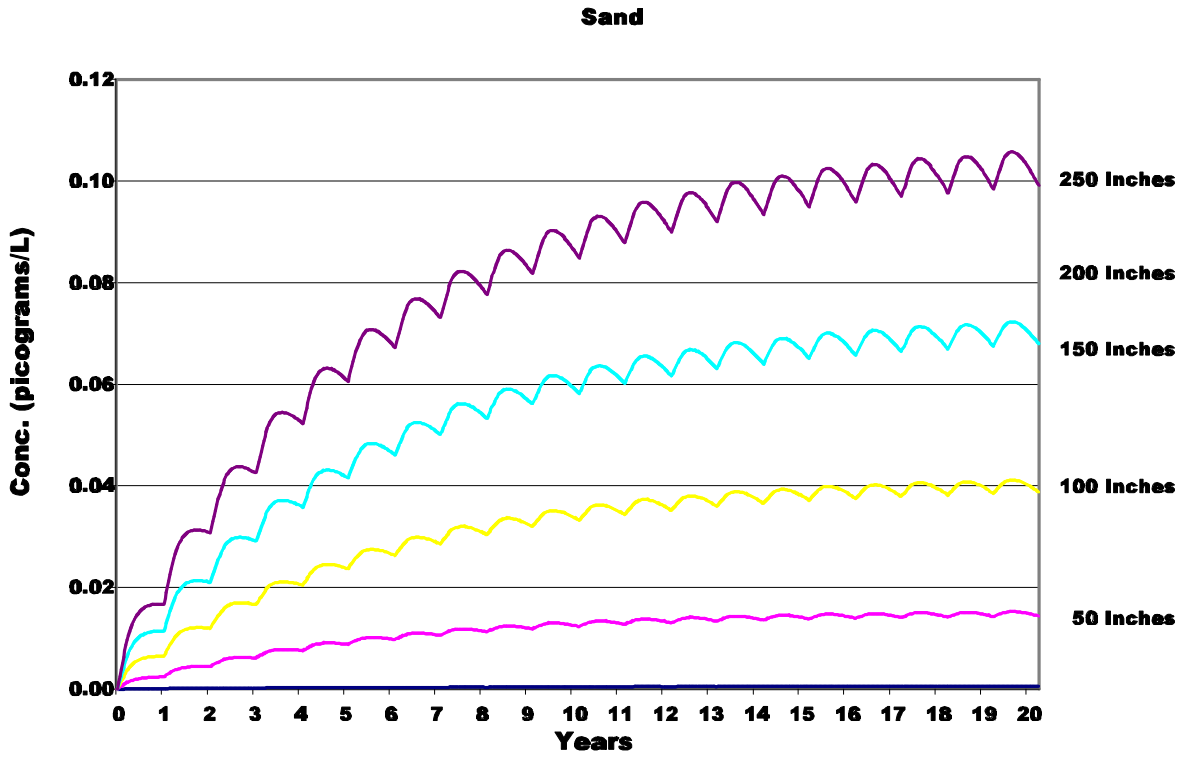

Figure A7-3: Estimated concentrations of hexachlorobenzene in water (in units of picograms/L or 10^{-9} mg/L) associated with runoff from sand at rainfall rates of 50 inches to 250 inches per year.

WORKSHEETS FOR
Clopyralid

Worksheet Table of Contents

Worksheet Table of Contents

Worksheet Table of Contents

GENERAL ASSUMPTIONS, VALUES, and MODELS

Worksheet A01: Constants and conversion factors used in calculations [CONST]		
Conversion	ID	Value
mg/lb	mg_lb	453,600
mL/gallon	ml_gal	3,785
lb/gallon to mg/mL	lbg_mgml	119.8
lb/acre to µg/cm^2	lbac_ugcm	11.21
lb/acre to mg/cm^2	lbac_mgcm	0.01121
gallons to liters	gal_lit	3.785

Worksheet A02: General Assumptions Used in Worker Exposure Assessments [STD]				
Parameter	ID	Value	Units	Reference
Body Weight (General)	BW	70	kg	ICRP (1975), p. 13
Surface area of hands	Hands	840	cm^2	U.S. EPA 1992
Surface area of lower legs	LLegs	2070	cm^2	U.S. EPA 1992
Weight of liquid adhering to surface of skin after a spill	Liq	0.008	mg/cm^2	Mason and Johnson 1987

Worksheet A03a: Directed Ground Sprays (includes backpack, cut surface, and streamline applications) - General Assumptions Used in Worker Exposure Assessments [BACKPACK]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		0.625	acres/hour	USDA 1989a,b,c
Lower estimate		0.25		
Upper estimate		1		
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	N/A[1]
Lower estimate	ACREL	1.5		
Upper estimate	ACREU	8		
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.0003		
Upper estimate	RATEU	0.01		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A03b: Hydraulic/Broadcast Ground Sprays - General Assumptions Used in Worker Exposure Assessments [HYDSPRAY]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		16	acres/hour	USDA 1989a,b,c
Lower estimate		11		
Upper estimate		21		
Acres treated per day				
Central estimate	ACREC	112	acres/day	N/A[1]
Lower estimate	ACREL	66		
Upper estimate	ACREU	168		
Absorbed dose rate				
Central estimate	RATEC	0.0002	(mg agent/kg bw) ÷ (lbs agent handled per day) [2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.00001		
Upper estimate	RATEU	0.0009		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of values are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Body Weights				
Male, Adult	BWM	70	kg	ICRP (1975), p. 13.
Female, Adult	BWF	64	kg	Burnmaster 1998; U.S. EPA 1985[1]
Child, 2-3 years old	BWC	13.3	kg	U.S. EPA, 1996, page 7-1, Table 7-2
Body Surface Areas				
Female, feet and lower legs	SAF1	2915	cm^2	U.S. EPA, 1992, p. 8-11, Table 8-3, total for feet and lower legs
Female, exposed skin when wearing shorts and a T-shirt	SAF2	5300	cm^2	U.S. EPA, 1992, p. 8-11, Table 8-3, total for arms, hands, lower legs, and feet
Child, male, 2-3 years old, total body surface area	SAC	6030	cm^2	U.S. EPA, 1996, p. 6-15, Table 6-6, 50th percentile
Water Intake				
Adult				
typical	WCAT	2	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (1.4 L/day) and 90th percentile (2.4 L/day) rounded to one significant place.
lower range for exposure assessment	WCAL	1.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCAH	2.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile
Child, <3 years old				
typical	WCT	1	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (0.61 L/day) and 90th percentile (1.5 L/day) rounded to one significant place
lower range for exposure assessment	WCL	0.61	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCH	1.50	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of values are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Fish Consumption				
Freshwater anglers, typical intake per day over a prolonged period	FAT	0.010	kg/day	U.S. EPA, 1996, p. 10-51, average of means from four studies
Freshwater anglers, maximum consumption for a single day	FAU	0.158	kg/day	Ruffle et al. 1994
Native American subsistence populations, typical intake per day	FNT	0.081	kg/day	U.S. EPA, 1996, p. 10-51, median value of 94 individuals
Native American subsistence populations, maximum for a single day	FNU	0.770	kg/day	U.S. EPA, 1996, p. 10-51, highest value of 94 individuals
Consumption of Fruits or Vegetables				
Amount of food consumed per kg bw per day for longer term exposures scenarios.				
Typical	VT	0.0043	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, mean intake of vegetables
Upper	VU	0.01	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, 95th percentile for intake of vegetables
Worst-case scenario for consumption in a single day, acute exposure scenario only.	VAcute	0.454	kg food	1 lb. The approximate mid-range of the above typical and upper limits based on the 64 kg body weight.
Miscellaneous				
Estimate of dislodgeable residue as a proportion of application rate shortly after application.	DisL	0.1	none	Harris and Solomon 1992, data on 2,4-D

[1]This is the average value (63.79 kg), rounded to the nearest kg for 3 different groups of women between 15-49 years old: control (62.07 kg), pregnant (65.90 kg), and lactating (63.48 kg). See Burnmaster 1998, p.218, Table III., Risk Analysis. 18(2): 215-219. This is identical to the body weight for females, 45-55 years old, 50th percentile from U.S. EPA, 1985, page 5, Table 2-2, rounded to nearest kilogram.

Worksheet A05a: Estimated concentrations of pesticides on or in various types of vegetation shortly after application at 1 lb a.i./acre [from Hoerger and Kenaga (1972), Table 9, p. 22]. [HK]

Type of Vegetation	Concentration (mg chemical/kg vegetation)			
	Typical		Upper Limit	
	ID	Value	ID	Value
Range grass	RGT	125	RGU	240
Grass	GST	92	GSU	110
Leaves and leafy crops	LVT	35	LVU	125
Forage crops	FCT	33	FCU	58
Pods containing seeds	PDT	3	PDU	12
Grain	GNT	3	GNU	10
Fruit	FRT	1.5	FRU	7

Worksheet A05b: Concentrations of chemical on spheres (berries) at the specified application rate. [FRUIT]

Diameter (cm)	Planar Surface Area (cm^2)[a]	Amount deposited (mg)[b]	Weight of sphere (kg)[c]	Concentration (mg/kg)[d]
1	0.7853981634	0.008796459	0.0005236	16.8
5	19.6349540849	0.21991148575	0.065449847	3.36
10	78.5398163397	0.87964594301	0.5235987756	1.68
	Application rate	1 lb/acre =	0.0112	mg/cm^2

a Planar surface area of a sphere = πr^2 where r is the radius in cm.

b Amount deposited is calculated as the application rate in mg/cm^2 multiplied by the planar surface area.

c Assumes a density of 1 g/cm^3 for the fruit. The volume of a sphere is$(1\div6)\times \pi \times d^3$ where d is the diameter in cm. Assuming a density of 1 g/cm^3, the weight of the sphere in kg is equal to:

$$kg= (1\div6)\times \pi \times d^3 \div 1000$$

d Amount of chemical in mg divided by the weight of the sphere in kg.

Worksheet A06: Central estimates of off-site drift associated with aerial application of pesticides (from Bird 1995, p. 205) [OFFSITE]

Distance Down Wind (meters)	ID	Drift as a proportion of application rate
100	DRFT100	0.05
200	DRFT200	0.02
300	DRFT300	0.01
400	DRFT400	0.008

Worksheet A07a: Estimate of first-order absorption rate (k_a in hours^{-1}) and 95% confidence intervals (from Durkin et al. 1998). [KAMODEL]

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.233255	
Coefficient for MW	C_MW	0.005657	
Model Constant	C	1.49615	
Number of data points	DP	29	
Degrees of Freedom (d.f.)	DF	26	
Critical value of $t_{0.025}$ with 26 d.f.[1]	CRIT	2.056	
Standard error of the estimate	SEE	16.1125	
Mean square error or model variance	MDLV	0.619712	
Standard deviation of model (s)	MSD	0.787218	$MDLV^{0.5}$
X′X, cross products matrix	0.307537	-0.00103089	0.00822769
	-0.00103089	0.000004377	-0.0000944359
	0.0082	-0.0000944359	0.0085286

[1] Mendenhall and Scheaffer, 1973, Appendix 3, 4, p. A31.

Central (maximum likelihood) estimate:

$$\log_{10} k_a = 0.233255 \log_{10}(\boldsymbol{k_{o/w}}) - 0.005657\ \boldsymbol{MW} - 1.49615$$

95% Confidence intervals for $\log_{10} k_a$

$$\log_{10} k_a \pm \boldsymbol{t}_{0.025} \times \boldsymbol{s} \times (\boldsymbol{a}'\boldsymbol{X}'\boldsymbol{X}\,\boldsymbol{a})^{0.5}$$

where $\boldsymbol{a}$ is a column vector of {1, MW, $\log_{10}(\boldsymbol{k_{o/w}})$}.

NB: Although the equation for the central estimate is presented with $k_{o/w}$ appearing before MW to be consistent with the way a similar equation is presented by EPA, MW must appear first in column vector $\boldsymbol{a}$ because of the way the statistical analysis was conducted to derive X′X .

See following page for details of calculating $\boldsymbol{a}'\boldsymbol{X}'\boldsymbol{X}\,\boldsymbol{a}$ without using matrix arithmetic.

Worksheet Worksheet A07a (continued)
Details of calculating a′X′X a

The term $\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a}$ requires matrix multiplication. While this is most easily accomplished using a program that does matrix arithmetic, the calculation can be done with a standard calculator.

Letting

$$\mathbf{a} = \{a\_1, a\_2, a\_3\}$$

and

$$(\mathbf{X}'\mathbf{X})^{-1} = \{ \{b\_1, b\_2, b\_3\}, \{c\_1, c\_2, c\_3\}, \{d\_1, d\_2, d\_3\} \},$$

$\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a}$ is equal to

Term 1: {a_1 ×([a_1×b_1] + [a_2×c_1] + [a_3×d_1])} +
Term 2: {a_2 ×([a_1×b_2] + [a_2×c_2] + [a_3×d_2])} +
Term 3: {a_3 ×([a_1×b_3] + [a_2×c_3] + [a_3×d_3])}.

Worksheet A07b: Estimate of dermal permeability (K_p in cm/hr) and 95% confidence intervals (data from U.S. EPA 1992). [PKMODEL]

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.706648	
Coefficient for MW	C_MW	0.006151	
Model Constant	C	2.72576	
Number of data points	DP	90	
Degrees of Freedom (d.f.)	DF	87	
Critical value of $t_{0.025}$ with 87 d.f.[1]	CRIT	1.96	
Standard error of the estimate	SEE	45.9983	
Mean square error or model variance	MDLV	0.528716	
Standard deviation of model (s)	MSD	0.727129	$MDLV^{0.5}$
X′X, cross products matrix	0.0550931	-0.0000941546	-0.0103443
	-0.0000941546	0.0000005978	-0.0000222508
	-0.0103443	-0.0000222508	0.00740677

[1] Mendenhall and Scheaffer, 1973, Appendix 3, Table 4, p. A31.

NOTE: The data for this analysis are taken from U.S. EPA (1992), Dermal Exposure Assessment: Principles and Applications, EPA/600/8-91/011B, Table 5-4, pp. 5-15 through 5-19. The EPA report, however, does not provide sufficient information for the calculation of confidence intervals. The synopsis of the above analysis was conducted in STATGRAPHICS Plus for Windows, Version 3.1 (Manugistics, 1995) as well as Mathematica, Version 3.0.1.1 (Wolfram Research, 1997). Although not explicitly stated in the EPA report, 3 of the 93 data points are censored from the analysis because they are statistical outliers: [Hydrocortisone-21-yl]-hemipimelate, n-nonanol, and n-propanol. The model parameters reported above are consistent with those reported by U.S. EPA but are carried out to greater number of decimal places to reduce rounding errors when calculating the confidence intervals. See notes to Worksheet A07a for details of calculating maximum likelihood estimates and confidence intervals.

CHEMICAL SPECIFIC VALUES

Worksheet B01: Anticipated Application and Dilution Rates for clopyralid [WSB01]				
Item	Code	Value	Units	Reference/Source
Typical application rate	Typ	0.1	lb a.e./acre	Section 2.4
Lowest application rate	Low	0.01	lb a.e./acre	Section 2.4
Highest application rate	Hi	1.0	lb a.e./acre	Section 2.4
Lowest dilution	LDil	20	gal./acre	C&P Press 1998*
Highest dilution	Hdil	40	gal./acre	judgmental
*Product label for Transline				

Typical concentration in applied solution:

Typical application rate divided by the average of the lowest and highest dilutions, converted to mg/mL, and rounded to two significant places after the decimal.

0.1 lb/acre ÷ [(20 gal/acre + 40 gal/acre)/2] × 119.8 (mg/mL)/(lb/gal) = **0.4 mg/mL** [TypDr]

Lowest estimated concentration in applied solution:

Lowest application rate divided by the highest dilution, converted to mg/mL, and rounded to two significant places after the decimal.

0.01 lb/acre ÷ 40 gal/acre × 119.8 (mg/mL)/(lb/gal) = **0.03 mg/mL** [LowDr]

Highest estimated concentration in applied solution:

Highest application rate divided by the lowest dilution, converted to mg/mL, and rounded to two significant decimal places after the decimal.

1 lb/acre ÷ 20 gal/acre × 119.8 (mg/mL)/(lb/gal) = **6.0 mg/mL** [HI_Dr]

Worksheet B02: Summary of central estimate and range of concentrations of clopyralid in field solutions.				
Parameter	ID	Value	Units	Reference/Source
Typical	TypDR	0.4	mg/mL	See calculations above
Low	LowDR	0.03	mg/mL	
High	Hi_DR	6	mg/mL	

Worksheet B03: Summary of chemical specific values used for clopyralid in exposure assessment worksheets. [WSB03]

Parameter	ID	Value	Units	Source/Reference
Molecular weight	MW	192	grams/mole	Budavari 1989
Water Solubility, pH 7	WS	1000	mg/L	Budavari 1989
$K_{o/w}$ (pH 7)	Kow	0.0023	unitless	Lade 1998
Foliar half-time ($t_{½}$)	FT12	2	days	[c] Knisel et al. 1992
Half-time on fruit, central	FrT12C	28.3	days	See details below
strawberries lower	FrT12L	21.2	days	
upper	FrT12U	42.8	days	
Measured Bioconcentration factor ($\boldsymbol{BCF}_{(kg\ fish/L)}$)	BCFT	1	kg fish/L	[a] Bidlack 1982
EPA RfD[b]	RfDP	0.5	mg/kg bw/day	Section 3.3.3

[a] No bioconcentration noted. This is equivalent to a BCF of 1 or unity.
[b] No RfD for clopyralid is listed on IRIS. This RfD is that derived by EPA/OPP.
[c] Much longer halftimes may be apparent on fruit. See section 3.2.3.

Details of Calculation of confidence limits for halftimes on fruit.

Data from Table 5 of McMurray et al. 1996, 8 observations, fit the exponential model:

ln(residue(mg/kg) = -0.024474 days + 4.91472 lb a.e./acre - 7.0336

with an r^2 of 0.9152.

Note that at t_0 the estimated residue for 1 lb a.e./acre is $e^{4.91-7.03} = e^{-2.12} \approx 0.12$ mg/kg fruit.

There are 5 degrees of freedom [8 observations - 3 parameters] and the associated critical value for the t-distribution at 0.025 is 2.571 (Mendenhall and Scheaffer, 1973, Appendix III, Table 4, p. A31).

The standard error for the time parameter (k_e) is 0.003226.

Central Estimate of Halftime: $\log_e(2) \div 0.024474 = 28.3$

Lower Limit of Halftime: $\log_e(2) \div (0.024474 + (2.571 \times 0.003226)) = 21.2$

Upper Limit of Halftime: $\log_e(2) \div (0.024474 - (2.571 \times 0.003226)) = 42.8$

Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for clopyralid.							
Parameters	Value	Units			Reference		
Molecular weight	192	g/mole					
$K_{o/w}$ at pH 7	0.0023	unitless					
$\log_{10} K_{o/w}$	-2.64						
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)							
a_1	1						
a_2	192						
a_3	-2.64						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet Worksheet A07a for details of calculation.							
Term 1	0.08795812						
Term 2	0.011290517						
Term 3	0.085587498						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.1848	calculation verified in Mathematica 3.0.1.1					
$\log_{10} k_a = 0.233255 \log_{10}(k_{o/w}) - 0.005657\ MW - 1.49615$					WSA07a		
$\log_{10}$ of first-order absorption rate (k_a)							
Central estimate	-3.19768417361	±	$t_{0.025}$	×	s	×	$(\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a})^{0.5}$
Lower limit	-3.89345963757	-	2.0560	×	0.787218	×	0.4298837052
Upper limit	-2.50190870965	+	2.0560	×	0.787218	×	0.4298837052
First order absorption rates (i.e., antilog or 10^x of above values).							
Central estimate	0.00063433	hours^{-1}					
Lower limit	0.0001278	hours^{-1}					
Upper limit	0.00314841	hours^{-1}					

Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for clopyralid.								
Parameters	Value	Units					Reference	
Molecular weight	192	g/mole						
$K_{o/w}$ at pH 7	0.0023	unitless						
$\log_{10} K_{o/w}$	-2.63827216398							
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)								
a_1	1							
a_2	192							
a_3	-2.63827216398							
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07b for details of calculation.								
Term 1	0.0643064955							
Term 2	0.0152307199							
Term 3	0.0901168572							
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.1697	calculation verified in Mathematica 3.0.1.1						
$\log_{10} k_p = 0.706648 \log_{10}(k_{o/w}) - 0.006151\ MW - 2.72576$							Worksheet A07b	
$\log_{10}$ of dermal permeability								
Central estimate	-5.77108174813	±	$t_{0.025}$	×	s	×	$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}^{0.5}$	
Lower limit	-6.35817685182	-	1.9600	×	0.727129	×	0.41194659848	
Upper limit	-5.18398664445	+	1.9600	×	0.727129	×	0.41194659848	
Dermal permeability								
Central estimate	0.0000017	cm/hour						
Lower limit	0.00000044	cm/hour						
Upper limit	0.0000065	cm/hour						

Worksheet B06: Summary of chemical specific dermal absorption values used for clopyralid dermal absorption. [WSB06]

Description	Code	Value	Units	Reference/Source
Zero-order absorption (K_p)				
Central estimate	KpC	0.00000170	cm/hour	Worksheet B05, values rounded to two significant figures
Lower limit	KpL	0.00000044	cm/hour	
Upper limit	KpU	0.00000650	cm/hour	
First-order absorption rates (k_a)				
Central estimate	AbsC	0.00063	$hour^{-1}$	Worksheet B04, values rounded to two significant figures
Lower limit	AbsL	0.00013	$hour^{-1}$	
Upper limit	AbsU	0.0031	$hour^{-1}$	

Worksheet B07: Estimates of the concentration of clopyralid in ambient water per lb a.i. applied per acre. [Used in chronic contaminated water exposure assessment.]

Scenario	Ambient Conc. mg/L	Appl. Rate (lb a.e./acre) [b]	ID	WCR[a] (mg/L) ÷ (lb a.e./acre)	Reference
Typical	0.004	1.9	AWT	0.0021	Leitch and Gagg 1985. Monitoring over a 19 day period after spray. See section 3.2.3.
Low	0.001	1.9	AWL	0.00053	
High	0.017	1.9	AWU	0.0089	

[a] Expected water contamination rate - mg/L in water after the application of clopyralid at a given rate in lb a.i./acre.

[b] Application rate report as 2.5 lb a.i./acre - i.e. monoethanolamine [MW 61] salt of clopyralid [MW 192]. This is equivalent to about 1.90 lb a.e./acre [2.5×192÷(192+61) ≈ 1.89723].

WORKER EXPOSURE ASSESSMENTS

Worksheet C01: Worker exposure estimates for directed foliar (backpack) applications of clopyralid				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	ApplC	0.1	lbs a.i./day	WSB01.TYP
Lower estimate	ApplL	0.01	lbs a.i./day	WSB01.LOW
Upper estimate	ApplU	1	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	WSA03.ACREC
Lower estimate	ACREL	1.5	acres/day	WSA03.ACREL
Upper estimate	ACREU	8	acres/day	WSA03.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	0.4375	lb/day	
Lower estimate	HANDLL	0.015	lb/day	
Upper estimate	HANDLU	8	lb/day	
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA03.RATEC
Lower estimate	RATEL	0.0003		WSA03.RATEL
Upper estimate	RATEU	0.01		WSA03.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.0013	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000005		
Upper estimate	DOSEU	0.080		

Worksheet C02: Worker exposure estimates for boom spray (broadcast ground spray) applications of clopyralid [WSC01]				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	APPLC	0.1	lbs a.i./day	WSB01.TYP
Lower estimate	APPLL	0.01	lbs a.i./day	WSB01.LOW
Upper estimate	APPLU	1	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	112	acres/day	WSA04.ACREC
Lower estimate	ACREL	66	acres/day	WSA04.ACREL
Upper estimate	ACREU	168	acres/day	WSA04.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	11.2	lb/day	
Lower estimate	HANDLL	0.66	lb/day	
Upper estimate	HANDLU	168	lb/day	
Absorbed dose rate				
Central estimate	RATEC	0.00020	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA04.RATEC
Lower estimate	RATEL	0.00001		WSA04.RATEL
Upper estimate	RATEU	0.00090		WSA04.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.00224	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000007		
Upper estimate	DOSEU	0.1512		

Worksheet C03: Workers: Accidental Dermal Exposure Assessments Using Zero-Order Absorption			
Parameter	Value	Units	Source
Body weight (*W*)	70	kg	WSA02.BW
Surface Area of hands (*S*)	840	cm^2	WSA02.Hands
Dermal permeability (K_p, cm/hour) [see Worksheet B05]			
Typical	0.0000017	cm/hour	WSB06.KpC
Lower	0.00000044	cm/hour	WSB06.KpL
Upper	0.0000065	cm/hour	WSB06.KpU
Concentration in solution (*C*) [see Worksheet B02]			
Typical	0.4	mg/mL	WSB02.TypDr
Lower	0.03	mg/mL	WSB02.LowDr
Upper	6	mg/mL	WSB02.HI_Dr

Note that 1 mL is equal to 1 cm^3 and thus mg/mL = mg/cm^3.

Details of calculations for worker zero-order dermal absorption scenarios.

Equation (U.S. EPA 1992)

$$K_p \cdot C \cdot Time(hr) \cdot S \cdot \div W = Dose(mg/kg)$$

where: C = concentration in mg/cm^3 or mg/mL, S = Surface area of skin in cm^2, W = Body weight in kg.

Immersion of Hands or Wearing Contaminated Gloves for One-Minute

Typical Value: Use typical concentration and central estimate of K_p.
0.0000017 cm/hr × 0.4 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 1.36e-07 mg/kg [WZHT1M]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.00000044 cm/hr × 0.03 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 2.64e-09 mg/kg [WZHL1M]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0000065 cm/hr × 6 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 0.000008 mg/kg [WZHU1M]

Wearing Contaminated Gloves for One-Hour

Typical Value: Use typical concentration and central estimate of K_p.
0.0000017 cm/hr × 0.4 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.000008 mg/kg [WZHT1H]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0000004 cm/hr × 0.03 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.58e-07 mg/kg [WZHL1H]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0000065 cm/hr × 6 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.00047 mg/kg [WZHU1H]

Worksheet C04: Worker Accidental Spill Based on the Assumption of First-Order Absorption			
Parameter	Value	Units	Source
Liquid adhering to skin after a spill (***L***)	0.008	mg/mL	WSA02.Liq
Body weight (***W***)	70	kg	WSA02.BW
Surface Areas (**A**)			
Hands	840	cm^2	WSA02.Hands
Lower legs	2070	cm^2	WSA02.LLegs
First-order dermal absorption rates (k_a)			
Central Estimate	0.00063	$hour^{-1}$	WSB06.ABSC
Lower limit of range	0.000130	$hour^{-1}$	WSB06.ABSL
Upper limit of range	0.00310	$hour^{-1}$	WSB06.ABSU
Concentration in solution (***C***) [see Worksheet Worksheet B01]			
Typical	0.4	mg/mL	TypDr
Lower	0.03	mg/mL	LowDr
Upper	6	mg/mL	HI_Dr

Details of calculations.

Equation (from Durkin et al. 1995)

$$Dose_{(mg/kg\ bw)} = k_{a\ (1/hours)} \times L_{(mg/cm\ sq)} \times C_{(mg/mL)} \times T_{(hours)} \times A_{(cm\ sq)} \div W_{(kg)}$$

where ***T*** is the duration of exposure in hours and other terms are defined as above.
Note that 1 mg/cm³ = 1 mg/mL.

Lower Legs: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFLT1H],
0.0006300 h^{-1} × 0.008 mL/cm × 0.4 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 6.0e-05 mg/kg
Lower range [WFLL1H],
0.0001300 h^{-1} × 0.008 mL/cm × 0.03 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 9.2e-07 mg/kg
Upper range [WFLU1H],
0.0031000 h^{-1} × 0.008 mL/cm × 6 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 4.4e-03 mg/kg

Hands: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFHT1H],
0.0006300 h^{-1} × 0.008 mL/cm × 0.4 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 2.4e-05 mg/kg
Lower range [WFHL1H],
0.0001300 h^{-1} × 0.008 mL/cm × 0.03 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 3.7e-07 mg/kg
Upper range [WFHU1H],
0.0031000 h^{-1} × 0.008 mL/cm × 6 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.8e-03 mg/kg

EXPOSURE ASSESSMENTS for the GENERAL PUBLIC

Worksheet D01: Direct spray of child.			
Verbal Description*: A naked child is accidentally sprayed over the entire body surface with a field dilution as it is being applied. The child is effectively washed - i.e., all of the compound is removed - after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	13.3	kg	WSA04.BWC
Exposed surface area (***A***)	6030	cm^2	WSA04.SAC
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	0.4	mg/mL	WSB02.TYPDR
Low	0.03	mg/mL	WSB02.LOWDR
High	6	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00063	$hour^{-1}$	WSB06.AbsC
Low	0.000130	$hour^{-1}$	WSB06.AbsL
High	0.0031	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.00091	mg/kg	SPRYC
Low	0.000014	mg/kg	SPRYL
High	0.067	mg/kg	SPRYH

Details of calculations

Equation: $L \times C \times A \times k_a \times T \div W$

Central Estimate [SPRYCC]:
0.008 mg/mL × 0.4 mg/mL × 6030 cm^2 × 0.00063 h^{-1} × 1 h ÷ 13.3 kg = 0.00091 mg/kg

Lower Range of Estimate [SPRYCL]:
0.008 mg/mL × 0.03 mg/mL × 6030 cm^2 × 0.00013 h^{-1} × 1 h ÷ 13.3 kg = 0.000014 mg/kg

Upper Range of Estimate [SPRYCH]:
0.008 mg/mL × 6 mg/mL × 6030 cm^2 × 0.0031 h^{-1} × 1 h ÷ 13.3 kg = 0.067 mg/kg

Worksheet D02: Direct spray of woman.			
Verbal Description*: A woman is accidentally sprayed over the feet and legs with a field dilution as it is being applied. The woman washes and removes all of the compound after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	2915	cm^2	WSA04.SAF1
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	0.4	mg/mL	WSB02.TYPDR
Low	0.03	mg/mL	WSB02.LOWDR
High	6	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00063	$hour^{-1}$	WSB06.AbsC
Low	0.000130	$hour^{-1}$	WSB06.AbsL
High	0.0031	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.000092	mg/kg	SPRYWC
Low	0.000001	mg/kg	SPRYWL
High	0.0068	mg/kg	SPRYWH

Details of calculations

Equation: $L \times C \times S \times k_a \times T \div W$

Central Estimate [SPRYWC]:
0.008 mg/mL × 0.4 mg/mL × 2915 cm^2 × 0.00063 h^{-1} × 1 h ÷ 64 kg = 0.000092 mg/kg

Lower Range of Estimate [SPRYWL]:
0.008 mg/mL × 0.03 mg/mL × 2915 cm^2 × 0.00013 h^{-1} × 1 h ÷ 64 kg = 0.0000014 mg/kg

Upper Range of Estimate [SPRYWH]:
0.008 mg/mL × 6 mg/mL × 2915 cm^2 × 0.0031 h^{-1} × 1 h ÷ 64 kg = 0.0068 mg/kg

Worksheet D03: Dermal contact with contaminated vegetation.			
Verbal Description*: A woman wearing shorts and a short sleeved shirt is in contact with contaminated vegetation for 1 hour shortly after application of the compound - i.e. no dissipation or degradation is considered. The chemical is effectively removed from the surface of the skin - i.e., washing - after 24 hours.*			
Parameter/Assumption	Value	Units	Source/Reference
Contact time (***Tc***)	1	hour	N/A
Exposure time (***Te***)	24	hours	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	5300	cm^2	WSA04.SAF2
Dislodgeable residue (***Dr***) as a proportion of application rate	0.1	none	WSA04.DisL
Application Rates(***R***)			
Typical/Central	0.1	lb a.i/acre	WSB01.TYP
Low	0.01	lb a.i/acre	WSB01.LOW
High	1	lb a.i/acre	WSB01.HI
First-order dermal absorption rate (k_a)			
Central	0.00063	$hour^{-1}$	WSB06.AbsC
Low	0.000130	$hour^{-1}$	WSB06.AbsL
High	0.00310	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations on next page.***			
Central	0.001590	mg/kg	VEGDWC
Low	0.000027	mg/kg	VEGDWL
High	0.0963	mg/kg	VEGDWH

Description of Calculations:

Step 1:

Use method of Durkin et al. (1995, p. 68, equation 4) to calculate dislodgeable residue (Dr) in units of µg/(cm^2·hr)) after converting application rate in lb a.i./acre to units of µg/cm^2:

$x = \log(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(\boldsymbol{R} \times \text{WSA01.lbac\_ugcm})) + 0.05$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^x$

Step 2:

Convert Dr from units of µg/(cm^2·hr)) to units of mg/(cm^2·hr)) by dividing by 1000:

$\boldsymbol{Dr}(mg/(cm^2 \cdot hr)) = \boldsymbol{Dr}(\mu g/(cm^2 \cdot hr))/1000$

Step 3:

Estimate amount (*Amnt*) transferred to skin in mg during the exposure period:

$\boldsymbol{Amnt}(mg) = \boldsymbol{Dr}(mg/(cm^2 \cdot hr)) \times \boldsymbol{Tc}\ (hours) \times \boldsymbol{A}\ (cm^2)$

Step 4:

Estimate the absorbed dose ($\boldsymbol{D_{Abs}}$) in mg/kg bw as the product of the amount on the skin, the first-order absorption rate, and the duration of exposure divided by the body weight:

$\boldsymbol{D_{Abs}} = \boldsymbol{Amnt}(mg) \times \mathbf{k_a}\ (hours^{-1}) \times \boldsymbol{Te}\ (hours) \div \boldsymbol{W}\ (kg)$

See next page for details of calculations.

Worksheet D03 Details of calculations: *Dermal Exposure to Contaminated Vegetation*

Central Estimate:

Step 1:

$\log_{10}$(***Dr*** (µg/(cm^2·hr)))0.104 = (1.09 × $\log_{10}$(0.1 ×11.21)) + 0.05 = 0.104 µg/(cm^2·hr)

Dr (µg/(cm^2·hr)) = $10^{0.104}$ = 1.27 µg/(cm^2·hr)

Step 2:

Dr (mg/(cm^2·hr)) = 1.27 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.00127 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.00127 mg/(cm^2·hr) × 1 hr × 5300 cm^2 = 6.731 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 6.731 mg × 0.00063 hr^{-1} × 24 hours ÷ 64 kg = 0.00159 [VEGDWC]

Lower Range of Estimate:

Step 1:

$\log_{10}$(***Dr*** (µg/(cm^2·hr))) = (1.09 × $\log_{10}$(0.01 ×11.21)) + 0.05 = -0.986µg/(cm^2·hr)

Dr (µg/(cm^2·hr)) = $10^{-0.986}$ = 0.103 µg/(cm^2·hr)

Step 2:

Dr (mg/(cm^2·hr)) = 0.103 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.000103 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.000103 mg/(cm^2·hr) × 1 hr × 5300 cm^2 =0.55 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 0.55 mg × 0.00013 hr^{-1} × 24 hours ÷ 64 kg = 0.0000268 [VEGDWL]

Upper Range of Estimate:

Step 1:

$\log_{10}$(***Dr*** (µg/(cm^2·hr))) = (1.09 × $\log_{10}$(1 ×11.21)) + 0.05 = 1.194 µg/(cm^2·hr)

Dr (µg/(cm^2·hr)) = $10^{1.194}$ = 15.63 µg/(cm^2·hr)

Step 2:

Dr (mg/(cm^2·hr)) = 15.63 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.01563 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.01563 mg/(cm^2·hr) × 1 hr × 5300 cm^2 = 82.8 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 82.8 mg × 0.0031 hr^{-1} × 24 hours ÷ 64 kg = 0.0963 [VEGDWH]

Worksheet D04: Consumption of contaminated fruit, acute exposure scenario.			
Verbal Description*: A woman consumes 1 lb (0.4536 kg) of contaminated fruit shortly after application of the chemical - i.e. no dissipation or degradation is considered. Residue estimates based on relationships from Hoerger and Kenaga (1972) summarized in WSA07.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	64	kg	`WSA04.BWF`
Amount of fruit consumed (***A***)	0.454	kg	`N/A`
Application rates (***R***)			
Typical	0.1	lb a.i./acre	`WSB01.Typ`
Lower	0.01	lb a.i./acre	`WSB01.Low`
Upper	1	lb a.i./acre	`WSB01.Hi`
Residue rates (***rr***)			
Typical	1.5	RUD[1]	`WSA05a.FRT`
Upper	7	RUD[1]	`WSA05a.FRU`
Dose estimates (***D***) - **see details of calculations below**			
Typical	0.0011	mg/kg bw	`VEGCWAT`
Lower	0.00011	mg/kg bw	`VEGCWAL`
Upper	0.05	mg/kg bw	`VEGCWAU`
[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on vegetation (mg chemical per kg of vegetation) for each l lb a.i./acre applied.			

Equation (terms defined in above table):

D (mg/kg bw) = ***A***(kg) × ***R***(lb a.i./acre) × ***rr***(mg/kg÷lb a.i./acre) ÷***W***(kg bw)

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.454 kg × 0.1 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.0011 mg/kg bw

Lower: Use lowest estimated application rate. Use typical RUD because no lower estimate of the RUD is available.

D = 0.454 kg × 0.01 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.00011 mg/kg bw

Upper: Use highest estimated application rate and highest RUD.

D = 0.454 kg × 1 lb a.i./acre × 7 mg/kg÷lb a.i./acre ÷ 64 kg = 0.05 mg/kg bw

Worksheet D05: Consumption of contaminated fruit, 90-day exposure scenario.

***Verbal Description**: A woman consumes contaminated fruit for a 90 day period starting shortly after application of the chemical. Initial residue estimates are based on relationships from Hoerger and Kenaga (1972) summarized in Worksheet A05a. The foliar half-time is used to estimate the concentration on vegetation after 90 days. The geometric mean of the initial and 90 day concentrations is used as a central/typical dose.*

Parameters/Assumptions		Value	Units	Source/Reference
Halftime on fruit ($t_{½}$)	central	28.3	days	WSB03.FrT12C
	lower	21.2	days	WSB03.FrT12L
	upper	42.8	days	WSB03.FrT12U
Duration of exposure (***t***)		90	days	N/A
Body weight (***W***)		64	kg	WSA04.BWF
Amount of vegetation consumed per unit body weight(***A***)				
	Typical	0.0043	kg veg./kg bw	WSA04.VT
	Upper	0.01	kg veg./kg bw	WSA04.VU
Application rates (***R***)				
	Typical	0.1	lb a.i./acre	WSB01.Typ
	Lower	0.01	lb a.i./acre	WSB01.Low
	Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)				
	Typical	1.5	RUD[1]	WSA05a.FRT
	Upper	7	RUD[1]	WSA05aFRU
Dose estimates (***D***) - **see details of calculations on next page**				
	Typical	0.00050	mg/kg bw/day	VEGCWCT
	Lower	0.000044	mg/kg bw/day	VEGCWCL
	Upper	0.059	mg/kg bw/day	VEGCWCU

[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on fruit (mg chemical per kg of vegetation) for each l lb a.i./acre applied.

Details of calculations on next page

Subchronic consumption of vegetation: Details of calculations

Equations (terms defined below or in table on previous page):

Step 1: Calculate $C_{0,}$ concentration in vegetation on Day 0 - i.e., day of application- as the product of the application rate (***R***) and the residue rate (***rr***):

C_0 (mg/kg) = ***R***(lb a.i./acre) × ***rr***(mg/kg÷lb a.i./acre)

Step 2: Calculate $C_{90,}$ concentration in vegetation on Day 90 (t=90 days) based on dissipation coefficient (k) derived from foliar half-life ($t_{½}$).

k ($days^{-1}$) = ln(2) ÷ $t_{½}$ (days)

C_{90} (mg/kg) = C_0 (mg/kg) × e^{-tk}

Step 3: Use the geometric mean of C_0 and C_{90} to get a central estimate of concentration in vegetation (mg/kg veg.) and multiply this value by the vegetation consumption (kg veg/kg bw) to calculate the daily dose (mg/kg bw) over the exposure period.

D (mg/kg bw) = $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw × ***W*** kg bw ÷ ***B***(kg bw)

= $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw

Central Estimate:

Use the typical application rate, the typical vegetation consumption rate, and the typical residue rate along with the central estimate of half-time on fruit.

Step 1:

C_0 = 0.1 lb a.i./acre × 1.5 mg/kg veg. = 0.15 mg/kg veg.

Step 2:

k = ln(2) ÷28.3 $days^{-1}$ = 0.024

C_{90} = 0.15 mg/kg × $e^{-0.024 \times 90}$ = 0.09 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(0.15 \times 0.09)^{0.5}$ (mg/kg veg.) × 0.0043 kg veg/kg bw = 0.0005 mg/kg bw

Lower Estimate:

Use the lowest anticipated application rate along with the lower limit of the half-time of fruit. Also the typical vegetation consumption rate and the typical residue rate because lower limits on these estimates are not available.

Step 1:

C_0 = 0.01 lb a.i./acre × 1.5 mg/kg veg. = 0.015 mg/kg veg.

Step 2:

k = ln(2) ÷21.2 $days^{-1}$ = 0.033

C_{90} = 0.015 mg/kg × $e^{-0.033 \times 90}$ = 0.007 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (0.015 \times 0.007)^{0.5}{}_{(mg/kg\ veg.)} \times 0.0043_{(kg\ veg/kg\ bw)} = 0.000044_{(mg/kg\ bw)}$

Upper Estimate:

Use the highest anticipated application rate, the upper range of the vegetation consumption rate and the upper range of the residue rate along with the upper limit of the half-time on fruit.

Step 1:

C_0 = 1 lb a.i./acre × 7 mg/kg veg. = 7 mg/kg veg.

Step 2:

k = ln(2) ÷42.8 $days^{-1}$ = 0.016

C_{90} = 7 mg/kg × $e^{-0.016 \times 90}$ = 5.0 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (7 \times 5)^{0.5}{}_{(mg/kg\ veg.)} \times 0.01_{(kg\ veg/kg\ bw)} = 0.059_{(mg/kg\ bw)}$

Worksheet D06: Consumption of contaminated water, acute exposure scenario.			
***Verbal Description**: A young child (2-3 years old) consumes 1 liter of contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. No dissipation or degradation is considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Field concentrations in solution ($C_{(mg/L)}$)			
Central	400	mg/L	WSB02.TypDR
Low	30	mg/L	WSB02.LowDR
High	6000	mg/L	WSB02.Hi_DR
Body weight (***W***)	13.3	kg	WSA04.BWC
Concentration in water			
Typical	0.3	mg/L	see next page for calculations.
Lower	0.023	mg/L	
Upper	4.54	mg/L	
Amount of water consumed (***A***)			
Typical	1	L/day	WSA04.WCT
Lower	0.61	L/day	WSA04.WCL
Upper	1.5	L/day	WSA04.WCH
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	0.023	mg/kg bw	WATCCAT
Lower	0.0011	mg/kg bw	WATCCAL
Upper	0.51	mg/kg bw	WATCCAU

Details of calculations on next page

Acute Consumption of Contaminated Water from an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: Calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$Conc._{(mg/L)} = VS_{(gal.)} \times 3.785_{L/gal} \times C_{(mg/L)} \div VL_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the amount of water consumed, and the body weight.

$$D_{(mg/kg\ bw)} = Conc._{(mg/L)} \times A_{(L)} \div W_{(kg)}$$

Calculations

Central Estimate:

Use the typical field dilution, and the typical water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 400_{(mg/L)} \div 1000000_{(liters)} = 0.3_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.3_{(mg/L)} \times 1_{(L)} \div 13.3_{(kg)} = 0.023_{(mg/kg\ bw)}$$ [WATCCAT]

Lower Estimate:

Use the lowest estimated field dilution and the lower range of water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 30_{(mg/L)} \div 1000000_{(liters)} = 0.023_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.023_{(mg/L)} \times 0.61_{(L)} \div 13.3_{(kg)} = 0.0011_{(mg/kg\ bw)}$$ [WATCCAL]

Upper Estimate:

Use the highest estimated field concentration and the upper range of water consumption.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 6000_{(mg/L)} \div 1000000_{(liters)} = 4.54_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 4.54_{(mg/L)} \times 1.5_{(L)} \div 13.3_{(kg)} = 0.51_{(mg/kg\ bw)}$$ [WATCCAU]

Worksheet D07: Consumption of contaminated water, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates (***R*** $_{(lb/acre)}$)			
Central	0.1	lb a.e./acre	WSB01.Typ
Low	0.01		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(mg/L)}$÷***R*** $_{(lb/./acre}$)			
Central	0.0021	mg/L/lb a.e./acre	WSB07.AWT
Low	0.00053		WSB07.AWL
High	0.0089		WSB07.AWU
Concentration in Water***(R×WCR, as specified above)***			
Central	0.00021	mg/L	
Low	5.30e-06		
High	0.0089		
Body weight (***W***)	70	kg	WSA046.BWM
Amount of water consumed (***A*** $_{(L/day)}$)			
Typical	2	L/day	WSA04.WCAT
Lower	1.4	L/day	WSA04.WCAL
Upper	2.4	L/day	WSA04.WCAH
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	0.00001	mg/kg bw/day	WATCMCT
Lower	0.0000001	mg/kg bw/day	WATCMCL
Upper	0.0003	mg/kg bw/day	WATCMCU

Details of calculations on next page

Chronic Consumption of Contaminated Ambient Water
Details of calculations

Equations (terms defined in table on previous page)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{\text{(lb a.i./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}}$) to get the concentration in ambient water. This product is in turn multiplied by the amount of water consumed per day ($\boldsymbol{A}_{\text{(L/day)}}$) and then divided by the body weight ($\boldsymbol{W}_{\text{(kg)}}$) to get the estimate of the absorbed dose ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.i./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}} \times \boldsymbol{A}_{\text{(L/day)}} \div \boldsymbol{W}_{\text{(kg)}}$$

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), and the typical water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.1_{\text{(lb a.i./acre)}} \times 0.0021_{\text{((mg/L)×(lb a.i./gal))}} \times 2_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.00001_{\text{(mg/kg bw)}}$$ [WATCMCT]

Lower Range of Estimate:

Use the lowest anticipated application rate, the low end of the range of the water contamination rate (WCR), and the low end of the range for water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.01_{\text{(lb a.i./acre)}} \times 0.00053_{\text{((mg/L)×(lb a.i./gal))}} \times 1.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0000001_{\text{(mg/kg bw)}}$$ [WATCMCL]

Upper range of Estimate:

Use the lowest anticipated application rate, the low end of the range of the water contamination rate (WCR), and the low end of the range for water consumption.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 1_{\text{(lb a.i./acre)}} \times 0.0089_{\text{((mg/L)×(lb a.i./gal))}} \times 2.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0003_{\text{(mg/kg bw)}}$$ [WATCMCU]

Worksheet D08: Consumption of contaminated fish, acute exposure scenario.

Verbal Description*: An adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre. No dissipation or degradation is considered. Because of the available and well documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations, separate exposure estimates are made for these two groups.*

Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in spilled solution (***C*** $_{(mg/L)}$)			
Central	400	mg/L	WSB02.TYPDR×1000
Low	30	mg/L	WSB02.LOWDR×1000
High	6000	mg/L	WSB02.HI_DR×1000
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population	0.158	kg/day	WSA04.FAU
Native American subsistence populations	0.77	kg/day	WSA04.FNU
Bioconcentration factor (***BCF*** $_{(kg\ fish/L)}$)	1	kg fish/L	WSB03.BCFT
Dose estimates (***D***) - **see details of calculations on next page.**			
General Population			
Typical	0.0007	mg/kg bw	FISHAMGPT
Lower	0.00005	mg/kg bw	FISHAMGPL
Upper	0.0102	mg/kg bw	FISHAMGPU
Native American subsistence populations			
Typical	0.0033	mg/kg bw	FISHAMNAT
Lower	0.00022	mg/kg bw	FISHAMNAL
Upper	0.05	mg/kg bw	FISHAMNAU

Details of calculations on next page

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: As in the acute drinking water scenario, calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$\textit{Conc.}_{(mg/L)} = \textit{VS}_{(gal.)} \times 3.785_{L/gal} \times \textit{C}_{(mg/L)} \div \textit{VL}_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the bioconcentration factor, the amount of fish consumed, and the body weight.

$$\textit{D}_{(mg/kg\ bw)} = \textit{Conc.}_{(mg/L)} \times \textit{BCF}_{(kg\ fish/L)} \times \textit{A}_{(kg\ fish)} \div \textit{W}_{(kg\ bw)}$$

General Public

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 400_{(mg/L)} \div 1000000_{(liters)} = 0.3_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 0.3_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.00070_{(mg/kg\ bw)}$$ `[FISHAMGPT]`

Lower End of Range for the Estimate:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 30_{(mg/L)} \div 1000000_{(liters)} = 0.023_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 0.023_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.00005_{(mg/kg\ bw)}$$ `[FISHAMGPL]`

Upper End of Range for the Estimate:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 6000_{(mg/L)} \div 1000000_{(liters)} = 4.54_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 4.54_{(mg/L)} \times 1_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 0.0102_{(mg/kg\ bw)}$$ `[FISHAMGPU]`

(continued on next page)

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations (continued)

Native American Subsistence Populations

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 400 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 0.3 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 0.3 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.0033 $_{(mg/kg\ bw)}$ [FISHAMNAT]

Estimate of Lower End of Range:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 30 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 0.020 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 0.02 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.00022 $_{(mg/kg\ bw)}$ [FISHAMNAL]

Estimate of Upper End of Range:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 6000 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 4.540 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 4.54 $_{(mg/L)}$ × 1 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 0.05 $_{(mg/kg\ bw)}$ [FISHAMNAU]

Worksheet D09: Consumption of contaminated fish, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes fish taken from contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates (***R*** $_{(lb\ a.i./acre)}$)			
Central	0.1	lb a.i./gal	WSB01.Typ
Low	0.01		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{(mg/L)}$÷***R*** $_{(lb\ a.i./gal)}$)			
Central	0.0021	mg/L/lb a.i./acre	WSB07.AWT
Low	0.00053		WSB07.AWL
High	0.0089		WSB07.AWU
Bioconcentration factor (***BCF*** $_{(kg\ fish/L)}$)	1	kg fish/L	WSB03.BCFT
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population typical	0.01	kg/day	WSA04.FAT
upper limit	0.158	kg/day	WSA04.FAU
Native American subsistence populations typical	0.081	kg/day	WSA04.FNT
upper limit	0.77	kg/day	WSA04.FNU
Dose estimates (***D***) - **see details of calculations on next page.**			
General Public			
Typical	0.00000003	mg/kg bw/day	FISHMCT
Lower	0.000000001	mg/kg bw/day	FISHMCL
Upper	0.00002	mg/kg bw/day	FISHMCU
Native American Subsistence Population			
Typical	0.0000002	mg/kg bw/day	FISHNMCT
Lower	0.00000001	mg/kg bw/day	FISHNMCL
Upper	0.00010	mg/kg bw/day	FISHNMCU

Details of calculations on next page

Chronic Consumption of Contaminated Fish, Details of calculations

Equations (terms defined below or in table on previous page)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{\text{(lb a.i./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}}$) to get the concentration in ambient water. This product is in turn multiplied by the bioconcentration factor ($\boldsymbol{BCF}_{\text{(kg fish/L)}}$) and the amount of fish consumed per day ($\boldsymbol{A}_{\text{(kg fish/day)}}$) and then divided by the body weight ($\boldsymbol{W}_{\text{(kg bw)}}$) to get the estimate of the absorbed dose ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.i./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}} \times \boldsymbol{A}_{\text{(kg/day)}} \times \boldsymbol{BCF}_{\text{(kg fish/L)}} \div \boldsymbol{W}_{\text{(kg)}}$$

General Public

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), the typical fish consumption, the measured bioconcentration factor, and standard body weight.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.1_{\text{(lb a.i./acre)}} \times 0.0021_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.00000003_{\text{(mg/kg bw)}}$ `[FISHMCT]`

Lower Range of Estimate:

Use the lowest anticipated application rate, lower range of contamination rate (WCR), the typical fish consumption, the measured bioconcentration factor, and standard body weight. Typical fish consumption is used because there is no published lower estimate.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.01_{\text{(lb a.i./acre)}} \times 0.00053_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.000000001_{\text{(mg/kg bw)}}$ `[FISHMCL]`

Upper Range of Estimate:

Use the highest labelled application rate, upper range of contamination rate (WCR), the maximum fish consumption, the measured bioconcentration factor, and standard body weight.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 1_{\text{(lb a.i./acre)}} \times 0.0089_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.158_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.00002_{\text{(mg/kg bw)}}$ `[FISHMCU]`

Chronic Consumption of Contaminated Fish
Details of calculations (continued)

Native American Subsistence Populations

Central Estimate:

Use the typical application rate, typical contamination rate (WCR), the typical fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.1_{\text{(lb a.i./acre)}} \times 0.0021_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.081_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.0000002_{\text{(mg/kg bw)}}$$ `[FISHNMCT]`

Lower Range of Estimate:

Use the lowest anticipated application rate, lower range of contamination rate (WCR), the typical fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight. Typical fish consumption is used because there is no published lower estimate.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 0.01_{\text{(lb a.i./acre)}} \times 0.00053_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.081_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.00000001_{\text{(mg/kg bw)}}$$ `[FISHNMCL]`

Upper Range of Estimate:

Use the highest labelled application rate, upper range of contamination rate (WCR), the maximum fish consumption for native American subsistence populations, the measured bioconcentration factor, and standard body weight.

$$\boldsymbol{D}_{(\text{mg/kg bw})} = 1_{\text{(lb a.i./acre)}} \times 0.0089_{\text{((mg/L)×(lb a.i./gal))}} \times 1_{\text{(kg fish/L)}} \times 0.77_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.00010_{\text{(mg/kg bw)}}$$ `[FISHNMCU]`

SUMMARY TABLES FOR HUMAN HEALTH RISK ASSESSMENT

Worksheet E01: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.0013	0.000005	0.08	WSC01
Broadcast ground spray (Boom spray)	0.0022	0.000007	0.15	WSC02
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	1.36e-07	2.64e-09	0.000008	WSC03
Contaminated Gloves, 1 hour	0.000008	1.58e-07	0.00047	WSC03
Spill on hands, 1 hour	0.000024	3.74e-07	0.0018	WSC04
Spill on lower legs, 1 hour	0.00006	9.23e-07	0.0044	WSC04

Worksheet E02: Summary of risk characterization for workers[1]

RfD	0.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.003	0.000009	0.2	WSC01
Broadcast ground spray (Boom spray)	0.004	0.00001	0.3	WSC02
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	3e-07	1e-08	0.00002	WSC03
Contaminated Gloves, 1 hour	0.00002	3e-07	0.0009	WSC03
Spill on hands, 1 hour	0.00005	7e-07	0.004	WSC04
Spill on lower legs, 1 hour	0.0001	0.000002	0.009	WSC04

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Worksheet E01 for summary of exposure assessment.

Worksheet E03: Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00091	0.00001	0.067	WSD01
Direct spray, lower legs	Woman	0.00009	0.0000014	0.0068	WSD02
Dermal, contaminated vegetation	Woman	0.00159	0.000027	0.0963	WSD03
Contaminated fruit, acute exposure	Woman	0.0011	0.00011	0.05	WSD04
Contaminated water, acute exposure	Child	0.023	0.0011	0.51	WSD06
Consumption of fish, general public	Man	0.0007	0.00005	0.0102	WSD08
Consumption of fish, subsistence populations	Man	0.0033	0.00022	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0005	0.00004	0.059	WSD05
Consumption of water	Man	0.00001	1.10e-07	0.0003	WSD07
Consumption of fish, general public	Man	3.00e-08	1.00e-09	0.00002	WSD09
Consumption of fish, subsistence populations	Man	2.00e-07	1.00e-08	0.0001	WSD09

Worksheet E04: Summary of risk characterization for the general public [1] .

Provisional RfD		0.5	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.002	0.00003	0.1	WSD01
Direct spray, lower legs	Woman	0.0002	3e-06	0.01	WSD02
Dermal, contaminated vegetation	Woman	0.003	0.00005	0.2	WSD03
Contaminated fruit, acute exposure	Woman	0.002	0.0002	0.1	WSD04
Contaminated water, acute exposure	Child	0.05	0.002	1	WSD06
Consumption of fish, general public	Man	0.001	0.0001	0.02	WSD08
Consumption of fish, subsistence populations	Man	0.007	0.0004	0.1	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.001	0.00009	0.1	WSD05
Consumption of water	Man	0.00002	2e-07	0.0006	WSD07
Consumption of fish, general public	Man	1e-07	2e-09	0.00004	WSD09
Consumption of fish, subsistence populations	Man	4e-07	2e-08	0.0002	WSD09

[1] Hazard quotient is the level of exposure divided by the provisional RfD then rounded to one significant decimal place or digit. See Worksheet E03 for summary of exposure assessments.

EXPOSURE ASSESSMENTS for Terrestrial Species

Worksheet F01: Direct spray of small mammal assuming first-order absorption kinetics.			
Verbal Description*: A 20 g mammal is directly sprayed over one half of the body surface as the chemical is being applied. The absorbed dose over the first day - i.e., a 24 hour period) is estimated using the assumption of first-order dermal absorption. In the absence of any data on dermal absorption in a small mammal, the estimated absorption rate for humans is used. An empirical relationship between body weight and surface area (Boxenbaum and D'Souze 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.020	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	87	cm^2	
Application rate (***R***)			
Typical/Central	0.1	lb a.e. /acre	WSB01.TYP
Low	0.01		WSB01.LOW
High	1		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
First-order dermal absorption rate (k_a)			
Central	0.00063	$hour^{-1}$	WSB06.AbsC
Low	0.000130	$hour^{-1}$	WSB06.AbsL
High	0.00310	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.037	mg/kg	SMDSDC
Low	0.00076	mg/kg	SMDSDL
High	1.75	mg/kg	SMDSDH

Details of calculations on next page.

Direct Spray of Small Mammal, first-order absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \times 1^{-ka \times T} \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Get the proportion of the amount that is absorbed using the assumption of first-order absorption kinetics. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate and dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.1 lb/acre × 87 cm^2
× 1-e$^{-0.00063/h \times 24h}$ ÷ 0.02 kg = 0.037 mg/kg [SMDSDC]

Lower Range of Estimate: Use the lowest anticipated application rate and lower 95% limit of the estimated dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.01 lb/acre × 87 cm^2
× 1-e$^{-0.00013/h \times 24 h}$ ÷ 0.02 kg = 0.00076 mg/kg [CMDSDL]

Upper Range of Estimate: Use the highest anticipated application rate and upper 95% limit of the estimated dermal absorption rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 1 lb/acre × 87 cm^2
× 0.0031/h × 24 h) ÷ 0.02 kg = 1.75 mg/kg [DMDSDH]

Worksheet F02: Direct spray of small mammal assuming 100% absorption over the first 24 hour period.			
Verbal Description*: A 20 g mammal is directly sprayed over one half of the body surface as the chemical is being applied. The deposited dose is assumed to be completely absorbed during the first day. An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.020	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	87	cm^2	
Application rate (***R***)			
Typical/Central	0.1	lb aei. /acre	WSB01.TYP
Low	0.01		WSB01.LOW
High	1		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	2.4	mg/kg	SMDS2DC
Low	0.24	mg/kg	SMDS2DL
High	24.4	mg/kg	SMDS2DH

Direct Spray of Small Mammal, Complete absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 0.1 lb/acre × 87 cm^2 ÷ 0.02 kg = 2.4 mg/kg [SMDS2DC]

Lower Range of Estimate [WSE042DL]: Use the lowest anticipated application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 0.01 lb/acre × 87 cm^2 ÷ 0.02 kg = 0.24 mg/kg [SMDS2DL]

Upper Range of Estimate [WSE042DH]: Use the highest anticipated application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 1 lb/acre × 87 cm^2 ÷ 0.02 kg = 24.4 mg/kg [SMDS2DU]

Worksheet F03: Direct spray of bee assuming 100% absorption over the first 24 hour period.			
Verbal Description*: A 0.093 g bee is directly sprayed over one half of the body surface as the chemical is being applied. The deposited dose is assumed to be completely absorbed during the first day. An empirical relationship between body weight and surface area (Boxenbaum and D'Souza 1990) is used to estimate the surface area of the animal.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	24	hour	N/A
Body weight (***W***)	0.000093	kg	Section 4.2.1.
Exposed surface area (***A***)	$cm^2=1110\times BW(kg)^{0.65}$		Boxenbaum and D'Souza 1990
	2.7	cm^2	
Application rate (***R***)			
Typical/Central	0.1	lb a.i. /acre	WSB01.TYP
Low	0.01		WSB01.LOW
High	1		WSB01.HI
Conversion Factor (***F***) for lb/acre to mg/cm^2	0.01121		WSA01.LBAC_MGCM
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	16	mg/kg	BEEDS2DC
Low	1.6	mg/kg	BEEDS2DL
High	163	mg/kg	BEEDS2DH

Direct Spray of Bee, Complete absorption, Details of calculations

Equation: $0.5 \times F \times R \times A \div W$

Verbal Description: *Multiply by 0.5 because only one half of the body surface is assumed to be sprayed. Calculate the amount deposited on the animal as the product of the application rate converted to mg/cm^2 and the surface area of the animal in cm^2. Divide by the body weight.*

Central Estimate: Use the central estimate of the application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 0.1 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 16 mg/kg [BEEDS2DC]

Lower Range of Estimate: Use the lowest anticipated application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 0.01 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 1.6 mg/kg [BEEDS2DL]

Upper Range of Estimate: Use the highest anticipated application rate,
0.5 × 0.01121 ($mg/cm^2 \div$ lb/acre) × 1 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 163 mg/kg [BEEDS2DH]

Worksheet F04: Consumption of contaminated vegetation by a small mammal, acute exposure scenario.

Verbal Description*: A 20 g mammal consumes vegetation shortly after application of the chemical - i.e. no dissipation or degradation is considered. The contaminated vegetation accounts for 100% of the diet. Residue estimates based on relationships for leaves and leafy vegetables from Hoerger and Kenaga (1972) summarized in Worksheet A05a.*

Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	0.020	kg	N/A
Food consumed per day (***A***)	0.003	kg	U.S. EPA 1989
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.1	lb a.i./acre	WSB01.Typ
Lower	0.01	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Dose estimates (***D***) - **see details of calculations below**			
Typical	0.53	mg/kg bw	VGCSMAC
Lower	0.05	mg/kg bw	VGCSMAL
Upper	18.8	mg/kg bw	VGCSMAU

[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on vegetation (mg chemical per kg of vegetation) for each l lb a.i./acre applied.

Equation (terms defined in above table):

D (mg/kg bw) = ***A***(kg) × ***R***(lb a.i./acre) × ***rr***(mg/kg veg.÷lb a.i./acre) ÷ ***W***(kg bw)

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.003 kg × 0.1 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 0.53 mg/kg bw [VGCSMAC]

Lower: Use lowest estimated application rate. Use typical RUD because no lower estimate of the RUD is available.

D = 0.003 kg × 0.01 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 0.05 mg/kg bw [VGCSMAL]

Upper: Use highest estimated application rate and highest RUD.

D = 0.003 kg × 1 lb a.i./acre × 125 mg/kg÷lb a.i./acre ÷ 0.02 kg = 18.8 mg/kg bw [VGCSMAU]

Worksheet F05: Consumption of contaminated vegetation by a small mammal, chronic exposure scenario.

Verbal Description*: A 20 g mammal consumes contaminated vegetation for a 90 day period starting shortly after application of the chemical. It is assumed that 100% of the diet is contaminated. Initial residue estimates are based on relationships for leaves and leafy vegetables from Hoerger and Kenaga (1972) summarized in Worksheet A05a. The foliar half-time is used to estimate the concentration on vegetation after 90 days. The geometric mean of the initial and 90 day concentrations is used as the estimate of the dose.*

Parameters/Assumptions	Value	Units	Source/Reference
Duration of exposure (***D***)	90	days	N/A
Body weight (***W***)	0.02	kg	
Food consumed per day (***A***)	0.003	kg	U.S. EPA 1989
kg food consumed per kg bw	0.15	Unitless	0.003/0.02
Application rates (***R***)			
Typical	0.1	lb a.i./acre	WSB01.Typ
Lower	0.01	lb a.i./acre	WSB01.Low
Upper	1	lb a.i./acre	WSB01.Hi
Residue rates (***rr***)			
Typical	35	RUD[1]	WSA05a.LVT
Upper	125	RUD[1]	WSA05a.LVU
Dose estimates (***D***) - **see details of calculations on next page**			
Typical	0.18	mg/kg bw	VGCSMCT
Lower	0.0250	mg/kg bw	VGCSMCL
Upper	4.3	mg/kg bw	VGCSMCU

[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on fruit (mg chemical per kg of vegetation) for each l lb a.i./acre applied.

Equations (terms defined below or in above table):

Step 1: Calculate $C_{0,}$ concentration in vegetation on Day 0 - i..e., day of application.

C_0 (mg/kg) = ***R***(lb a.i./acre) × ***rr***(mg/kg÷lb a.i./acre)

Step 2: Calculate $C_{90,}$ concentration in vegetation on Day 90 (t=90 days) based on dissipation coefficient (k) derived from foliar half-life ($t_{½}$).

k ($days^{-1}$) = ln(2) ÷ $t_{½}$ (days)

C_{90} (mg/kg) = C_0 (mg/kg) × e^{-tk}

Step 3: Use the geometric mean of C_0 and C_{90} to get a central estimate of concentration in vegetation (mg/kg veg.) and multiply this value by the vegetation consumption (kg veg/kg bw) to calculate the daily dose (mg/kg bw) over the exposure period.

D (mg/kg bw) = $(C_0 \times C_{90})^{0.5}$ (mg/kg veg.) × ***A*** kg veg./kg bw

Details of calculations on next page

Subchronic consumption of vegetation by a small mammal:
Details of calculations

Central Estimate:

Use the typical application rate, the typical vegetation consumption rate, and the typical residue rate along with the central estimate of half-time on fruit.

Step 1:

C_0 = 0.1 lb a.i./acre × 35 mg/kg veg. = 3.5 mg/kg veg.

Step 2:

k = ln(2) ÷ 28.3 $days^{-1}$ = 0.0245

C_{90} = 3.5 mg/kg × $e^{-0.0245 \times 90}$ = 0.39 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(3.5 \times 0.39)^{0.5}$ (mg/kg veg.) × 0.15 kg veg/kg bw = 0.18 mg/kg bw [VGCSMCT]

Lower Estimate:

Use the lowest anticipated application rate along with the upper estimate of the half-time on fruit. Also the typical vegetation consumption rate and the typical residue rate because lower limits on these estimates are not available.

Step 1:

C_0 = 0.01 lb a.i./acre × 35 mg/kg veg. = 0.35 mg/kg veg.

Step 2:

k = ln(2) ÷42.8 $days^{-1}$ = 0.0162

C_{90} = 0.35 mg/kg × $e^{-0.0162 \times 90}$ = 0.081 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (0.35 \times 0.081)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 0.025_{(mg/kg\ bw)}$ [VGCSMCL]

Upper Estimate:

Use the highest anticipated application rate, the upper range of the vegetation consumption rate and the upper range of the residue rate along with the lower range of the estimated of half-time on fruit.

Step 1:

C_0 = 1 lb a.i./acre × 125 mg/kg veg. = 125 mg/kg veg.

Step 2:

k = ln(2) ÷21.2 $days^{-1}$ = 0.0327

C_{90} = 125 mg/kg × $e^{-0.0327 \times 90}$ = 6.6 mg/kg veg.

Step 3:

$D_{(mg/kg\ bw)} = (125 \times 6.6)^{0.5}{}_{(mg/kg\ veg.)} \times 0.15_{(kg\ veg/kg\ bw)} = 4.3_{(mg/kg\ bw)}$ [VGCSMCU]

Worksheet F06: Consumption of contaminated water by a small mammal, acute exposure scenario.			
Verbal Description*: A small (20g) mammal consumes contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in solution ($C_{(mg/L)}$)			
Central	400	mg/L	WSB02.TYPDR×1000
Low	30	mg/L	WSB02.LOWDR×1000
High	6000	mg/L	WSB02.HI_DR×1000
Body weight (***W***)	0.02	kg	N/A
Amount of water consumed (***A***)	0.005	L/day	U.S. EPA 1989
Dose estimates (***D***) - **see details of calculations below.**			
Typical	0.075	mg/kg bw	WTCSMAT
Lower	0.0060	mg/kg bw	WTCSMAL
Upper	1.14	mg/kg bw	WTCSMAU

Equations (terms defined below or in table)

Step 1: Calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$\text{Conc.}_{(mg/L)} = VS_{(gal.)} \times 3.785_{L/gal} \times C_{(mg/L)} \div VL_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the amount of water consumed, and the body weight.

$$D_{(mg/kg\ bw)} = \text{Conc.}_{(mg/L)} \times A_{(L)} \div W_{(kg)}$$

Central Estimate: Use the typical field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 400_{(mg/L)} \div 1000000_{(liters)} = 0.3_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 0.3_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.075_{(mg/kg\ bw)}$ [WTCSMAT]

Lower Estimate: Use the lowest estimated field dilution,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 30_{(mg/L)} \div 1000000_{(liters)} = 0.023_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 0.023_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 0.006_{(mg/kg\ bw)}$ [WTCSMAL]

Upper Estimate: Use the highest estimated field concentration,

Step 1: $\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 6000_{(mg/L)} \div 1000000_{(liters)} = 4.54_{(mg/L)}$

Step 2: $D_{(mg/kg\ bw)} = 4.54_{(mg/L)} \times 0.005_{(L)} \div 0.02_{(kg)} = 1.14_{(mg/kg\ bw)}$ [WTCSMAU]

Worksheet F07: Consumption of contaminated water by a small mammal, chronic exposure scenario.			
Verbal Description*: A small (20 g) mammal consumes contaminated ambient water for a lifetime. The levels in water are estimated from monitoring data and thus dissipation, degradation and other environmental processes are implicitly considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates ($\boldsymbol{R}_{\text{(lb a.i./acre)}}$)			
Central	0.1	lb a.i./gal	WSB01.Typ
Low	0.01		WSB01.Low
High	1		WSB01.Hi
Water Contamination Rate (WCR)($\boldsymbol{C}_{\text{(mg/L)}} \div \boldsymbol{R}_{\text{(lb a.i./gal)}}$)			
Central	0.0021	mg/L/lb a.i./acre	WSB07.AWT
Low	0.00053		WSB07.AWL
High	0.0089		WSB07.AWU
Body weight ($\boldsymbol{W}$)	0.02	kg	U.S. EPA 1989
Amount of water consumed ($\boldsymbol{A}_{\text{(L/day)}}$)	0.005	L/day	U.S. EPA 1989
Dose estimates ($\boldsymbol{D}$) - **see details of calculations on next page.**			
Typical	0.0001	mg/kg bw	WTCSMCT
Lower	0.000001	mg/kg bw	WTCSMCL
Upper	0.002	mg/kg bw	WTCSMCU

Equations (terms defined in table)

Verbal Description: Multiply the application rate ($\boldsymbol{R}_{\text{(lb a.i./acre)}}$) by the water contamination rate ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}}$) to get the concentration in ambient water. This product is in turn multiplied by the amount of water consumed per day ($\boldsymbol{A}_{\text{(L/day)}}$) and then divided by the body weight ($\boldsymbol{W}_{\text{(kg)}}$)to get the estimate of the absorbed dose ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = \boldsymbol{R}_{\text{(lb a.i./acre)}} \times \boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./gal))}} \times \boldsymbol{A}_{\text{(L/day)}} \div \boldsymbol{W}_{\text{(kg)}}$$

Central Estimate: Use the typical application rate and typical water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.1_{\text{(lb a.i./acre)}} \times 0.0021_{\text{((mg/L)×(lb a.i./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.0001_{\text{(mg/kg bw)}}$$ [WTCSMCT]

Lower Range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.01_{\text{(lb a.i./acre)}} \times 0.00053_{\text{((mg/L)×(lb a.i./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.000001_{\text{(mg/kg bw)}}$$ [WTCSMCL]

Upper range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 1_{\text{(lb a.i./acre)}} \times 0.0089_{\text{((mg/L)×(lb a.i./gal))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.002_{\text{(mg/kg bw)}}$$ [WTCSMCU]

Worksheet G01: Summary of Exposure Scenarios for terrestrial animals

Scenario	Dose (mg/kg/day)			Worksheet
	Typical	Lower	Upper	
Acute/Accidental Exposures				
Direct spray, small mammal, first-order absorption	0.037	0.00076	1.75	WSF01
Direct spray, small animal, 100% absorption	2.4	0.24	24.4	WSF02
Direct spray, bee, 100% absorption	16	1.6	163	WSF03
Consumption of contaminated vegetation, acute exposure	0.53	0.05	18.8	WSF04
Consumption of contaminated water, acute exposure	0.075	0.006	1.14	WSF06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.18	0.025	4.3	WSF05
Consumption of contaminated water, chronic exposure	0.0001	0.000001	0.002	WSF07

Worksheet G02: Summary of quantitative risk characterization for terrestrial animals[1]

Scenario	Hazard Quotient[2]		
	Typical	Lower	Upper
Acute/Accidental Exposures			
Direct spray, small mammal, first-order absorption	0.0007	0.00002	0.04
Direct spray, small animal, 100% absorption	0.05	0.005	0.5
Direct spray, bee, 100% absorption[3]	0.02	0.002	0.2
Consumption of contaminated vegetation, acute exposure	0.01	0.001	0.4
Consumption of contaminated water, acute exposure	0.002	0.0001	0.001
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.004	0.0005	0.1
Consumption of contaminated water, chronic exposure	0.000002	2e-08	0.00004
Toxicity value for mammal [2]		50	mg/kg/day
Toxicity value for bee [3]		1000	mg/kg

[1] See Worksheet F07 for details of exposure assessment.
[2] Except for the honey bee, the hazard quotient is calculated as the estimated exposure divided by the chronic rats NOAEL of 50 mg/kg/day and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on the marginally-lethal acute dose level of 1000 mg/kg from the study by (Hinken et al. 1986) .

WORKSHEETS FOR
Hexachlorobenzene
in Clopyralid

Worksheet Table of Contents

Worksheet Table of Contents

GENERAL ASSUMPTIONS, VALUES, and MODELS

Worksheet A01: Constants and conversion factors used in calculations [CONST]		
Conversion	ID	Value
mg/lb	mg_lb	453,600
mL/gallon	ml_gal	3,785
lb/gallon to mg/mL	lbg_mgml	119.8
lb/acre to µg/cm^2	lbac_ugcm	11.21
lb/acre to mg/cm^2	lbac_mgcm	0.01121
gallons to liters	gal_lit	3.785

Worksheet A02: General Assumptions Used in Worker Exposure Assessments [STD]				
Parameter	ID	Value	Units	Reference
Body Weight (General)	BW	70	kg	ICRP (1975), p. 13
Surface area of hands	Hands	840	cm^2	U.S. EPA 1992
Surface area of lower legs	LLegs	2070	cm^2	U.S. EPA 1992
Weight of liquid adhering to surface of skin after a spill	Liq	0.008	mg/cm^2	Mason and Johnson 1987

Worksheet A03a: Directed Ground Sprays (includes backpack, cut surface, and streamline applications) - General Assumptions Used in Worker Exposure Assessments [BACKPACK]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		0.625	acres/hour	USDA 1989a,b,c
Lower estimate		0.25		
Upper estimate		1		
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	N/A[1]
Lower estimate	ACREL	1.5		
Upper estimate	ACREU	8		
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.0003		
Upper estimate	RATEU	0.01		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A03b: Hydraulic/Broadcast Ground Sprays - General Assumptions Used in Worker Exposure Assessments [HYDSPRAY]

Parameter/Assumption	ID	Value	Units	Reference
Hours of application per day				
Central estimate		7	hours	USDA 1989a,b,c
Lower estimate		6		
Upper estimate		8		
Acres treated per hour				
Central estimate		16	acres/hour	USDA 1989a,b,c
Lower estimate		11		
Upper estimate		21		
Acres treated per day				
Central estimate	ACREC	112	acres/day	N/A[1]
Lower estimate	ACREL	66		
Upper estimate	ACREU	168		
Absorbed dose rate				
Central estimate	RATEC	0.0002	(mg agent/kg bw) ÷ (lbs agent handled per day) [2]	Rubin et al. 1988, Table 5
Lower estimate	RATEL	0.00001		
Upper estimate	RATEU	0.0009		

[1] Calculated as the product of the number of hours of application and the number of acres treated per hour for each category - i.e., central estimate, lower estimate, and upper estimate.

[2] "Agent" refers to the material being handled and may be expressed in units of a.i. or a.e. Depending on the agent under consideration, additional exposure conversions may be made in the exposure assessment and dose response assessment. For the risk assessment, the only important point is that the exposure and dose/response assessments must use the same units - that is, a.i., a.e., etc. - or the units must be converted to some equivalent form in the risk characterization.

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of value are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Body Weights				
Male, Adult	BWM	70	kg	ICRP (1975), p. 13.
Female, Adult	BWF	64	kg	Burnmaster 1998; U.S. EPA 1985[1]
Child, 2-3 years old	BWC	13.3	kg	U.S. EPA, 1996, page 7-1, Table 7-2
Body Surface Areas				
Female, feet and lower legs	SAF1	2915	cm^2	U.S. EPA, 1992a, p. 8-11, Table 8-3, total for feet and lower legs
Female, exposed skin when wearing shorts and a T-shirt	SAF2	5300	cm^2	U.S. EPA, 1992a, p. 8-11, Table 8-3, total for arms, hands, lower legs, and feet.
Child, male, 2-3 years old, total body surface area	SAC	6030	cm^2	U.S. EPA, 1996, p. 6-15, Table 6-6, 50th percentile.
Water Intake				
Adult				
typical	WCAT	2	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (1.4 L/day) and 90th percentile (2.4 L/day) rounded to one significant place.
lower range for exposure assessment	WCAL	1.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCAH	2.4	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile
Child, <3 years old				
typical	WCT	1	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, midpoint of mean (0.61L/day) and 90th percentile (1.5 L/day) rounded to one significant place.
lower range for exposure assessment	WCL	0.61	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, mean
upper range	WCH	1.50	L/day	U.S. EPA, 1996, p. 3-28, Table 3-30, 90th percentile

Worksheet A04: General Assumptions Used in Exposure Assessments for the General Public [PUBL]

Narrative: This table contains various values used in the exposure assessments for the general public. Three general groups of individuals are considered: adult male, adult female, and a 2 year old child. Values are specified for body weight, surface areas for various parts of the body, water intake, fish consumption, and the consumption of fruits or vegetables. ***NOTE****: Not all types of value are specified for each group. The only values specified are those used in the risk assessment.*

Description	ID	Value	Units	Reference
Fish Consumption				
Freshwater anglers, typical intake per day over a prolonged period	FAT	0.010	kg/day	U.S. EPA, 1996, p. 10-51, average of means from four studies
Freshwater anglers, maximum consumption for a single day	FAU	0.158	kg/day	Ruffle et al. 1994
Native American subsistence populations, typical intake per day	FNT	0.081	kg/day	U.S. EPA, 1996, p. 10-51, median value of 94 individuals
Native American subsistence populations, maximum for a single day	FNU	0.770	kg/day	U.S. EPA, 1996, p. 10-51, highest value of 94 individuals
Consumption of Fruits or Vegetables				
Amount of food consumed per kg bw per day for longer term exposures scenarios.				
Typical	VT	0.0043	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, mean intake of vegetables
Upper	VU	0.01	kg food/kg bw/day	U.S. EPA, 1996, Table 9-21, p. 9-39, 95th percentile for intake of vegetables
Worst-case scenario for consumption in a single day, acute exposure scenario only.	VAcute	0.454	kg food	1 lb. The approximate mid range of the above typical and upper limits based on the 64 kg body weight.
Miscellaneous				
Estimate of dislodgeable residue as a proportion of application rate shortly after application.	DisL	0.1	none	Harris and Solomon 1992, data on 2,4-D

[1]This is the average value (63.79 kg), rounded to the nearest kg for 3 different groups of women between 15-49 years old: control (62.07 kg), pregnant (65.90 kg), and lactating (63.48 kg). See Burnmaster 1998, p.218, Table III., Risk Analysis. 18(2): 215-219. This is identical to the body weight for females, 45-55 years old, 50th percentile from U.S. EPA, 1985, page 5, Table 2-2, rounded to nearest kilogram.

Worksheet A05a: Estimated concentrations of pesticides on or in various types of vegetation shortly after application at 1 lb a.i./acre [from Hoerger and Kenaga (1972), Table 9, p. 22]. [HK]

Type of Vegetation	Concentration (mg chemical/kg vegetation)			
	Typical		Upper Limit	
	ID	Value	ID	Value
Range grass	RGT	125	RGU	240
Grass	GST	92	GSU	110
Leaves and leafy crops	LVT	35	LVU	125
Forage crops	FCT	33	FCU	58
Pods containing seeds	PDT	3	PDU	12
Grain	GNT	3	GNU	10
Fruit	FRT	1.5	FRU	7

Worksheet A05b: Concentrations of chemical on spheres (berries) at the specified application rate. [FRUIT]

Diameter (cm)	Planar Surface Area (cm^2)[a]	Amount deposited (mg)[b]	Weight of sphere (kg)[c]	Concentration (mg/kg)[d]
1	0.7853981634	0.008796459	0.0005236	16.8
5	19.6349540849	0.21991148575	0.065449847	3.36
10	78.5398163397	0.87964594301	0.5235987756	1.68
	Application rate	1 lb/acre =	0.0112	mg/cm^2

a Planar surface area of a sphere = πr^2 where r is the radius in cm.

b Amount deposited is calculated as the application rate in mg/cm^2 multiplies by the planar surface area.

c Assumes a density of 1 g/cm^3 for the fruit. The volume of a sphere is$(1\div6)\times \pi \times d^3$ where d is the diameter in cm. Assuming a density of 1 g/cm^3, the weight of the sphere in kg is equal to:

$$kg= (1\div6)\times \pi \times d^3 \div 1000$$

d Amount of chemical in mg divided by the weight of the sphere in kg.

Worksheet A06: Central estimates of off-site drift associated with aerial application of pesticides (from Bird 1995, p. 205) [OFFSITE]

Distance Down Wind (meters)	ID	Drift as a proportion of application rate
100	DRFT100	0.05
200	DRFT200	0.02
300	DRFT300	0.01
400	DRFT400	0.008

Worksheet A07a: Estimate of first-order absorption rate (k_a in hours^{-1}) and 95% confidence intervals (from Durkin et al. 1998). [KAMODEL]

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.233255	
Coefficient for MW	C_MW	0.005657	
Model Constant	C	1.49615	
Number of data points	DP	29	
Degrees of Freedom (d.f.)	DF	26	
Critical value of $t_{0.025}$ with 26 d.f.[1]	CRIT	2.056	
Standard error of the estimate	SEE	16.1125	
Mean square error or model variance	MDLV	0.619712	
Standard deviation of model (s)	MSD	0.787218	$MDLV^{0.5}$
X′X, cross products matrix	0.307537	-0.00103089	0.00822769
	-0.00103089	0.000004377	-0.0000944359
	0.0082	-0.0000944359	0.0085286

[1] Mendenhall and Scheaffer, 1973, Appendix 3, 4, p. A31.

Central (maximum likelihood) estimate:

$$\log_{10} k_a = 0.233255 \log_{10}(k_{o/w}) - 0.005657\ MW - 1.49615$$

95% Confidence intervals for $\log_{10} k_a$

$$\log_{10} k_a \pm t_{0.025} \times s \times (a'X'X\ a)^{0.5}$$

where a is a column vector of {1, MW, $\log_{10}(k_{o/w})$}.

NB: Although the equation for the central estimate is presented with $k_{o/w}$ appearing before MW to be consistent with the way a similar equation is presented by EPA, MW must appear first in column vector a because of the way the statistical analysis was conducted to derive X′X .

See following page for details of calculating $a'X'X\ a$ without using matrix arithmetic.

Worksheet Worksheet A07a (continued)
Details of calculating a′X′X a

The term $\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a}$ requires matrix multiplication. While this is most easily accomplished using a program that does matrix arithmetic, the calculation can be done with a standard calculator.

Letting

$\mathbf{a}$ = {a_1, a_2, a_3}

and

$(\mathbf{X}'\mathbf{X})^{-1}$ = {
{b_1, b_2, b_3},
{c_1, c_2, c_3},
{d_1, d_2, d_3}
},

$\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a}$ is equal to

Term 1: {a_1 ×([a_1×b_1] + [a_2×c_1] + [a_3×d_1])} +
Term 2: {a_2 ×([a_1×b_2] + [a_2×c_2] + [a_3×d_2])} +
Term 3: {a_3 ×([a_1×b_3] + [a_2×c_3] + [a_3×d_3])}.

Worksheet A07b: Estimate of dermal permeability (K_p in cm/hr) and 95% confidence intervals (data from U.S. EPA 1992). [PKMODEL]

Model parameters	ID	Value	
Coefficient for $k_{o/w}$	C_KOW	0.706648	
Coefficient for MW	C_MW	0.006151	
Model Constant	C	2.72576	
Number of data points	DP	90	
Degrees of Freedom (d.f.)	DF	87	
Critical value of $t_{0.025}$ with 87 d.f.[1]	CRIT	1.96	
Standard error of the estimate	SEE	45.9983	
Mean square error or model variance	MDLV	0.528716	
Standard deviation of model (s)	MSD	0.727129	$MDLV^{0.5}$
X′X, cross products matrix	0.0550931	-0.0000941546	-0.0103443
	-0.0000941546	0.0000005978	-0.0000222508
	-0.0103443	-0.0000222508	0.00740677

[1] Mendenhall and Scheaffer, 1973, Appendix 3, Table 4, p. A31.

NOTE: The data for this analysis is taken from U.S. EPA (1992), Dermal Exposure Assessment: Principles and Applications, EPA/600/8-91/011B, Table 5-4, pp. 5-15 through 5-19. The EPA report, however, does not provide sufficient information for the calculation of confidence intervals. The synopsis of the above analysis was conducted in STATGRAPHICS Plus for Windows, Version 3.1 (Manugistics, 1995) as well as Mathematica, Version 3.0.1.1 (Wolfram Research, 1997). Although not explicitly stated in the EPA report, 3 of the 93 data points are censored from the analysis because they are statistical outliers: [Hydrocortisone-21-yl]-hemipimelate, n-nonanol, and n-propanol. The model parameters reported above are consistent with those reported by U.S. EPA but are carried out to greater number of decimal places to reduce rounding errors when calculating the confidence intervals. See notes to Worksheet A07a for details of calculating maximum likelihood estimates and confidence intervals.

LIMITATIONS: This equation is based on measured K_p values for 95 organic compounds (Flynn 1990, Table 5-4 in U.S. EPA 1992) with log K_{ow} values ranging from about -2.5 to 5.5 and molecular weights ranging from about 30 to 770. As reviewed by U.S. EPA (1992), some analyses (e.g., Flynn 1990) suggest that the effects of both molecular weight and lipophilicity on permeability may be linear only within certain limits. Based on the analysis by Flynn (1990), relatively lipophobic compounds with log Kow values <0.5 appear to have log Kp values of approximately -3 (MW<150) or -5 (MW>150). At the upper limit, highly lipophilic compounds with log Kow values >3 and molecular weights <150 appear to have log Kp values of about -0.5. Compounds with log Kow values>3.5 and molecular weights >150 appear to have log Kp values of about -1.5 (Flynn 1990).

CHEMICAL SPECIFIC VALUES

Worksheet B01: Anticipated Application and Dilution Rates for hexachlorobenzene [WSB01]				
Item	Code	Value	Units	Reference/Source
Typical application rate[1]	Typ	0.00000025	lb a.i../acre	See note below and Section 2.4 for application rate of clopyralid.
Lowest application rate	Low	0.000000025	lb a.i./acre	
Highest application rate	Hi	0.0000025	lb a.i./acre	
Lowest dilution	LDil	20	gal./acre	C&P Press 1998[*]
Highest dilution	Hdil	40	gal./acre	judgmental
[*]Product label for Transline				

[1] Based on 2.5 ppm of HCB in technical grade clopyralid. For example, the typical application rate for clopyralid is taken as 0.1 lb a.i./acre. Since the proportion of HCB in clopyralid is 0.0000025 [2.5 ppm], the 'application' rate of HCB is thus 0.00000025 [0.0000025×0.1]

Typical concentration in applied solution:

Typical application rate divided by the average of the lowest and highest dilutions, converted to mg/mL, and rounded to two significant places after the decimal.

2.50e-07 lb/acre ÷ [(20 gal/acre + 40 gal/acre)/2] × 119.8 (mg/mL)/(lb/gal) = **9.98e-07 mg/mL** [TypDr]

Lowest estimated concentration in applied solution:

Lowest application rate divided by the highest dilution, converted to mg/mL, and rounded to two significant places after the decimal.

2.50e-08 lb/acre ÷ 40 gal/acre) × 119.8 (mg/mL)/(lb/gal) = **7.49e-08 mg/mL** [LowDr]

Highest estimated concentration in applied solution:

NOTE: This value is typically calculated as the highest application rate divided by the lowest dilution, converted to mg/mL, and rounded to two significant decimal places after the decimal. This standard calculation would be: 2.50e-06 lb/acre ÷ 20 gal/acre × 119.8 (mg/mL)/(lb/gal) = 1.5e-05 mg/mL = 1.5e-02 mg/L = 0.015 mg/L. This exceeds the water solubility of hexachlorobenzene, 0.006 mg/L (ATSDR 1998), which is equivalent to 0.000006 mg/mL or 6.00e-05 mg/mL. Thus, the water solubility of hexachlorobenzene is used to set the maximum concentration rate in an applied solution:

6.00e-05 mg/mL [HI_Dr]

Worksheet B02: Summary of central estimate and range of concentrations of hexachlorobenzene in field solutions.				
Parameter	ID	Value	Units	Reference/Source
Typical	TypDR	9.98e-07	mg/mL	See calculations above
Low	LowDR	7.49e-08	mg/mL	
High	Hi_DR	6.00e-05	mg/mL	

Worksheet B03: Summary of chemical specific values used for hexachlorobenzene in exposure assessment worksheets. [WSB03]				
Parameter	ID	Value	Units	Source/Reference
Molecular weight	MW	284	grams/mole	Budavari 1989
Water Solubility	WS	0.006	mg/L	ATSDR 1998
$K_{o/w}$ (given as log $K_{o/w}$ of 6.18)	Kow	1510000	unitless	ATSDR 1998
Measured Bioconcentration factor ($\boldsymbol{BCF}_{(\text{kg fish/L})}$)	BCFT	10000	kg fish/L	Section 3.4.4.3
ATSDR Acute MRL	RfDA	0.008	mg/kg bw/day	Section 3.3.3
EPA RfD	RfDP	0.0008	mg/kg bw/day	Section 3.3.3
EPA Cancer Potency Factor	Q1	1.6	(mg/kg/day)-1	Section 3.3.3

Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for hexachlorobenzene.							
Parameters	Value	Units					Reference
Molecular weight	284	g/mole					
$K_{o/w}$ at pH 7	1510000	unitless					
$\log_{10} K_{o/w}$	6.18						
Column vector ***a*** for calculating confidence intervals (see Worksheet 08 for definitions.)							
a_1	1						
a_2	284						
a_3	6.18						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet Worksheet A07a for details of calculation.							
Term 1	0.06544024						
Term 2	-0.10548778481						
Term 3	0.21082849003						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.1708	calculation verified in Mathematica 3.0.1.1					
$\log_{10} k_a = 0.233255 \log_{10}(k_{o/w}) - 0.005657\ MW - 1.49615$							WSA07a
$\log_{10}$ of first order absorption rate (k_a)							
Central estimate	-1.66146073216	±	$t_{0.025}$	×	s	×	$(\mathbf{a}'\cdot(\mathbf{X}'\mathbf{X})^{-1}\cdot\mathbf{a})^{0.5}$
Lower limit	-2.33036206192	-	2.0560	×	0.787218	×	0.4132795664
Upper limit	-0.99255940239	+	2.0560	×	0.787218	×	0.4132795664
First order absorption rates (i.e., antilog or 10^x of above values).							
Central estimate	0.0218041554	hours^{-1}					
Lower limit	0.004673454	hours^{-1}					
Upper limit	0.1017280214	hours^{-1}					

Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for hexachlorobenzene.								
Parameters	Value	Units					Reference	
Molecular weight	284	g/mole						
$K_{o/w}$	1510000	unitless						
$\log_{10} K_{o/w}$	6.17897694729							
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)								
a_1	1							
a_2	284							
a_3	6.17897694729							
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07b for details of calculation.								
Term 1	-0.0355639976							
Term 2	-0.0175701088							
Term 3	0.17982512177							
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.12669101534	calculation verified in Mathematica 3.0.1.1						
$\log_{10} k_p = 0.706648 \log_{10}(k_{o/w}) - 0.006151\ MW - 2.72576$							Worksheet A07b	
$\log_{10}$ of dermal permeability								
Central estimate	-0.10628229815	±	$t_{0.025}$	×	s	×	$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}^{0.5}$	
Lower limit	-0.61355377778	-	1.9600	×	0.727129	×	0.35593681369	
Upper limit	0.40098918148	+	1.9600	×	0.727129	×	0.35593681369	
Dermal permeability								
Central estimate	0.7829206	cm/hour						
Lower limit	0.2434704	cm/hour						
Upper limit	2.5176142	cm/hour						

NOTE: U.S. EPA (1992) gives an estimated Kp of 0.21 cm/hr based on a Log Ko/w of 5.31. The U.S. EPA (1992) does not provide a reference for this lower Ko/w. The more conservative and documented Log(Ko/w) of about 6.18 is used in this risk assessment and documented in Worksheet B03. As discussed by Flynn, compounds with log Kow values>3.5 and molecular weights >150 appear to have log Kp values of about -1.5 or Kp values of about 0.03. Thus, the use of the central estimate of 0.78 may over-estimate exposure by a factor of about 25. As discussed in Section 3.4, this very conservative approach has no impact on the risk characterization.

Worksheet B06: Summary of chemical specific dermal absorption values used for hexachlorobenzene dermal absorption. [WSB06]				
Description	Code	Value	Units	Reference/Source
Zero-order absorption (K_p)				
Central estimate	KpC	0.78292057	cm/hour	Worksheet B05
Lower limit	KpL	0.24347043	cm/hour	
Upper limit	KpU	2.51761421	cm/hour	
First-order absorption rates (k_a)				
Central estimate	AbsC	0.0218041554	$hour^{-1}$	Worksheet B04
Lower limit	AbsL	0.004673454	$hour^{-1}$	
Upper limit	AbsU	0.1017280214	$hour^{-1}$	

WORKER EXPOSURE ASSESSMENTS

Worksheet C01: Worker exposure estimates for directed foliar (backpack) applications of hexachlorobenzene				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	ApplC	2.50e-07	lbs a.i./day	WSB01.TYP
Lower estimate	ApplL	2.50e-08	lbs a.i./day	WSB01.LOW
Upper estimate	ApplU	2.50e-06	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	4.375	acres/day	WSA03.ACREC
Lower estimate	ACREL	1.5	acres/day	WSA03.ACREL
Upper estimate	ACREU	8	acres/day	WSA03.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	1.09e-06	lb/day	
Lower estimate	HANDLL	3.75e-08	lb/day	
Upper estimate	HANDLU	2.00e-05	lb/day	
Absorbed dose rate (mg/day)				
Central estimate	RATEC	0.003	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA03.RATEC
Lower estimate	RATEL	0.0003		WSA03.RATEL
Upper estimate	RATEU	0.01		WSA03.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	3.28e-09	mg/kg bw/day	N/A
Lower estimate	DOSEL	1.13e-11		
Upper estimate	DOSEU	2.00e-07		

Worksheet C02: Worker exposure estimates for boom spray (hydraulic ground spray) applications of hexachlorobenzene [WSC01]				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	APPLC	2.50e-07	lbs a.i./day	WSB01.TYP
Lower estimate	APPLL	2.50e-08	lbs a.i./day	WSB01.LOW
Upper estimate	APPLU	2.50e-06	lbs a.i./day	WSB01.HI
Acres treated per day				
Central estimate	ACREC	112	acres/day	WSA04.ACREC
Lower estimate	ACREL	66	acres/day	WSA04.ACREL
Upper estimate	ACREU	168	acres/day	WSA04.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	2.80e-05	lb/day	
Lower estimate	HANDLL	1.65e-06	lb/day	
Upper estimate	HANDLU	4.20e-04	lb/day	
Absorbed dose rate				
Central estimate	RATEC	2.00e-04	(mg agent/kg bw) ÷ (lbs agent handled per day)	WSA04.RATEC
Lower estimate	RATEL	1.00e-05		WSA04.RATEL
Upper estimate	RATEU	9.00e-04		WSA04.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	5.60e-09	mg/kg bw/day	N/A
Lower estimate	DOSEL	1.65e-11		
Upper estimate	DOSEU	3.78e-07		

Worksheet C03: Workers: Accidental Dermal Exposure Assessments Using Zero-Order Absorption			
Parameter	Value	Units	Source
Body weight (*W*)	70	kg	WSA02.BW
Surface Area of hands (*S*)	840	cm^2	WSA02.Hands
Dermal permeability (K_p, cm/hour) [see Worksheet B05]			
Typical	0.7829206	cm/hour	WSB06.KpC
Lower	0.24347043	cm/hour	WSB06.KpL
Upper	2.5176142	cm/hour	WSB06.KpU
Concentration in solution (*C*) [see Worksheet B02]			
Typical	9.98e-07	mg/mL	WSB02.TypDr
Lower	7.49e-08	mg/mL	WSB02.LowDr
Upper	6.00e-05	mg/mL	WSB02.HI_Dr

Note that 1 mL is equal to 1 cm^3 and thus mg/mL = mg/cm^3.

Details of calculations for worker zero-order dermal absorption scenarios.

Equation (U.S. EPA 1992)

$$K_p \cdot C \cdot Time(hr) \cdot S \cdot \div W = Dose(mg/kg)$$

where: C = concentration in mg/cm^3 or mg/mL, S = Surface area of skin in cm^2, W = Body weight in kg.

Immersion of Hands or Wearing Contaminated Gloves for One-Minute

Typical Value: Use typical concentration and central estimate of K_p.
0.7829206 cm/hr × 9.98e-07 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 1.56e-07 mg/kg [WZHT1M]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.2434704 cm/hr × 7.49e-08 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 3.65e-09 mg/kg [WZHL1M]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
2.5176142 cm/hr × 6.00e-05 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 0.0000302 mg/kg [WZHU1M]

Wearing Contaminated Gloves for One-Hour

Typical Value: Use typical concentration and central estimate of K_p.
0.7829206 cm/hr × 9.98e-07 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.000009 mg/kg [WZHT1H]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.2434704 cm/hr × 7.49e-08 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 2.19e-07 mg/kg [WZHL1H]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
2.5176142 cm/hr × 6.00e-05 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.00181 mg/kg [WZHU1H]

Worksheet C04: Worker Accidental Spill Based on the Assumption of First-Order Absorption			
Parameter	Value	Units	Source
Liquid adhering to skin after a spill (***L***)	0.008	mg/mL	WSA02.Liq
Body weight (***W***)	70	kg	WSA02.BW
Surface Areas (**A**)			
Hands	840	cm^2	WSA02.Hands
Lower legs	2070	cm^2	WSA02.LLegs
First-order dermal absorption rates (k_a)			
Central Estimate	0.02180	$hour^{-1}$	WSB06.ABSC
Lower limit of range	0.004673	$hour^{-1}$	WSB06.ABSL
Upper limit of range	0.10173	$hour^{-1}$	WSB06.ABSU
Concentration in solution (***C***) [see Worksheet B01]			
Typical	9.98e-07	mg/mL	TypDr
Lower	7.49e-08	mg/mL	LowDr
Upper	6.00e-05	mg/mL	HI_Dr

Details of calculations.

Equation (from Durkin et al. 1995)

$$Dose_{(mg/kg\ bw)} = k_{a\ (1/hours)} \times L_{(mg/cmsq)} \times C_{(mg/mL)} \times T_{(hours)} \times A_{(cm\ sq)} \div W_{(kg)}$$

where ***T*** is the duration of exposure in hours and other terms are defined as above.

Lower Legs: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFLT1H],
0.0218042 h^{-1} × 0.008 mL/cm × 9.98e-07 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 5.2e-09 mg/kg
Lower range [WFLL1H],
0.0046735 h^{-1} × 0.008 mL/cm × 7.49e-08 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 8.3e-11 mg/kg
Upper range [WFLU1H],
0.1017280 h^{-1} × 0.008 mL/cm × 6.00e-05 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 1.4e-06 mg/kg

Hands: Spill with 1 Hour (*T*) Exposure Period

Typical Value [WFHT1H],
0.0218042 h^{-1} × 0.008 mL/cm × 9.98e-07 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 2.1e-09 mg/kg
Lower range [WFHL1H],
0.0046735 h^{-1} × 0.008 mL/cm × 7.49e-08 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 3.4e-11 mg/kg
Upper range [WFHU1H],
0.1017280 h^{-1} × 0.008 mL/cm × 6.00e-05 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 5.9e-07 mg/kg

EXPOSURE ASSESSMENTS for the GENERAL PUBLIC

Worksheet D01: Direct spray of child.			
Verbal Description*: A naked child is accidentally sprayed over the entire body surface with a field dilution as it is being applied. The child is effectively washed - i.e., all of the compound is removed - after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	13.3	kg	WSA04.BWC
Exposed surface area (***A***)	6030	cm^2	WSA04.SAC
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	9.98e-07	mg/mL	WSB02.TYPDR
Low	7.49e-08	mg/mL	WSB02.LOWDR
High	6.00e-05	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	2.18e-02	$hour^{-1}$	WSB06.AbsC
Low	4.67e-03	$hour^{-1}$	WSB06.AbsL
High	1.02e-01	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	7.90e-08	mg/kg	SPRYC
Low	1.27e-09	mg/kg	SPRYL
High	2.21e-05	mg/kg	SPRYH

Details of calculations

Equation: $L \times C \times A \times k_a \times T \div W$

Central Estimate [SPRYCC]:
0.008 mg/mL × 9.98e-07 mg/mL × 6030 cm^2 × 2.18e-02 h^{-1} × 1 h ÷ 13.3 kg = 7.90e-08 mg/kg

Lower Range of Estimate [SPRYCL]:
0.008 mg/mL × 7.49e-08 mg/mL × 6030 cm^2 × 4.67e-03 h^{-1} × 1 h ÷ 13.3 kg = 1.27e-09 mg/kg

Upper Range of Estimate [SPRYCH]:
0.008 mg/mL × 6.00e-05 mg/mL × 6030 cm^2 × 1.02e-01 h^{-1} × 1 h ÷ 13.3 kg = 2.21e-05 mg/kg

Worksheet D02: Direct spray of woman.			
Verbal Description*: A woman is accidentally sprayed over the feet and legs with a field dilution as it is being applied. The woman washes and removes all of the compound after 1 hour. The absorbed dose is estimated using the assumption of first-order dermal absorption.*			
Parameter/Assumption	Value	Units	Source/Reference
Period of exposure (***T***)	1	hour	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	2915	cm^2	WSA04.SAF1
Liquid adhering to skin per cm^2 of exposed skin.(***L***)	0.008	mL/cm^2	WSA02.LIQ
Concentrations in solution (***C***)			
Typical/Central	9.98e-07	mg/mL	WSB02.TYPDR
Low	7.49e-08	mg/mL	WSB02.LOWDR
High	6.00e-05	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	2.18e-02	$hour^{-1}$	WSB06.AbsC
Low	4.67e-03	$hour^{-1}$	WSB06.AbsL
High	1.02e-01	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	7.93e-09	mg/kg	SPRYWC
Low	1.28e-10	mg/kg	SPRYWL
High	2.22e-06	mg/kg	SPRYWH

Details of calculations

Equation: $L \times C \times S \times k_a \times T \div W$

Central Estimate [SPRYWC]:
0.008 mg/mL × 9.98e-07 mg/mL × 2915 cm^2 × 0.0218041554 h^{-1} × 1 h ÷ 64 kg = 7.93e-09 mg/kg

Lower Range of Estimate [SPRYWL]:
0.008 mg/mL × 7.49e-08 mg/mL × 2915 cm^2 × 0.004673454 h^{-1} × 1 h ÷ 64 kg = 1.28e-10 mg/kg

Upper Range of Estimate [SPRYWH]:
0.008 mg/mL × 6.00e-05 mg/mL × 2915 cm^2 × 0.1017280214 h^{-1} × 1 h ÷ 64 kg = 2.22e-06 mg/kg

Worksheet D03: Dermal contact with contaminated vegetation.			
Verbal Description*: A woman wearing shorts and a short sleeved shirt is in contact with contaminated vegetation for 1 hour shortly after application of the compound - i.e. no dissipation or degradation is considered. The chemical is effectively removed from the surface of the skin - i.e., washing - after 24 hours.*			
Parameter/Assumption	Value	Units	Source/Reference
Contact time (***Tc***)	1	hour	N/A
Exposure time (***Te***)	24	hours	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Exposed surface area (***A***)	5300	cm^2	WSA04.SAF2
Dislodgeable residue (***Dr***) as a proportion of application rate	0.1	none	WSA04.DisL
Application Rates(***R***)			
Typical/Central	2.50e-07	lb a.i/acre	WSB01.TYP
Low	2.50e-08	lb a.i/acre	WSB01.LOW
High	2.50e-06	lb a.i/acre	WSB01.HI
First-order dermal absorption rate (k_a)			
Central	2.18e-02	$hour^{-1}$	WSB06.AbsC
Low	4.67e-03	$hour^{-1}$	WSB06.AbsL
High	1.02e-01	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations on next page.***			
Central	4.31e-08	mg/kg	VEGDWC
Low	7.52e-10	mg/kg	VEGDWL
High	2.48e-06	mg/kg	VEGDWH

Description of Calculations:

Step 1:

Use method of Durkin et al. (1995, p. 68, equation 4) to calculate dislodgeable residue (Dr) in units of µg/(cm^2·hr)) after converting application rate in lb a.i./acre to units of µg/cm^2:

$x = \log(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr))) = (1.09 \times \log_{10}(\boldsymbol{R} \times \text{WSA01.lbac\_ugcm})) + 0.05$

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^x$

Step 2:

Convert Dr from units of µg/(cm^2·hr)) to units of mg/(cm^2·hr)) by dividing by 1000:

$\boldsymbol{Dr}(mg/(cm^2 \cdot hr)) = \boldsymbol{Dr}(\mu g/(cm^2 \cdot hr))/1000$

Step 3:

Estimate amount (*Amnt*) transferred to skin in mg during the exposure period:

$\boldsymbol{Amnt}(mg) = \boldsymbol{Dr}(mg/(cm^2 \cdot hr)) \times \boldsymbol{Tc}\ (hours) \times \boldsymbol{A}\ (cm^2)$

Step 4:

Estimate the absorbed dose ($\boldsymbol{D_{Abs}}$) in mg/kg bw as the product of the amount on the skin , the first-order absorption rate, and the duration of exposure divided by the body weight:

$\boldsymbol{D_{Abs}} = \boldsymbol{Amnt}(mg) \times \mathbf{k_a}\ (hours^{-1}) \times \boldsymbol{Te}\ (hours) \div \boldsymbol{W}\ (kg)$

See next page for details of calculations.

Worksheet D03 Details of calculations: *Dermal Exposure to Contaminated Vegetation*

Central Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)))$-6.002 = (1.09 × $\log_{10}$(0 ×11.21)) + 0.05 = -6.002 µg/(cm²·hr)

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-6.002}$ = 9.95e-07 µg/(cm²·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm²·hr)) = 9.95e-07 µg/(cm²·hr) ÷ 1000 µg/mg = 9.95e-10 mg/(cm²·hr)

Step 3:

$\boldsymbol{Amnt}$(mg) = 9.95e-10 mg/(cm²·hr) × 1 hr × 5300 cm² = 5.28e-06 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 5.28e-06 mg × 0.0218041554 hr^{-1} × 24 hours ÷ 64 kg = 4.31e-08 `[VEGDWC]`

Lower Range of Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)))$ = (1.09 × $\log_{10}$(0 ×11.21)) + 0.05 = -7.092µg/(cm²·hr)

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-7.092}$ = 8.09e-08 µg/(cm²·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm²·hr)) = 8.09e-08 µg/(cm²·hr) ÷ 1000 µg/mg = 8.09e-11 mg/(cm²·hr)

Step 3:

$\boldsymbol{Amnt}$(mg) = 8.09e-11 mg/(cm²·hr) × 1 hr × 5300 cm² =4.29e-07 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 4.29e-07 mg × 0.004673454 hr^{-1} × 24 hours ÷ 64 kg = 7.52e-10 `[VEGDWL]`

Upper Range of Estimate:

0.008Step 1:

$\log_{10}(\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)))$ = (1.09 × $\log_{10}$(0.000003 ×11.21)) + 0.05 = -4.912 µg/(cm²·hr)

$\boldsymbol{Dr}\ (\mu g/(cm^2 \cdot hr)) = 10^{-4.912}$ = 1.22e-05 µg/(cm²·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm²·hr)) = 1.22e-05 µg/(cm²·hr) ÷ 1000 µg/mg = 1.22e-08 mg/(cm²·hr)

Step 3:

$\boldsymbol{Amnt}$(mg) = 1.22e-08 mg/(cm²·hr) × 1 hr × 5300 cm² = 6.49e-05 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 6.49e-05 mg × 0.1017280214 hr^{-1} × 24 hours ÷ 64 kg = 2.48e-06 `[VEGDWH]`

Worksheet D04: Consumption of contaminated fruit, acute exposure scenario.			
Verbal Description*: A woman consumes 1 lb (0.4536 kg) of contaminated fruit shortly after application of the chemical - i.e. no dissipation or degradation is considered. Residue estimates based on relationships from Hoerger and Kenaga (1972) summarized in WSA07.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	64	kg	`WSA04.BWF`
Amount of fruit consumed (***A***)	0.454	kg	`N/A`
Application rates (***R***)			
Typical	2.50e-07	lb a.i./acre	`WSB01.Typ`
Lower	2.50e-08	lb a.i./acre	`WSB01.Low`
Upper	2.50e-06	lb a.i./acre	`WSB01.Hi`
Residue rates (***rr***)			
Typical	1.5	RUD[1]	`WSA05a.FRT`
Upper	7	RUD[1]	`WSA05a.FRU`
Dose estimates (***D***) - **see details of calculations below**			
Typical	2.66e-09	mg/kg bw	`VEGCWAT`
Lower	2.66e-10	mg/kg bw	`VEGCWAL`
Upper	1.24e-07	mg/kg bw	`VEGCWAU`
[1] RUD: Residue Unit Dosage, term used by Hoerger and Kenaga (1972) for anticipated concentration on vegetation (mg chemical per kg of vegetation) for each l lb a.i./acre applied.			

Equation (terms defined in above table):

D (mg/kg bw) = ***A***(kg) × ***R***(lb a.i./acre) × ***rr***(mg/kg÷lb a.i./acre) ÷***W***(kg bw)

Details of Calculations

Typical: Use typical application rate and typical RUD.

D = 0.454 kg × 2.50e-07 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 2.66e-09 mg/kg bw

Lower: Use lowest estimated application rate. Use typical RUD because no lower estimate of the RUD is available.

D = 0.454 kg × 2.50e-08 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 2.66e-10 mg/kg bw

Upper: Use highest estimated application rate and highest RUD.

D = 0.454 kg × 2.50e-06 lb a.i./acre × 7 mg/kg÷lb a.i./acre ÷ 64 kg = 1.24e-07 mg/kg bw

Worksheet D05: Consumption of vegetation, chronic exposure scenario.			
Verbal Description*: A woman consumes contaminated vegetation daily for a life time. This scenario makes the assumption that concentration of hexachlorobenzene in the lower surface layers is essentially constant.*			
Parameters/Assumptions	Value	Units	Source/Reference
Concentration in soil			Section 3.2.4.2.
0.1 lb clopyralid a.e./acre	3.00e-08	mg/kg	
0.01 lb clopyralid a.e./acre	3.00e-09	mg/kg	
1.0 lb clopyralid a.e./acre	3.00e-07	mg/kg	
Bioconcentration factor in vegetation	19	value for carrots	ATSDR 1998
Concentration in vegetation central	5.70e-07	mg/kg	Concentration in soil multiplied by bioconcentration factor for vegetation.
lower	5.70e-08	mg/kg	
upper	5.70e-06	mg/kg	
Duration of exposure (***t***)	365	days	N/A
Body weight (***W***)	64	kg	WSA04.BWF
Amount of vegetation consumed per unit body weight(***A***)			
Typical	0.0043	kg veg./kg bw	WSA04.VT
Upper	0.01	kg veg./kg bw	WSA04.VU
Dose estimates (***D***)[1]			
Typical	3.83e-11	mg/kg bw/day	VEGCWCT
Lower	3.83e-12	mg/kg bw/day	VEGCWCL
Upper	8.91e-10	mg/kg bw/day	VEGCWCU

[1] The product of the concentration in vegetation and the amount of vegetation consumed divided by the body weight. Typical and lower ranges are based on the typical consumption of vegetation as well as the central and lower ranges, respectively, of the application rates. The upper range is based on the upper ranges of the application rate and resulting upper range on contaminated vegetation as well as the upper range of consumption of vegetation.

Worksheet D06: Consumption of contaminated water, acute exposure scenario.			
Verbal Description*: A young child (2-3 years old) consumes 1 liter of contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in solution ($C_{(mg/L)}$)			
Central	9.98e-04	mg/L	WSB02.TypDR
Low	7.49e-05	mg/L	WSB02.LowDR
High	1.50e-01	mg/L	Section 3.2.4.
Body weight (***W***)	13.3	kg	WSA04.BWC
Amount of water consumed (***A***)			
Typical	1	L/day	WSA04.WCT
Lower	0.61	L/day	WSA04.WCL
Upper	1.5	L/day	WSA04.WCH
Estimated Concentration in Water (***Conc***) - **see details of calculations on next page.**			
Typical	7.56e-07	mg/kg bw	
Lower	5.67e-08	mg/kg bw	
Upper	1.14e-04	mg/kg bw	
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	5.68e-08	mg/kg bw	WATCCAT
Lower	2.60e-09	mg/kg bw	WATCCAL
Upper	1.28e-05	mg/kg bw	WATCCAU

Details of calculations on next page

Acute Consumption of Contaminated Water from an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: Calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$Conc._{(mg/L)} = VS_{(gal.)} \times 3.785_{L/gal} \times C_{(mg/L)} \div VL_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the amount of water consumed, and the body weight.

$$D_{(mg/kg\ bw)} = Conc._{(mg/L)} \times A_{(L)} \div W_{(kg)}$$

Calculations

Central Estimate:

Use the typical field dilution, and the typical water consumption.

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 9.98e\text{-}04_{(mg/L)} \div 1000000_{(liters)} = 7.56e\text{-}07_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 7.56e\text{-}07_{(mg/L)} \times 1_{(L)} \div 13.3_{(kg)} = 5.68e\text{-}08_{(mg/kg\ bw)}$$ [WATCCAT]

Lower Estimate:

Use the lowest estimated field dilution and the lower range of water consumption.

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 7.49e\text{-}05_{(mg/L)} \div 1000000_{(liters)} = 5.67e\text{-}08_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 5.67e\text{-}08_{(mg/L)} \times 0.61_{(L)} \div 13.3_{(kg)} = 2.60e\text{-}09_{(mg/kg\ bw)}$$ [WATCCAL]

Upper Estimate:

Use the highest estimated field concentration and the upper range of water consumption.

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 1.50e\text{-}01_{(mg/L)} \div 1000000_{(liters)} = 1.14e\text{-}04_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 1.14e\text{-}04_{(mg/L)} \times 1.5_{(L)} \div 13.3_{(kg)} = 1.28e\text{-}05_{(mg/kg\ bw)}$$ [WATCCAU]

Worksheet D07: Consumption of contaminated fish, acute exposure scenario.

Verbal Description*: An adult angler consumes fish taken from contaminated water shortly after an accidental spill of 200 gallons of a field solution into a pond that has an average depth of 1 m and a surface area of 1000 m^2 or about one-quarter acre . No dissipation or degradation is considered. Because of the available and well documented information and substantial differences in the amount of caught fish consumed by the general public and native American subsistence populations, separate exposure estimates are made for these two groups.*

Parameters/Assumptions	Value	Units	Source/Reference
Surface area of pond [SA]	1000	m^2	N/A
Average depth [DPTH]	1	m	N/A
Volume of pond in cubic meters [VM]	1000	m^3	N/A
Volume of pond in Liters [VL]	1000000	L	1 m^3 = 1,000 L
Volume of spill [VS]	200	gallons	N/A
Concentrations in spilled solution (***C*** $_{(mg/L)}$)			
Central	9.98e-04	mg/L	WSB02.TYPDR×1000
Low	7.49e-05	mg/L	WSB02.LOWDR×1000
High	1.50e-02	mg/L	Section 3.2.4.
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population	0.158	kg/day	WSA04.FAU
Native American subsistence populations	0.77	kg/day	WSA04.FNU
Bioconcentration factor (***BCF*** $_{(kg\ fish/L)}$)	10000	kg fish/L	WSB03.BCFT
Dose estimates (***D***) - **see details of calculations on next page.**			
General Population			
Typical	1.71e-05	mg/kg bw	FISHAMGPT
Lower	1.28e-06	mg/kg bw	FISHAMGPL
Upper	2.56e-04	mg/kg bw	FISHAMGPU
Native American subsistence populations			
Typical	8.31e-05	mg/kg bw	FISHAMNAT
Lower	6.23e-06	mg/kg bw	FISHAMNAL
Upper	1.25e-03	mg/kg bw	FISHAMNAU

Details of calculations on next page

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations

Equations (terms defined below or in table on previous page)

Step 1: As in the acute drinking water scenario, calculate the concentration in the pond based on the concentration in the spilled solution, the volume spilled and the volume of the pond, assuming instantaneous mixing.

$$\textbf{\textit{Conc.}}_{(mg/L)} = \textbf{\textit{VS}}_{(gal.)} \times 3.785_{L/gal} \times \textbf{\textit{C}}_{(mg/L)} \div \textbf{\textit{VL}}_{(liters)}$$

Step 2: Calculate the dose based on the concentration in the water, the bioconcentration factor, the amount of fish consumed, and the body weight.

$$\textbf{\textit{D}}_{(mg/kg\ bw)} = \textbf{\textit{Conc.}}_{(mg/L)} \times \textbf{\textit{BCF}}_{(kg\ fish/L)} \times \textbf{\textit{A}}_{(kg\ fish)} \div \textbf{\textit{W}}_{(kg\ bw)}$$

General Public

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 9.98\text{e-}04_{(mg/L)} \div 1000000_{(liters)} = 7.56\text{e-}07_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 7.56\text{e-}07_{(mg/L)} \times 10000_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 1.71\text{e-}05_{(mg/kg\ bw)}$$ `[FISHAMGPT]`

Lower End of Range for the Estimate:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 7.49\text{e-}05_{(mg/L)} \div 1000000_{(liters)} = 5.67\text{e-}08_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 5.67\text{e-}08_{(mg/L)} \times 10000_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 1.28\text{e-}06_{(mg/kg\ bw)}$$ `[FISHAMGPL]`

Upper End of Range for the Estimate:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the general public.

Step 1:

$$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 0.015_{(mg/L)} \div 1000000_{(liters)} = 1.14\text{e-}05_{(mg/L)}$$

Step 2:

$$\text{D}_{(mg/kg\ bw)} = 1.14\text{e-}05_{(mg/L)} \times 10000_{(L/kg)} \times 0.158_{(kg\ fish)} \div 70_{(kg)} = 2.56\text{e-}04_{(mg/kg\ bw)}$$ `[FISHAMGPU]`

(continued on next page)

Acute Consumption of Contaminated Fish after an Accidental Spill Details of calculations (continued)

Native American Subsistence Populations

Central Estimate:

Use the typical field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 0.00099833 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 7.56e-07 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 7.56e-07 $_{(mg/L)}$ × 10000 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 8.31e-05 $_{(mg/kg\ bw)}$ [FISHAMNAT]

Estimate of Lower End of Range:

Use the lower field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 0.0000749 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 5.67e-08 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 5.67e-08 $_{(mg/L)}$ × 10000 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 6.23e-06 $_{(mg/kg\ bw)}$ [FISHAMNAL]

Estimate of Upper End of Range:

Use the upper field dilution as well as the experimental BCF and upper range of daily fish consumption for the native American subsistence populations.

Step 1:

Conc. $_{(mg/L)}$ = 200 $_{(gal.)}$ × 3.785 $_{L/gal}$ × 0.015 $_{(mg/L)}$ ÷ 1000000 $_{(liters)}$ = 1.14e-05 $_{(mg/L)}$

Step 2:

D $_{(mg/kg\ bw)}$ = 1.14e-05 $_{(mg/L)}$ × 10000 $_{(L/kg)}$ × 0.77 $_{(kg\ fish)}$ ÷ 70 $_{(kg)}$ = 1.25e-03 $_{(mg/kg\ bw)}$ [FISHAMNAU]

Worksheet D08: Consumption of contaminated water, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes contaminated ambient water for a lifetime. The levels in water are estimated from GLEAMS model as detailed in Worksheet D08.*			
Parameters/Assumptions	Value	Units	Source/Reference
Body weight (***W***)	70	kg	WSA046.BWM
Amount of water consumed ($\boldsymbol{A}_{(L/day)}$)			
Typical	2	L/day	WSA04.WCAT
Lower	1.4	L/day	WSA04.WCAL
Upper	2.4	L/day	WSA04.WCAH
Estimated Concentration in Water (**Conc**)			
Typical	3.00e-12	mg/L	Section 3.2.4.3, last paragraph
Lower	0.00e+00	mg/L	
Upper	2.00e-10	mg/L	
Dose estimates : *Conc × A / W*			
Typical	8.57e-14	mg/kg bw/day	WATCMCT
Lower	0.00e+00	mg/kg bw/day	WATCMCL
Upper	6.86e-12	mg/kg bw/day	WATCMCU

Worksheet D09: Consumption of contaminated fish, chronic exposure scenario.			
Verbal Description*: An adult (70 kg male) consumes fish taken from contaminated ambient water for a lifetime. The levels in water are estimated from GLEAMS model as detailed in Worksheet D08.*			
Parameters/Assumptions	Value	Units	Source/Reference
Bioconcentration factor (***BCF***$_{(kg\ fish/L)}$)	10000	kg fish/L	WSB03.BCFT
Estimated Concentration in Water (**Conc**)			
Typical	3.00e-12	mg/L	Section 3.2.4.3, last paragraph
Lower	0.00e+00	mg/L	
Upper	2.00e-10	mg/L	
Body weight (***W***)	70	kg	WSA04.BWM
Amount of fish consumed (***A***)			
General Population typical	0.01	kg/day	WSA04.FAT
upper limit	0.158	kg/day	WSA04.FAU
Native American subsistence populations typical	0.081	kg/day	WSA04.FNT
upper limit	0.77	kg/day	WSA04.FNU
Dose estimates: ***BCF*** × **Conc** × ***A*** ÷ ***W***			
General Public			For the lower range of dose, the typical fish consumption is used because there is no published lower estimate of typical food consumption.
Typical	4.29e-12	mg/kg bw/day	
Lower	0.00e+00	mg/kg bw/day	
Upper	4.51e-09	mg/kg bw/day	
Native American Subsistence Population			
Typical	3.47e-11	mg/kg bw/day	
Lower	0.00e+00	mg/kg bw/day	
Upper	2.20e-08	mg/kg bw/day	

SUMMARY TABLES FOR HUMAN HEALTH RISK ASSESSMENT

Worksheet E01: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event)			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	3.28e-09	1.13e-11	2.00e-07	WSC01
Broadcast ground spray (Boom spray)	5.60e-09	1.65e-11	3.78e-07	WSC02
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	1.56e-07	3.65e-09	3.02e-05	WSC03
Contaminated Gloves, 1 hour	9.38e-06	2.19e-07	1.81e-03	WSC03
Spill on hands, 1 hour	2.09e-09	3.36e-11	5.86e-07	WSC04
Spill on lower legs, 1 hour	5.15e-09	8.28e-11	1.44e-06	WSC04

Worksheet E02a: Summary of risk characterization for workers[1]

ATSDR Acute MRL	0.008	mg/kg/day	Sect. 3.3.3.	
Chronic RfD	0.0008	mg/kg/day	Sect. 3.3.3.	

Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	4e-06	1e-08	0.0003	WSC01
Broadcast ground spray (Boom spray)	7e-06	2e-08	0.0005	WSC02
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	2e-05	5e-07	0.004	WSC03
Contaminated Gloves, 1 hour	0.001	3e-05	0.2	WSC03
Spill on hands, 1 hour	3e-07	4e-09	7e-05	WSC04
Spill on lower legs, 1 hour	6e-07	1e-08	0.0002	WSC04

[1] For acute exposures, the hazard quotient is the level of exposure divided by the acute MRL. For chronic exposures, the hazard quotient is the level of exposure divided by the chronic RfD. See Worksheet E01 for a summary of the exposure assessments.

Worksheet E02b: Summary of cancer risk assessment for workers expressed as increased cancer risk per day of exposure.[1]

Adjusted Cancer potency parameter	6.26e-05	$(mg/kg/day)^{-1}$	see note below [1]	
Scenario	Cancer Risk			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	2.05e-13	7.05e-16	1.25e-11	WSC01
Broadcast ground spray (Boom spray)	3.51e-13	1.03e-15	2.37e-11	WSC02
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	9.79e-12	2.28e-13	1.89e-09	WSC03
Contaminated Gloves, 1 hour	5.87e-10	1.37e-11	1.13e-07	WSC03
Spill on hands, 1 hour	1.31e-13	2.10e-15	3.67e-11	WSC04
Spill on lower legs, 1 hour	3.22e-13	5.18e-15	9.04e-11	WSC04
Forest Service Reference Cancer Risk Level	1.00e-06	one in one million		

[1] Based on the cancer potency factor of 1.6 $(mg/kg/day)^{-1}$ for lifetime exposure. To get an estimate of daily cancer risk, this factor is divided by the number of days in the reference human life span of 70 years - i.e., 365 days/year × 70 years = 25,550 days. Thus, the adjusted potency is 1.6 $(mg/kg/day)^{-1}$ ÷ 25,550 days or 0.000062622 $(mg/kg)^{-1}$.

Worksheet E02c: Summary of risk characterization for cancer risk assessment for workers relative to risk level of 1 in 1 million.[1]

Adjusted Cancer potency parameter	6.26e-05	$(mg/kg/day)^{-1}$	see note below [2]

Scenario	Cancer risk divided one in one-million			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	2e-07	7e-10	1e-05	WSC01
Broadcast ground spray (Boom spray)	4e-07	1e-09	2e-05	WSC02
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	1e-05	2e-07	0.002	WSC03
Contaminated Gloves, 1 hour	0.0006	1e-05	0.1	WSC03
Spill on hands, 1 hour	1e-07	2e-09	4e-05	WSC04
Spill on lower legs, 1 hour	3e-07	5e-09	9e-05	WSC04
Forest Service Reference Cancer Risk Level	1.00e-06	one in one million		

[1] Cancer risk from Table E02a divided by the reference cancer risk level used by the Forest Service.
[2] Estimated daily cancer potency factor based on the cancer potency factor of 1.6 $(mg/kg/day)^{-1}$ for lifetime exposure. See Worksheet E02a for details.

Worksheet E03: Summary of Exposure Scenarios for the General Public

Scenario	Target	Dose (mg/kg/day)			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	7.90e-08	1.27e-09	2.21e-05	WSD01
Direct spray, lower legs	Woman	7.93e-09	1.28e-10	2.22e-06	WSD02
Dermal, contaminated vegetation	Woman	4.31e-08	7.52e-10	2.48e-06	WSD03
Contaminated fruit, acute exposure	Woman	2.66e-09	2.66e-10	1.24e-07	WSD04
Contaminated water, acute exposure	Child	5.68e-08	2.60e-09	1.28e-05	WSD06
Consumption of fish, general public	Man	1.71e-05	1.28e-06	2.56e-04	WSD07
Consumption of fish, subsistence populations	Man	8.31e-05	6.23e-06	1.25e-03	WSD07
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	3.83e-11	7.66e-13	8.91e-10	WSD05
Consumption of water	Man	8.57e-14	0.00e+00	6.86e-12	WSD08
Consumption of fish, general public	Man	4.29e-12	0.00e+00	4.51e-09	WSD09
Consumption of fish, subsistence populations	Man	3.47e-11	0.00e+00	2.20e-08	WSD09

Worksheet E04a: Summary of risk characterization for the general public [1] .

ATSDR Acute MRL	0.008	mg/kg/day	Sect. 3.3.3.	
U.S. EPA RfD	0.0008	mg/kg/day	Sect. 3.3.3.	

Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	9.87e-06	1.59e-07	0.003	WSD01
Direct spray, lower legs	Woman	9.91e-07	1.59e-08	0.0003	WSD02
Dermal, contaminated vegetation	Woman	5.39e-06	9.39e-08	0.0003	WSD03
Contaminated fruit, acute exposure	Woman	3.33e-07	3.33e-08	1.55e-05	WSD04
Contaminated water, acute exposure	Child	7.10e-06	3.25e-07	0.002	WSD06
Consumption of fish, general public	Man	0.002	0.0002	0.03	WSD07
Consumption of fish, subsistence populations	Man	0.01	0.0008	0.2	WSD07
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	4.79e-08	9.58e-10	1.11e-06	WSD05
Consumption of water	Man	1.07e-10	0.00e+00	8.57e-09	WSD08
Consumption of fish, general public	Man	5.36e-09	0.00e+00	5.64e-06	WSD09
Consumption of fish, subsistence populations	Man	4.34e-08	0.00e+00	2.75e-05	WSD09

[1] For acute exposures, the hazard quotient is the level of exposure divided by the acute MRL. For chronic exposures, the hazard quotient is the level of exposure divided by the chronic RfD. See Worksheet E03 for a summary of the exposure assessments.

Worksheet E04b: Summary of cancer risk assessment for the general public [1] .

Adjusted Cancer Potency parameter	6.26e-05	$(mg/kg/day)^{-1}$	Sect. 3.3.3.	

Scenario	Target	Cancer risk			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	4.94e-12	7.95e-14	1.39e-09	WSD01
Direct spray, lower legs	Woman	4.97e-13	7.98e-15	1.39e-10	WSD02
Dermal, contaminated vegetation	Woman	2.70e-12	4.71e-14	1.55e-10	WSD03
Contaminated fruit, acute exposure	Woman	1.67e-13	1.67e-14	7.77e-12	WSD04
Contaminated water, acute exposure	Child	3.56e-12	1.63e-13	8.02e-10	WSD06
Consumption of fish, general public	Man	1.07e-09	8.01e-11	1.61e-08	WSD07
Consumption of fish, subsistence populations	Man	5.21e-09	3.90e-10	7.82e-08	WSD07
Longer Term Exposures					
Contaminated fruit[2]	Woman	6.13e-11	1.23e-12	1.43e-09	WSD05
Consumption of water	Man	1.37e-13	0.00e+00	1.10e-11	WSD08
Consumption of fish, general public	Man	6.86e-12	0.00e+00	7.22e-09	WSD09
Consumption of fish, subsistence populations	Man	5.55e-11	0.00e+00	3.52e-08	WSD09

[1] Based on the cancer potency factor of 1.6 $(mg/kg/day)^{-1}$ for lifetime exposure. To get an estimate of daily cancer risk, this factor is divided by the number of days in the reference human life span of 70 years - i.e., 365 days/year × 70 years = 25,550 days. Thus, the adjusted potency is 1.6 $(mg/kg/day)^{-1}$ ÷ 25,550 days or 0.000062622 $(mg/kg)^{-1}$.

[2] Based on the cancer potency factor of 1.6 $(mg/kg/day)^{-1}$ for lifetime exposure and the assumption of daily lifetime exposure.

Worksheet E04c: Summary of risk characterization of cancer risk assessment for the general public relative to a risk level of 1 in 1 million [1] .

Acute Cancer Potency Parameter		6.26e-05	(mg/kg/day)$^{-1}$	see note[1] below	
Scenario	Target	**Cancer risk divided by one in one-million**			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures [2]					
Direct spray, entire body	Child	4.94e-06	7.95e-08	1.39e-03	WSD01
Direct spray, lower legs	Woman	4.97e-07	7.98e-09	1.39e-04	WSD02
Dermal, contaminated vegetation	Woman	2.70e-06	4.71e-08	1.55e-04	WSD03
Contaminated fruit, acute exposure	Woman	1.67e-07	1.67e-08	7.77e-06	WSD04
Contaminated water, acute exposure	Child	3.56e-06	1.63e-07	8.02e-04	WSD06
Consumption of fish, general public	Man	1.07e-03	8.01e-05	1.61e-02	WSD07
Consumption of fish, subsistence populations	Man	5.21e-03	3.90e-04	7.82e-02	WSD07
Longer Term Exposures [3]					
Contaminated fruit	Woman	6.13e-05	1.23e-06	1.43e-03	WSD05
Consumption of water	Man	1.37e-07	0.00e+00	1.10e-05	WSD08
Consumption of fish, general public	Man	6.86e-06	0.00e+00	7.22e-03	WSD09
Consumption of fish, subsistence populations	Man	5.55e-05	0.00e+00	3.52e-02	WSD09
Forest Service Reference Cancer Risk Level	1.00e-06	one in one million			

[1] Cancer risk from Worksheet E04a divided by the reference cancer risk level used by the Forest Service.
[2] Estimated daily cancer potency factor based on the cancer potency factor of 1.6 (mg/kg/day)$^{-1}$ for lifetime exposure. See Worksheet E04a for details.
[3] Based on the cancer potency factor of 1.6 (mg/kg/day)$^{-1}$ for lifetime exposure and the assumption of daily lifetime exposure.