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Metsulfuron methyl (Escort) - Final Report

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ACRONYMS, ABBREVIATIONS, AND SYMBOLS

a.e.	acid equivalents
a.i.	active ingredient
AEL	adverse-effect level
ACGIH	American Conference of Governmental Industrial Hygienists
AChE	acetylcholinesterase
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
DF	dry flowable
d.f.	degrees of freedom
EC_{25}	concentration causing 25% 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

ACRONYMS, ABBREVIATIONS, AND SYMBOLS (*continued*)

NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NRC	National Research Council
OPPTS	Office of Pesticide Planning and Toxic Substances
ppm	parts per million
PSP	phenolsulfonphthalein
RBC	red blood cells
RfD	reference dose
UF	uncertainty factor
ULW	ultra low weight
U.S.	United States
U.S. EPA	U.S. Environmental Protection Agency
$>$	greater than
$\geq$	greater than or equal to
$<$	less than
$\leq$	less than or equal to
$=$	equal to
$\simeq$	approximately equal to
$\sim$	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 ($\mu g/cm^2$)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm^2)	square inches (in^2)	0.155
square centimeters (cm^2)	square meters (m^2)	0.0001
square meters (m^2)	square centimeters (cm^2)	10,000
yards	meters	0.9144

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

OVERVIEW

Metsulfuron methyl is a selective pre-emergence and post-emergence sulfonyl urea herbicide used primarily to control broadleaf weeds and some grasses. Based on a review of published studies as well as unpublished studies submitted to the U.S. EPA, there is no basis for contending that terrestrial or aquatic animals will be exposed to toxic levels of metsulfuron methyl in Forest Service applications. Conversely, under normal and anticipated conditions of use, metsulfuron methyl contamination of soil or water could cause adverse effects (i.e., reduction in growth) in sensitive plant species (terrestrial broadleaf plants and aquatic macrophytes). The actual duration and magnitude of these effects will depend heavily on rainfall, the pH of the water or soil, and, to a somewhat lesser extent, on microorganisms that can degrade metsulfuron methyl.

PROGRAM DESCRIPTION

The Forest Service uses only one commercial formulation of metsulfuron methyl, Escort. Escort is manufactured by Du Pont as a dry flowable granule. The composition of the product is 60% metsulfuron methyl and 40% inert ingredients. Noxious weed control is the only use of Escort by the Forest Service. Metsulfuron methyl usually is applied as the sole herbicide. Occasionally, it is 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 Escort used by the Forest Service involve boom spray (broadcast foliar) operations. Although Escort is registered for aerial applications (helicopter and sometimes fixed wing), the Forest Service does use this application method for metsulfuron methyl. Nonetheless, the aerial application method is included in this risk assessment in the event that the Forest Service may need to consider this option. The typical application rate in Forest Service programs is 0.02 lbs a.i./acre. The range of application rates specified on the product label is 0.0125 to 0.15 lbs a.i./acre, which is encompassed in the current risk assessment. The Forest Service used about 40 lbs of metsulfuron methyl in 1997, the most recent year for which use statistics are available. Much greater amounts of metsulfuron methyl are used in agriculture (e.g., about 35,543 lbs in 1994).

HUMAN HEALTH EFFECTS

Hazard Identification

Although the mechanism of action of sulfonylurea herbicides, including metsulfuron methyl, is fairly well characterized in plants, the mechanism of toxicity of the compound in mammals or other animal species is less clear. A variety of sulfonylureas reduce blood glucose by stimulating the release of insulin from pancreatic B cells, and some sulfonylureas reduce the hepatic extraction of insulin. Secondarily, sulfonylureas may affect levels of blood cholesterol and serum triglycerides. There is some evidence that metsulfuron methyl may cause both of these effects, at least at high doses. Metsulfuron methyl can cause both skin and eye irritation.

Metsulfuron methyl has a low order of acute oral toxicity with an acute oral LD_{50} of greater than 5000 mg/kg. Nonetheless, substantial mortality (20%) was observed at doses of 2000 mg/kg, and non-lethal signs of toxicity were apparent after single oral doses as low as 50 mg/kg.

The most common sign of acute, subchronic, and chronic toxicity is decreased body weight gain. The only other commonly noted effect involves changes in various hematological parameters as well as changes in absolute and relative organ weights. None of these changes, however, suggest a clear or specific target organ toxicity. While speculative, the effects of metsulfuron methyl on the blood could be related to saccharin, which is a metabolite of metsulfuron methyl. At very high doses, saccharin has been shown to cause hematologic effects in mice. There is no evidence that metsulfuron methyl presents any reproductive risks or causes malformations or cancer.

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

Very little information is available on the inhalation toxicity of metsulfuron methyl. Metsulfuron methyl can induce irritant effects at very high exposure levels. The potential inhalation toxicity of metsulfuron methyl, however, is not of substantial concern to this risk assessment because of the implausibility of inhalation exposure involving high concentrations of this compound.

Exposure Assessment

There are no occupational exposure studies in the available literature that are associated with the application of metsulfuron methyl. 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. Separate exposure assessments are given for backpack, boom spray, and aerial applications.

For both types of ground applications, central estimates of worker exposure are similar: 0.0003 mg/kg/day for backpack applications and 0.0004 mg/kg/day for boom spray applications. The upper limits of the exposure estimates are 0.012 mg/kg/day for backpack applications and 0.02 mg/kg/day for boom spray applications. Although Escort is labeled for aerial applications, the Forest Service is not using and does not plan to use that application method for Escort. Nonetheless, aerial applications are considered in this risk assessment in the event that the Forest Service must consider the option. The central estimates of worker exposure associated with aerial application are similar to those for ground application, 0.0003 mg/kg/day, although the upper limit of the exposure estimate, 0.0016, is much lower than those for ground applications.

Except in the case of accidental exposure, the levels of metsulfuron methyl to which the general public might be exposed should be far less than the levels for workers. Longer-term exposure scenarios for the general public lead to central estimates of daily doses in the range of

0.000001-0.0002 mg/kg/day with upper limits of exposure in the range of 0.0001-0.003 mg/kg/day. While these exposure scenarios are intended to be conservative, they are nonetheless plausible. Accidental exposure scenarios result in central estimates of exposure up to 0.000001 mg/kg/day with upper ranges of 0.17 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.

Dose-Response Assessment

The Office of Pesticide Programs of the U.S. EPA derived an RfD of 0.3 mg/kg/day for metsulfuron methyl. This is identical to the Agency wide RfD of 0.25 mg/kg/day but rounded to one significant digit. This RfD is based on a chronic rat NOEL of 500 ppm in the diet with an estimated daily dose of 25 mg/kg/day and an uncertainty factor of 100. In the same study, the LOAEL was 250 mg/kg/day (5000 ppm in the diet) and the only effect noted was a decrease in body weight. No frank signs of toxicity were seen.

All estimated levels of exposure for metsulfuron methyl are substantially below the RfD, and most are below the RfD by factors of more than 100 to nearly 10 billion. Thus, there is no need to develop elaborate dose-severity relationships to characterize risk. Furthermore, there is essentially no basis for developing dose-severity relationships because the available data indicate that metsulfuron methyl will not cause severe signs of toxicity even at extremely high dose levels, relative to any reasonable estimates of exposure based on current application rates and projected uses.

Risk Characterization

None of the exposure scenarios for workers or members of the general public result in levels that exceed the RfD. Based on central estimates, the levels of exposure will be below the RfD by factors of 1000 to well over 1 million. Thus, there is no basis for contending that metsulfuron methyl is likely to pose an identifiable risk to human health. This is consistent with the recent evaluation of metsulfuron methyl by the U.S. EPA.

The only reservation associated with this assessment of metsulfuron methyl is the same reservation associated with any risk assessment in which no plausible hazards can be identified: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated***. No chemical, including metsulfuron methyl, is studied for all possible effects, and the use of data from laboratory animals to estimate hazard or the lack of hazard to humans is an uncertain process. 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 metsulfuron methyl in Forest Service programs does not pose any identifiable hazard to workers or members of the general public.

Irritation and damage to the skin and eyes can result from exposure to relatively high levels of metsulfuron methyl. From a practical perspective, eye or skin irritation is likely to be the only overt effect resulting from the mishandling of metsulfuron methyl. These effects can be minimized or avoided by prudent industrial hygiene practices by workers handling metsulfuron methyl.

ECOLOGICAL EFFECTS

Hazard Identification

The toxicity of metsulfuron methyl is relatively well characterized in experimental mammals; however, there is relatively little information regarding non-target wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., decreased body weight gain). Several acute toxicity studies as well as two reproduction studies regarding the toxicity of metsulfuron methyl to birds indicate that birds do not appear to be more sensitive than experimental mammals to the toxic effects of metsulfuron methyl. Again, the major adverse effect observed is weight loss. There are also several acute honey bee assays indicating that bees are no more sensitive than either mammals or birds to metsulfuron methyl. At exposure rates exceeding the highest recommended application rate by about a factor of 3, metsulfuron methyl appears to be somewhat toxic to the Rove beetle, *Aleochara bilineata*, causing a 15% decrease in egg hatching.

The toxicity of metsulfuron methyl to terrestrial plants is well studied and well characterized. Metsulfuron methyl inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. These effects are considered quantitatively in the dose-response assessment and are one of the principal effects of concern in this risk assessment.

Terrestrial microorganisms also have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. There are both laboratory and field studies on the effects of metsulfuron methyl to soil microorganisms that suggest that transient effects on soil bacteria are plausible.

Not surprising for an herbicide, metsulfuron methyl seems to be much more toxic to aquatic plants than to aquatic animals. Frank toxic effects in fish are not likely to be observed at concentrations less than or equal to 1000 mg/L. Aquatic plants are far more sensitive than aquatic animals to the effects of metsulfuron methyl, although there appear to be substantial differences in sensitivity among species of macrophytes and unicellular algae. In general, the macrophytes appear to be more sensitive.

Exposure Assessment

Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation. In acute exposure scenarios, the highest exposure levels for small terrestrial vertebrates will occur after a direct spray and could amount to approximately 4 mg/kg under typical exposure conditions and up to about 60 mg/kg under more extreme conditions. Other routes of exposure such as the consumption of contaminated water or contaminated vegetation will generally lead to much lower levels of exposure. In chronic exposures, estimated daily doses for a small vertebrate are generally below 0.5 mg/kg/day, although daily doses up to about 4 mg/kg/day are possible for the consumption of contaminated vegetation. Based on general relationships of body size to body volume, larger vertebrates, compared with smaller animals, like insects, will be exposed to lower doses of the herbicide under comparable exposure conditions. Because of the apparently low toxicity of metsulfuron methyl to animals, the rather substantial variation in the exposure assessments has little impact on the assessment of risk to terrestrial animals.

The primary hazards to non-target terrestrial plants are associated with unintended direct deposition or spray drift as well as the persistence and migration of the compound in soil. Unintended direct spray will result in an exposure level equivalent to the application rate. At least some plants that are sprayed directly with metsulfuron methyl at or near the recommended range of application rates will be damaged. Based on a monitoring study involving a ground application with a hydraulic sprayer, no more than 0.001 of the application rate is expected to drift 100 m offsite. Based on monitoring studies involving low-flight agricultural applications of various pesticides and employing 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, are approximately 0.03 at 100 feet, 0.002 at 500 feet, 0.0006 at 1000 feet, and 0.0002 at 2500 feet. Estimates of off-site deposition can also be based on Stoke's Law. Using this method and assuming a wind velocity of no more than 5 miles/hour perpendicular to the line of application, 100 µ particles falling from 3 feet above the surface could drift as far as 23 feet. A raindrop or 400 µ particle applied at 6 feet above the surface could drift about 3 feet.

There are major areas of uncertainty and variability in assessing potential levels of exposure in soil. In general, metsulfuron methyl adsorption to a variety of different soil types will increase as the pH decreases (i.e., the soil becomes more acidic). The persistence of metsulfuron methyl in soil is highly variable, and reported soil half-times range from a few days to several months, depending on factors like temperature, rainfall, pH, organic matter, and soil depth.

In order to encompass a wide range of field conditions, GLEAMS simulations were conducted for clay and sand at annual rainfall rates ranging from 5 to 250 inches and the typical application rate of 0.02 lb a.i./acre. In sand or clay under arid conditions (i.e., annual rainfall of about 10 inches or less) there is no percolation or runoff and the rate of decrease of metsulfuron methyl concentrations in soil is attributable solely to degradation rather than dispersion. At higher rainfall rates, plausible concentrations in soil range as high as 0.007 ppm, and under a variety of conditions, concentrations of 0.0005 ppm and greater may be anticipated in the root zone for appreciable periods of time.

Metsulfuron methyl exposure to aquatic species is affected by the same factors that influence terrestrial plants, except the directions of the impact are reversed. In other words, in very arid environments (i.e., where the greatest persistence in soil is expected) substantial contamination of water is unlikely. In areas with increasing levels of rainfall, toxicologically significant exposures to aquatic plants are more likely to occur.   As summarized in Appendix 2, peak water levels of about 0.003 to 0.006 mg/L can be anticipated under worst case conditions and concentrations on the order of 0.001 mg/L or more could be anticipated under a variety of conditions at rainfall rates of 25 to 50 inches per year after a single application. With multiple applications per year, concentrations in water would not be expected to increase.

These estimates of persistence in soil and transport to water should be considered only as crude approximations of plausible levels of exposure. A substantial impact on these assessments could result from a variety of site-specific factors, particularly, application rate, microbial activity, soil binding of metsulfuron methyl, depth of the water table, proximity to open water, and rates of flow in and volumes of groundwater, streams, ponds, or lakes, and specific patterns of rainfall. These site-specific considerations could lead to substantial variations from the modeled values upward or downward.

Dose-Response Assessment

For terrestrial mammals, the dose-response assessment is based on the same data as the human health risk assessment (i.e., a NOEL of 25 mg/kg/day NOEL from a 2-year feeding study in rats). All of the potential longer-term exposures and all but one of the acute exposures of terrestrial mammals to metsulfuron methyl are substantially below the NOEL of 25 mg/kg/day. Consequently, a dose of 25 mg/kg/day is used to assess the consequences of all exposures. The limited available data suggests that the sensitivity of birds and terrestrial invertebrates to metsulfuron methyl is similar to that of mammals.

The toxicity of metsulfuron methyl to terrestrial plants is well characterized. Metsulfuron methyl is a potent herbicide that causes adverse effects in various target and non-target plant species. For exposures associated with direct sprays or drift, functional application rates as low as 0.000037 lb/acre could be associated with growth inhibition in sensitive species and rates as high as 0.015 lb/acre might be required to cause the growth inhibition in more tolerant species, like wheat. For the assessment of soil contamination, soil concentrations as low as 0.00025 ppm could cause growth inhibition in some relatively sensitive species, like maize, lentil, and sugar beet. At soil concentrations of 0.1 ppm, growth inhibition could be evident in several species.

Metsulfuron methyl has a low order of toxicity to fish. Mortality is not likely to occur in fish exposed to metsulfuron methyl concentrations less than or equal to1000 mg/L. For longer-term effects (e.g., hatching, larval survival, or larval growth over 90-day exposure period) the NOEC is 4.7 mg/L for a corresponding effect level at 8 mg/L. Similarly, aquatic invertebrates do not appear to be sensitive to metsulfuron methyl with an acute LC_{50} value of 720 mg/L for immobility and an NOEC of 150 mg/L for reproduction.

Aquatic plants are much more sensitive than aquatic animals to metsulfuron methyl. For macrophytes, the most sensitive species appears to be *Lemna gibba* with a reported EC_{50} value of 0.00036 mg/L and a NOEC value of approximately 0.00016 mg/L. There appears to be substantial variation in the toxicity of metsulfuron methyl to algal species with reported EC_{50} values ranging from about 0.01 to about 1 mg/L.

Risk Characterization

As in the human health risk assessment, the weight of evidence suggests that no adverse effects in terrestrial animals are plausible using typical or even very conservative worst case exposure assumptions. For the small mammals, the hazard quotients are based on the long term NOAEL of 25 mg/kg/day that was used in the human health risk assessment to derive the RfD. None of the hazard quotients for the small mammal approach a level of concern, even at the upper limit of exposure. For the honey bee, the hazard quotient is based on the non-lethal acute dose level of 270 mg/kg from a standard bioassay required for pesticide registration. There is no basis for contending that adverse effects in bees are plausible. One study reports a reduction in egg hatching in the Rove beetle after direct spray of metsulfuron methyl that corresponds to an application rate of 8.04 $\mu g/cm^2$. This rate is more than 30 times greater than the typical application and more than twice the rate of the highest labeled application. Although these ratios cannot be treated as hazard quotients, they suggest that adverse effects are not likely to occur at the typical application rate. At the highest labeled rate, however, the observation of adverse effects on the Rove beetle may be plausible. **Given the multitude of terrestrial invertebrates on which no data are available, caution in applying metsulfuron methyl at the highest labeled rate seems warranted. Applications of that magnitude are not anticipated in any Forest Service programs.**

Under certain circumstances, terrestrial plants may be affected by exposure to metsulfuron methyl. There is not likely to be a substantial impact on less sensitive plant species unless they are sprayed directly at the typical application rate of 0.02 lbs ai/acre or greater. Sensitive plant species will be adversely effected not only by accidental direct spray but also from on-site soil contamination and possibly through the use of irrigation water contaminated with metsulfuron methyl. Notably, however, any plausible adverse effects associated with soil contamination are likely to be restricted to the application site since leaching, as opposed to runoff, would account for most of the offsite movement of the compound. Accordingly, despite the relatively high potential for water contamination, there seems to be a relatively low potential for significant runoff to offsite soil. There also seems to be a relatively low potential for offsite damage due to wind erosion.

1. INTRODUCTION

The USDA Forest Service uses the herbicide, metsulfuron methyl, in its vegetation management programs. Only one commercial formulation, Escort, is used by the Forest Service. In 1992, the Forest Service prepared a risk assessment covering the use of metsulfuron methyl (USDA 1992). The present document provides updated risk assessments for human health effects and ecological effects to support a reassessment of the environmental consequences of using metsulfuron methyl 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 Escort, the commercial formulation of metsulfuron methyl used by the Forest Service, 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.

This is a technical support document and it addresses some specialized technical areas. Nevertheless an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 1998). Furthermore, the technical terms are defined in the glossary (chapter 6) 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. Some of the literature on metsulfuron methyl is summarized in the earlier risk assessment on this compound (USDA 1992). Only one other very brief review of metsulfuron methyl was encountered (ExToxNet 1996). Moreover, almost all of the mammalian toxicology studies and many of the ecotoxicology and environmental fate studies are unpublished reports submitted to the U.S. EPA as part of the registration process for this compound. Although some of these studies are summarized briefly by the U.S. EPA (1998a,b), there are no detailed reviews regarding the human health or ecological effects of metsulfuron methyl.

Because of the lack of a detailed, recent review concerning metsulfuron methyl and the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA files was conducted in the preparation of this risk assessment. Full text copies of the most relevant studies [n=81] were kindly provided by the U.S. EPA Office of Pesticide Programs. The studies were reviewed, and synopses of the most relevant studies are included in the appendices to this document.

The information presented in the appendices and the discussions in chapters 2, 3, and 4 of the risk assessment are intended to be detailed enough to support a review of the risk analyses; however, they are not intended to be as detailed as the information generally presented in Chemical Background documents or other comprehensive reviews.

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 (1998a), 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 metsulfuron methyl 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, a set of worksheets is included as an attachment to the risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on non-target organisms.

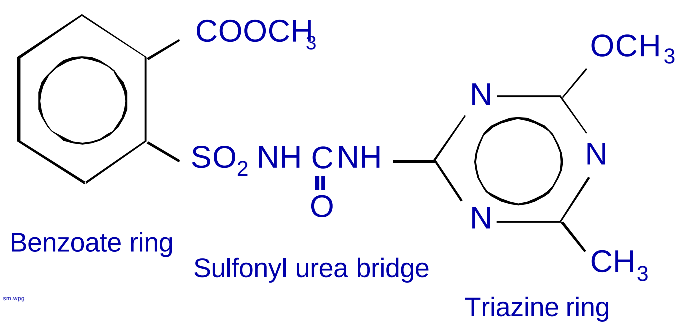
2. PROGRAM DESCRIPTION

2.1. OVERVIEW

Metsulfuron methyl is a selective pre-emergence and post-emergence sulfonyl urea herbicide used primarily to control broadleaf weeds and some grasses. The Forest Service uses only one commercial formulation of metsulfuron methyl, Escort. Escort is manufactured by Du Pont as a dry flowable granule. The composition of the product is 60% metsulfuron methyl and 40% inert ingredients. Noxious weed control is the only use of Escort by the Forest Service. Metsulfuron methyl is usually applied as the sole herbicide. Occasionally, it is 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 Escort used by the Forest Service involve boom spray (broadcast foliar) operations. Although Escort is registered for aerial applications (helicopter and sometimes fixed wing), the Forest Service does not currently engage in this application method. Nonetheless, the aerial application method is included in this risk assessment in the event that the Forest Service considers it an option. The typical application rate in Forest Service programs is 0.02 lbs a.i./acre. The range of application rates specified on the product label is 0.0125 to 0.15 lbs a.i./acre, which is encompassed in the current risk assessment. The Forest Service used about 40 lbs of metsulfuron methyl in 1997, the most recent year for which use statistics are available. Much greater amounts of metsulfuron methyl are used in agriculture (e.g., about 35,543 lbs in 1994).

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Metsulfuron methyl is the common name for Methyl-2-[[[[(4-methoxy-6-methyl-1,3,4-triazin-2-yl)amino]-carbonyl]amino]sulfonyl]benzoate] and is essentially a methyl benzoate ring linked to a methyl (-CH_3) and methoxy (-0CH_3) substituted triazine ring by a sulfonyl urea bridge:



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

Two commercial formulations of metsulfuron methyl are available in the United States, Ally and Escort, both produced by Du Pont as a dry flowable granule, which is mixed with water and a surfactant and then applied as a spray (section 2.4). Both of these formulations contain 60% (w/w) metsulfuron methyl and 40% (w/w) inerts, and both formulations have specific gravities of 1.47 and bulk densities of 33.9 lb/ft^3 (MSDS from C&P Press 1999). Except for differences in targeted crops specified on the product labels, it is not clear that these two formulations differ from one another. Ally is labeled for agricultural uses and is recommended for the control of weeds in fields of wheat or barley, fallow, pastures, and rangeland. Escort is labeled for non-agricultural uses and is recommended for the control of annual and perennial weeds and woody plants in non-crop areas and conifer plantations.

The identity of the inerts in Escort are considered proprietary information; therefore, Du Pont does not identify the inerts on the general or supplemental product labels or material safety data sheets (C&P Press 1999). This lack of disclosure indicates that none of the inerts present at a concentration of 0.1% or greater are classified as hazardous. Nonetheless, as discussed by Levine (1996), the testing requirements for inerts are less rigorous than the testing requirements for active ingredients (i.e., metsulfuron methyl).

Information about the impurities in technical grade metsulfuron methyl was submitted to the U.S. EPA (Brennan 1990, Brennan 1995) and reviewed during the preparation of this risk assessment. Since the identities of the impurities are considered proprietary by Du Pont, this information cannot be addressed specifically in this document. The potential impact of impurities on this risk assessment is discussed in section 3.1.

2.3. APPLICATION METHODS

Detailed descriptions of herbicide use in silviculture and the various methods by which to apply the herbicides exist in the general literature [e.g., Cantrell and Hyland (1985)] and in risk assessments conducted previously 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 for metsulfuron methyl (sections 3.2 and 4.2).

The general product label for Escort indicates that ground or aerial (helicopter only) applications are permitted. A supplemental label for the western United States (including Arizona, Colorado, Hawaii, Idaho, Kansas, Montana, Nebraska, North Dakota, Nevada, New Mexico, Oklahoma, Oregon, South Dakota, Texas, Utah, Washington, and Wyoming) allows helicopter or fixed wing aerial applications for rights-of-way, rangeland, pastures, and military installations (C&P Press 1999). Although the Forest Service has not conducted and is not planning to conduct aerial applications of metsulfuron methyl, the application method is considered in this risk assessment in the event that the Forest Service needs to consider aerial treatment options.

The most common methods of ground application for Escort are 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 to 1.0 acre/hour (Worksheet A03a).

Boom spray is used primarily in rights-of-way management or along roadways. 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). 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). These values are used to bracket the range of acres treated by a worker per hour with a central estimate of 16 acres per hour, the arithmetic mean between 11 and 21 (Worksheet A03b).

In aerial applications, Escort is applied under pressure through specially designed spray nozzles and booms. The nozzles are designed to minimize turbulence and maintain a large droplet size, both of which contribute to a reduction in spray drift. In aerial applications, approximately 40-100 acres may be treated per hour (Worksheet A03b).

2.4. MIXING AND APPLICATION RATES

The use of metsulfuron methyl by the Forest Service in 1997, the most recent year for which statistics are available (USDA 1998a), is summarized in Table 2-2. As indicated in this table, the sole use of metsulfuron methyl by the Forest Service involved noxious weed control. In 1997, the Forest Service treated about 2100 acres with approximately 38 lbs of metsulfuron methyl as the only herbicide for an average application rate of 0.018 lbs a.i./acre. Much smaller areas were treated with mixtures of 2,4-D and metsulfuron methyl (121 acres) or 2,4-D, picloram, and metsulfuron methyl (2 acres), again for noxious weed control.

In contrast, the annual use of metsulfuron methyl in agricultural applications in 1992, the most recent year for which data are available, amounted to 35,534 lbs, 97.34% of which was used on wheat or grains. As illustrated in Figure 2-1, all of the metsulfuron methyl was used in states east of the Mississippi, excluding California, Nevada, Arizona, and New Mexico (USGS 1998). Thus, the use of metsulfuron methyl by the Forest Service is a factor of over 900 less than agricultural uses [35,534 lbs ÷ 38 lbs = 935].

The highest labeled application rate for metsulfuron methyl is 4 ounces of Escort/acre, corresponding to 2.4 ounces of metsulfuron methyl (a.i.)/acre [4 ounces × 0.6 = 2.4 ounces] or 0.15 lbs a.i./acre [2.4 oz/acre ÷ 16 oz/lb = 0.15 lb/acre]. This rate is recommended only for the control of Kudzu.

The lowest recommended application rate is a ounces Escort/acre, which corresponds to an application rate of 0.2 ounces of metsulfuron methyl (a.i.)/acre [a ounces × 0.6 = 0.2 ounces] or 0.0125 lbs a.i./acre [0.2 oz/acre ÷ 16 oz/lb = 0.0125 lb/acre].   This rate is the lower limit of application rates recommended for the control of 53 species of weeds [C&P Press 1999, Escort Product Label p. 3].

For this risk assessment, the typical application rate is taken as 0.02 lbs a.i./acre, which is approximated from the average application rate of 0.018 lbs ai/acre used by the Forest Service in

1997 when metsulfuron methyl was applied as the sole herbicide (see Table 2-2). This typical application rate corresponds to an application rate of about 0.5 oz Escort/acre [0.02 lb a.i./acre ÷ 0.6 = 0.033 lb Escort/acre; 0.033 lb/acre × 16 oz/lb = 0.528 oz/acre], which approximates the upper the range of application rates recommended for 53 species of weeds and the lower range of application rates recommended for an additional 22 species of weeds.

The lower and upper limits of the application rates used in this risk assessment are 0.0125 and 0.15 lbs a.i./acre, respectively, and they correspond to the lower and upper limits of the labeled rates. They are used only to illustrate the consequences of applying metsulfuron methyl according to the range of rates specified on the label.

Mixing volumes for metsulfuron methyl vary substantially, depending on the type of vegetation to be treated as well as the application method. For aerial applications, 15-25 gallons of water per acre are recommended. Recommended mixing volumes for ground applications range from 100 to 400 gallons of water per acre for high volume applications, from 25 to 50 gallons of water per acre for low volume ground applications, and from 10 to 20 gallons of water per acre for ultra-low volume applications (C&P Press 1999, Escort Label, p. 4).

For this risk assessment, the extent to which a formulation of metsulfuron methyl is diluted prior to application primarily influences dermal and direct spray scenarios, both of which are dependent on ‘field dilution’(i.e., the concentration of metsulfuron methyl in the applied spray). In all cases, the higher the concentration of metsulfuron methyl, the greater the risk. For this risk assessment, the lowest dilution is taken as 10 gallons/acre, the minimum recommended for ultra-low volume applications. The highest dilution (i.e., that which results in the lowest risk) is based on 100 gallons of water per acre, the lowest application volume recommended for high volume ground applications. This range also encompasses the range of concentrations that might be used in aerial applications. Details regarding the calculation of field dilution rates are given in worksheet B01, and the calculations following this worksheet are summarized in worksheet B02.

Table 2-1. Selected physical and chemical properties of metsulfuron methyl with selected additional properties for the commercial formulations Escort.

Synonyms	Escort and Ally [formulations] (C&P Press 1999)
CAS number	74223-64-6 (C&P Press 1999; USDA/ARS 1995)
Molecular weight	381.4 (USDA/ARS 1995)
Bulk Density	Ally and Escort: 33.9 lb/ft^3 loose (C&P Press 1999)
Specific Gravity	Ally and Escort: 1.47 (C&P Press 1999)
Appearance, ambient	Ally and Escort: odorless off-white dry flowable granule, dispersable in water (C&P Press 1999)
Vapor pressure (mm Hg)	3.3×10^{-7} (USDA/ARS 1995) 2.5×10^{-12} (Peterson et al. 1994)
pH	4.1 in distilled water (Du Pont 1985a,b,c) 5.0 for 60 DF formulation
Water solubility (mg/L)	109 mg/L at 25°C in distilled water (pH 4.1) (Du Pont 1985a,b,c) 9500 mg/L at 25°C, pH 6.7 (Du Pont 1984) 1750 mg/L at 25°C, pH 5.4 (Du Pont 1984) 270 mg/L at 25°C, pH 4.6 (Du Pont 1984) 548 mg/L at 25ºC, pH 5 (USDA/ARS 1995; Barefoot and Cooke 1990) 2790 mg/L at 25ºC, pH 7 (USDA/ARS 1995; Barefoot and Cooke 1990) 213,000 mg/L at 25ºC, pH 9 (USDA/ARS 1995; Barefoot and Cooke 1990)
Henry's law constant	2.32×10^{-10} at 25ºC, pH 5 (USDA/ARS 1995) 4.50×10^{-11} at 25ºC, pH 7 (USDA/ARS 1995) 5.97×10^{-13} at 25ºC, pH 9 (USDA/ARS 1995)
pKa	3.3 (USDA/ARS 1995) 3.64 (Chamberlain et al. 1996) 3.7 (Berger and Wolfe 1996a)
log $K_{o/w}$	-1.7 at 25ºC, pH 7 (USDA/ARS 1995) -1.74 ($K_{o/w}$ = 0.018, Du Pont 1985a,b,c) 1.58 , acidic pH (Chamberlain et al. 1996)
Soil adsorption, K_d (L/kg)	0.05 to ~5 (USDA/ARS 1995) 0.54 (Baskaran et al. 1996)
Soil sorption, $K_{o/c}$	42 (4 to 206) (USDA/ARS 1995) 30 (Knisel et al. 1992)
Field dissipation half-time (days)	4 to 105 (USDA/ARS 1995) 7 to 180 (USDA/FS 1995 Fact Sheet) 29 to 84 dissipation from water (Thompson et al. 1992)
Hydrolysis half-time (days)	0.625 at pH 2 (Du Pont 1985a,b,c) 33 at pH 5 (Du Pont 1985a,b,c) stable at pH ≥ 7 (Du Pont 1985a,b,c) 3650 (Bastide et al. 1994) 660 (Berger and Wolfe 1996b)
Foliar half-time (days)	30 (Knisel et al. 1992)
Foliar wash-off fraction	0.8 (Knisel et al. 1992)
Soil half-time (days)	10 to 38 (USDA/ARS 1995) 120 to 180 (USDA/FS 1995 Fact Sheet) 120 (Knisel et al. 1992) 30 (14 to 180) (ExToxNet 1996) 4.3 [photolysis rate of 0.16/day@4.7%OM] (USDA/ARS 1995) 1 to 8 [photolysis] (USDA/FS 1995 Fact Sheet) 27 to 60 (Bastide et al. 1994) 8 to 36 (James et al. 1995)
Water half-time (days)	16.9 [photolysis rate of 0.041/day] (USDA/ARS 1995) 21.0 [hydrolysis rate of 0.033/day @ pH 5] (USDA/ARS 1995) stable to hydrolysis at pH 7 to 9 (USDA/ARS 1995) 1-8 days (USDA 1998b)

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

Herbicide or Herbicide Mixture	Use	Acres Treated	Amount Used (lbs)	lbs/acre[1]
as sole herbicide	noxious weed control	2131.61	38.12	0.018
with 2,4-D	noxious weed control	121	185.5	
with 2,4-D and picloram	noxious weed control	2	0.12	
	mixture subtotal	123		
Total (sole herbicide plus mixture subtotals)		2254.61		

[1] For metsulfuron methyl 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 metsulfuron methyl or other herbicides are not calculated.

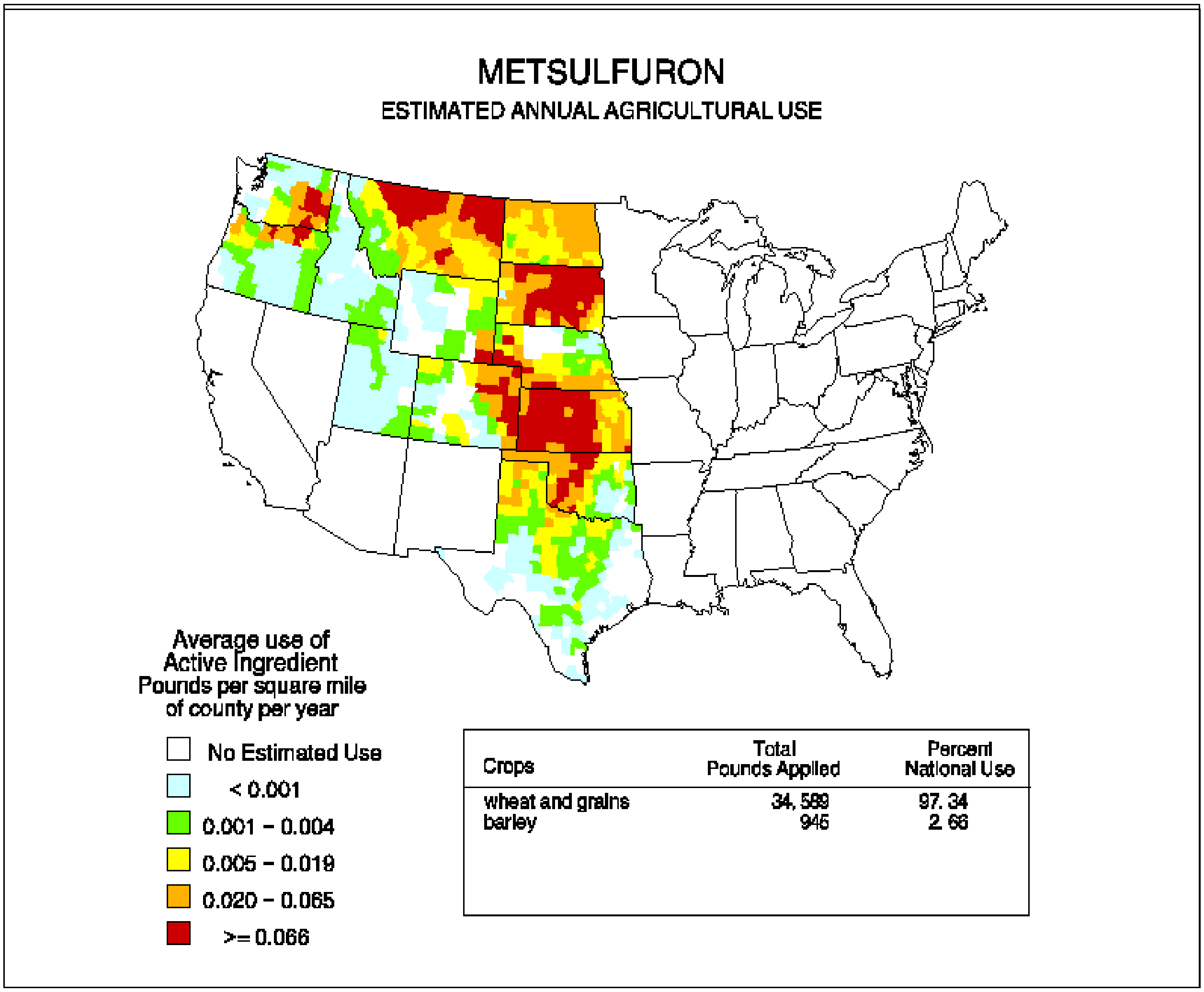


Figure 2-1: Agricultural Use of Metsulfuron Methyl in 1992 (USGS 1998).

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview. The mechanism of action of sulfonylurea herbicides, including metsulfuron methyl, is fairly well characterized in plants; however, the mechanism by which metsulfuron methyl is toxic to mammals and other animals is less clear. A variety of sulfonylureas reduce blood glucose by stimulating the release of insulin from pancreatic B cells, and some sulfonylureas reduce the hepatic extraction of insulin. Secondarily, sulfonylureas may affect levels of blood cholesterol and serum triglycerides. There is some evidence that metsulfuron methyl may cause both of these effects, at least at high doses. Metsulfuron methyl also is irritating to the skin and eyes.

In experimental mammals, the acute oral LD_{50} for metsulfuron methyl is greater than 5000 mg/kg, which indicates a low order of toxicity. Nevertheless, an oral dose 2000 mg/kg caused substantial mortality (20%). In addition, non-lethal signs of toxicity were apparent after single oral doses as low as 50 mg/kg.

The most common sign of acute, subchronic, and chronic toxicity is decreased body weight gain. The only other commonly noted effect involves changes in various hematological parameters as well as changes in absolute and relative organ weights. None of these changes, however, suggest a clear or specific target organ toxicity. There is speculation that the effects of metsulfuron methyl on the blood might be related to saccharin, which is a metabolite of metsulfuron methyl. At very high doses, saccharin caused hematological effects in mice. Appropriate tests have provided no evidence that metsulfuron methyl presents any reproductive risks or causes malformations or cancer.

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

The inhalation toxicity of metsulfuron methyl is not well documented in the literature. Available studies indicate that metsulfuron methyl induces irritant effects at very high exposure levels. Regardless, the potential inhalation toxicity of metsulfuron methyl is not of substantial concern to this risk assessment because of the implausibility of inhalation exposure involving high concentrations of this compound.

3.1.2. Acute Toxicity. Other than standard bioassays for acute toxicity that were conducted as part of the registration process, there is not much information regarding the acute toxicity of metsulfuron methyl. The most common measure of acute oral toxicity is the LD_{50}, the estimate of a dose that is most likely to cause 50% mortality in the test species after a single oral dose. As summarized in Appendix 1, there are only three acute oral studies involving exposure to metsulfuron methyl: Sarver (1990; 1991) and Ullman (1985a). These studies demonstrate that a single oral dose of up to 5000 mg/kg did not cause 50% mortality in any of the treated animal groups. Thus, the acute oral LD_{50} for metsulfuron methyl is correctly referenced as >5,000 mg/kg by ExToxNet (1996), USDA/FS (1998), and the U.S. EPA (1998b), and the compound is classified as *practically non-toxic*. Notably, however, a mortality rate of 20% was observed after a dose of 2000 mg/kg (Sarver 1991), and clinical signs of toxicity, including discharges (not otherwise specified) from eyes, nose, or mouth were observed after single oral doses as low as 50 mg/kg (Ullman 1985a). Other signs of toxicity after single oral doses of 500 mg/kg or greater include lethargy, weight loss, and sensitivity to touch. So, although metsulfuron methyl is not regarded as highly toxic, the compound is reported to have caused adverse effects at doses that are 100 times lower than the acute oral LD_{50}.

3.1.3. Subchronic or Chronic Systemic Toxic Effects. The subchronic or chronic toxicity of metsulfuron methyl to humans or mammals is not documented in the published literature, and all of the available toxicological data comes from unpublished studies that were conducted to support the registration of metsulfuron methyl as a herbicide. As summarized in Appendix 1, there are several subchronic studies in rats (Brock 1985; Burdock et al. 1982; Daly 1985; Pastoor 1985; Wiechman et al. 1982) and one subchronic study in dogs (Daly 1985). Two rat studies (Brock 1985; Wiechman et al. 1982) also involved assays for reproductive performance and are discussed further in section 3.1.4.

All of the subchronic rat studies report a decrease in body weight and/or growth rate (Brock 1985; Burdock et al. 1982; Daly 1985; Pastoor 1985; Wiechman et al. 1982). Brock (1985) noted that the decrease in body weight was accompanied by a decreased food conversion efficiency, which suggests that the effect could be associated with an underlying change in metabolism rather than a simple decrease in food intake. In the same study, a significantly lower serum glucose and higher serum cholesterol was observed in females at 1 and 3 months. The other effects commonly reported in the available subchronic studies involve changes in various hematological parameters and changes in absolute and relative organ weights. None of these changes, however, suggest a clear or specific target organ toxicity.

The chronic toxicity of metsulfuron methyl was investigated in rats (Burns 1984; Burdock and Hamada 1985), mice (Stadler 1984), and dogs (Burdock 1984). Like the subchronic studies, the chronic studies report decreased body weight as the most consistently observed adverse effect. Similarly, with respect to the subchronic studies, other signs of chronic toxicity included various changes in organ weights and changes in some hematological parameters that do not suggest any specific target organ toxicity.

As discussed in section 3.3., the U.S. EPA (1998a) derived an RfD for metsulfuron methyl and used body weight gain as the most sensitive effect. Based on a review of the studies considered by the U.S. EPA, this approach seems reasonable and appropriate.

3.1.4. Reproductive and Teratogenic Effects. Metsulfuron methyl was tested for its ability to cause birth defects (i.e., teratogenicity) as well as its ability to cause reproductive impairment. All of these studies are detailed in Appendix 1.

Teratogenicity studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Two such studies (each of which is detailed in Appendix 1) were conducted on metsulfuron methyl: one in rats (Feussner et al. 1982a) and one in rabbits (Feussner et al. 1982b). No signs of teratogenicity or fetal toxicity were noted in either study. Decreased weight gain was the only effect noted in the dams.

Another type of reproduction study involves exposing more than one generation of the test animal to the compound. One such study (Shriram Institute for Industrial Research, 1995) was conducted on metsulfuron methyl. In this study, the only effect noted was a decrease in growth rate at doses of 50 mg/kg/day or greater. As noted in section 3.1.3, this effect is also commonly seen in standard subchronic toxicity studies.

As discussed above, some test animals were allowed to mate in two of the subchronic oral toxicity studies in order to assay for potential reproductive effects. In the dietary study (Wiechman et al. 1982), no adverse effects were noted. In a gavage study (Christian and Doll 1985), there were no significant dose-related incidences of specific fetal malformations observed by external, soft tissue, or skeletal examination although various non-specific effects were noted in the offspring at maternally toxic doses.

In a recent review of these studies, the U.S. EPA (1998b) concluded that:

> *The results of a series of studies indicated that there were no reproductive, developmental or teratogenic hazards associated with the use of metsulfuron methyl. ... In studies conducted to evaluate developmental toxicity potential, metsulfuron methyl was neither teratogenic nor uniquely toxic to the conceptus (i.e., not considered a developmental toxin).*

The current review of these studies supports this assessment.

3.1.5. Carcinogenicity and Mutagenicity. As summarized in section 3.1.3, none of the chronic toxicity studies conducted on metsulfuron methyl found evidence of carcinogenic activity. In addition, *in vivo* and *in vitro* studies conducted in rats and mice indicate that metsulfuron methyl is not mutagenic. Single exposure to ≤5000 mg/kg bw by gavage did not induce chromosome aberrations in the bone marrow cells of male or female Sprague-Dawley rats (Ullman 1985a, MRID 00148642) or CD-1 mice (Ullman 1985b, MRID 00148644). And *in vitro* studies indicate that concentrations ≤3000 μg/mL metsulfuron methyl failed to induce unscheduled DNA synthesis in primary rat hepatocyte cultures (Vincent 1985, MRID 00148643; Bentley 1993, MRID 43035601). Furthermore, metsulfuron methyl was negative in a CHO/HPRT gene mutation assay with and without S-9 activation (Rickard 1985, MRID 00149671). Based on a review of these studies, the U.S. EPA (1998b) concluded that: *"the weight-of-evidence indicates that metsulfuron methyl is neither genotoxic nor mutagenic* and that *"Metsulfuron methyl was not oncogenic in the chronic rat and mouse bioassays"*. Thus, there is no basis for contending that exposure to metsulfuron methyl will pose an increased risk of cancer.

3.1.6. Effects on the Skin and Eyes.
Metsulfuron methyl was tested for irritant effects on the skin and eyes of rabbits (Appendix 1). When applied directly to the skin, technical grade metsulfuron methyl caused slight to moderate edema, erythema, and thickening of the skin (associated with adherence of the compound to the skin) (Gargus 1985a,b).   Similarly, Finlay (1996) report that a dermal application of 0.5 g/animal of the commercial formulation, Escort caused edema and erythema in rabbits. When applied directly into the eyes of rabbits, metsulfuron methyl caused mild conjunctival redness in all six animals tested and slight corneal opacity and slight chemosis in one rabbit (Brock 1987). Accordingly, the MSDS for both Ally and Escort warn that exposure to these formulations may cause eye and skin irritation (C&P Press 1999).

3.1.7. Systemic Toxic Effects from Dermal Exposure. Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared to an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies. Thus, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which metsulfuron methyl is likely to be absorbed from the surface of the skin.

The available toxicity studies summarized in Appendix 1 indicate that dermal exposure to 2000 mg/kg metsulfuron methyl (Gargus 1985a;b) caused weight loss similar to that observed in experimental mammals after acute, subchronic and chronic oral exposure (see section 3.1.3). The dermal studies, however, are much less detailed than the oral studies and did not assay for hematological changes or other signs of systemic toxicity. As discussed in sections 3.1.2. and 3.1.3, hematological effects were observed in experimental mammals after oral exposure to metsulfuron methyl.

The kinetics of dermal absorption of metsulfuron methyl are not documented in the available literature. 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. Using the method recommended by U.S. EPA (1992), the estimated dermal permeability coefficient for metsulfuron methyl is 0.0000005 cm/hour with a 95% confidence interval of 0.0000001-0.000002 cm/hour. These estimates are used in all exposure assessments that are based on Fick's first law. The calculations for these estimates are presented in worksheet B05.

For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the skin's surface, dermal absorption rates (proportion of the deposited dose per unit time) rather than dermal permeability rates are used in the exposure assessment. Using the methods detailed in Durkin et al. (1998), the estimated first-order dermal absorption coefficient is 0.000087 $hour^{-1}$ with 95% confidence intervals of 0.000012-0.00063 $hour^{-1}$. The calculations for these estimates are presented in worksheet B04.

The lack of experimental data regarding the dermal absorption of metsulfuron methyl adds substantial uncertainties to this risk assessment. Nonetheless, the available data, albeit relatively sparse, do not suggest that metsulfuron methyl is likely to be absorbed through the skin in amounts that may cause systemic toxic effects. Uncertainties in the rates of dermal absorption, although they are substantial, can be estimated quantitatively and are incorporated in the human health exposure assessment (section 3.2).

3.1.8. Inhalation Exposure. As summarized in Appendix 1, there are two inhalation toxicity studies on metsulfuron methyl (Burgess et al. 1983; Hutt 1985). Both studies follow a relatively standard protocol involving acute (4-hour) exposure to relatively high concentrations (>1.3 mg/L or >13,000 mg/m^3). No mortality or gross tissue pathology was observed in either study. A transient decrease in body weight was observed, consistent with both oral and dermal routes of administration. The only other signs of toxicity were hair loss, nasal discharges (probably attributable to irritation), and, in one rat, abnormal lung sounds (Hutt 1985).

These extremely limited data suggest only that metsulfuron methyl can induce irritant effects and perhaps systemic toxic effects at very high exposure levels. As discussed in section 3.3, this finding is not directly relevant to this risk assessment because of the implausibility of exposure to such high concentrations of the compound.

3.1.9. Impurities, Metabolites, and Formulation Additives.

3.1.9.1. Impurities -- There is no published information regarding the impurities in technical grade metsulfuron methyl or any of its commercial formulations. Information on all of the impurities in technical grade metsulfuron methyl were disclosed to the U.S. EPA (Brennan 1995), and the information was obtained and reviewed as part of this risk assessment. Because this information is classified as confidential business information, details about the impurities cannot be disclosed. Nonetheless, all of the toxicology studies on metsulfuron methyl involve technical metsulfuron methyl, which is presumed to be the same as or comparable to the active ingredient in the formulation used by the Forest Service. Thus, if toxic impurities are present in technical metsulfuron methyl, they are likely to be encompassed by the available toxicity studies using technical grade metsulfuron methyl.

3.1.9.2. Metabolites -- The metabolism of metsulfuron methyl was studied in rats (Hundley 1985), hens (Charlton and Bookhart. 1996), and, as summarized by U.S. EPA (1998b), in goats. In all species, metsulfuron methyl is eliminated rapidly with a half-time of 1 day or less. Most of the material is excreted as the unchanged compound. The major metabolites (5-15% of the administered dose) are associated with cleavage of the urea bridge (i.e., aminosulfonyl benzoate or sulfonamide and the triazine amine derivative). Other metabolites are formed by demethylation and include saccharin and benzoic acid, which are environmental metabolites.

The toxicity of the metabolites of metsulfuron methyl is likely to be encompassed by the available mammalian toxicity studies. An exception to this would be metabolites that are formed in the environment but not in mammals. As discussed by the U.S. EPA (1998b):

> *There were two major plant specific metabolites identified, that were not detected in the rat. However, in residue studies, no detectable residues of parent or major plant unique metabolites, were found in the feed and food items of cereal crops treated at the maximum seasonal use rate. Hence, toxicity testing of other degradation products of metsulfuron methyl was not needed.*

3.1.9.3. Inerts -- Escort, the commercial formulation of metsulfuron methyl used by the Forest Service, contains materials other than metsulfuron methyl that are included as adjuvants to improve either efficacy or ease of handling and storage. The identity of these materials is confidential. The additives were disclosed to the U.S. EPA (Du Pont 1985b,c) and were reviewed in the preparation of this risk assessment. All that can be disclosed explicitly is that none of the additives are classified by the U.S. EPA as toxic.

As reviewed by Levine (1996), testing requirements for pesticide inerts that have been used as additives or adjuvants for many years are minimal, and this is a general problem in many pesticide risk assessments. For new inerts, the U.S. EPA does require more extensive testing (Levine 1996).

3.1.10. Toxicological Interactions. As indicated in section 2.3, the Forest Service may apply Escort in combination with other herbicides, particularly 2,4-D. There is no published literature or information in the FIFRA files that would permit an assessment of potential toxicological interactions between metsulfuron methyl and 2,4-D or any other compounds.

3.1.11. Mechanism of Action. Although the mechanism of phytotoxic action of sulfonylurea herbicides including metsulfuron methyl is characterized in some detail (section 4.1.2.4), the mechanism of toxic action in mammals or other animal species is not well characterized.

As noted in the recent review on a closely related herbicide, sulfometuron methyl (Cox 1993), and described in detail by Melander et al. (1989), several of the sulfonylureas are biologically active in humans and are used or were considered for use in the treatment of non-insulin-dependent diabetes mellitus (NIDDM or type 2 diabetes). A variety of sulfonylureas reduce blood glucose, stimulating the release of insulin from pancreatic B cells, and some sulfonylureas may reduce the hepatic extraction of insulin. Secondarily, some sulfonylureas may affect levels of blood cholesterol and serum triglycerides. As noted above, decreased blood glucose levels and increased cholesterol were observed in rats after subchronic exposure to metsulfuron methyl (Brock 1985).

Hematological changes were observed in some of the mammalian toxicity studies. Recently, exposure to some sulfonamides are associated (p=0.004) with the development of hemolytic anemia in humans (Issaragrisil et al. 1997). This finding is supported by an earlier, more qualitative association of sulfonamide with anemia in humans (Dickerman 1981). Moreover, saccharin, which is a metabolite of metsulfuron methyl, was shown to cause hematological effects in mice (Prasad and Rai 1987). The doses of saccharin associated with hematological effects in mice—500, 1000, and 1500 mg/kg/day—are much higher than the doses of metsulfuron methyl that caused similar effects in rats and dogs (i.e., 20-30 mg/kg/day) (section 3.3).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. There are no occupational exposure studies in the available literature that are associated with the application of metsulfuron methyl. 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 both types of applications, central estimates of worker exposure are similar: 0.0003 mg/kg/day for backpack applications and 0.0004 mg/kg/day for boom spray applications. The upper limits of the exposure estimates are 0.012 mg/kg/day for backpack applications and 0.02 mg/kg/day for boom spray applications. Although Escort is registered for aerial applications (helicopter and sometimes fixed wing), the Forest Service does currently used this method. Nonetheless, the aerial application method is included in this risk assessment in the event that the Forest Service considers it an option. The central estimates of worker exposure associated with aerial application are similar to those for ground application, 0.0003 mg/kg/day, although the upper limit of the exposure estimate, 0.0016, is much lower than those for ground applications.

Except in the case of accidental exposure, the levels of metsulfuron methyl to which the general public might be exposed should be far less than the levels for workers. Longer-term exposure scenarios for the general public lead to central estimates of daily doses in the range of 0.000001-0.0002 mg/kg/day with upper limits of exposure in the range of 0.0001-0.003 mg/kg/day. While these exposure scenarios are intended to be conservative, they are nonetheless plausible. Accidental exposure scenarios result in central estimates of exposure of up to 0.000001 mg/kg/day with upper ranges of 0.17 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.

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 worksheets that accompany this risk assessment, as indicated in Table 3-1.

3.2.2.1. General Exposures **--** The assumptions used in worker exposure assessments are detailed in worksheets A03a (backpack), A03b (boom spray), and A03c (aerial). No worker exposure studies with metsulfuron methyl 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, the molecular weight of metsulfuron methyl is 381.4 and the log K_{ow} at pH 7 is about -1.7. Because the K_{ow} for metsulfuron methyl is beyond the range of K_{ow} values used in formulating the regression model, confidence in these assessments are diminished. This uncertainty is compounded by the uncertainties inherent in the available data on worker exposure. As described in 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); however, pharmacokinetic differences among individuals (i.e., how individuals absorb and excrete the compound) also may be important.

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 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, like 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 0.02 lbs metsulfuron methyl/acre is almost equal to the 1997 average application rate of 0.018 lbs a.i./acre when metsulfuron methyl was used as the sole herbicide (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 range of exposure rates and the ranges for the amounts handled per day. The lower and upper limits are similarly calculated using the lower and upper ranges of the amount handled, acres treated per day, and worker exposure rate.

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 to involve various dermal exposure scenarios.

Metsulfuron methyl can cause irritant effects to the skin and 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, there appear to be no reasonable approaches to modeling this type of exposure scenario quantitatively. Consequently, accidental exposure scenarios of this type are considered qualitatively in the risk characterization (section 3.4).

There are various methods for estimating absorbed doses associated with accidental dermal exposure (U.S. EPA 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. As specified in Table 3-1, the details of these exposure estimates are presented in the worksheets appended to this risk assessment.

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 metsulfuron methyl. Nonetheless, there is a noteworthy similarity between the exposure scenario in which contaminated gloves are worn for 1 hour and the exposure scenario in which a chemical solution is spilled on to the skin surface of the hands and cleaned after 1 hour. Confidence in these assessments is enhanced somewhat by the fact that two similar scenarios based on different empirical relationships yield similar estimates of exposure.

3.2.3. General Public.

3.2.3.1. General Considerations -- Under normal conditions, members of the general public should not be exposed to substantial levels of metsulfuron methyl. 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, and the details regarding the assumptions and calculations involved in these exposure assessments are provided in worksheets D01-D09. The remainder of this section focuses on a qualitative description 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 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 direct spray scenarios, it is assumed that during a ground application, a naked child is sprayed directly with metsulfuron methyl. The scenario also assumes that the child is completely covered (that is, 100% of the surface area of the body is exposed), which makes this an extremely conservative exposure scenario that is likely to represent the 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. These assumptions are taken from various U.S. EPA reports (U.S. EPA 1985, 1992, 1996) and are relatively well documented.

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 metsulfuron methyl, 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.

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. Although metsulfuron methyl is chemically stable in pure aqueous solutions, it is degraded in natural waters by hydrolysis and photolysis (Bastide et al. 1994; Du Pont 1985a,b,c), and concentrations of metsulfuron methyl in water are further reduced by dispersal. For this risk assessment, the two types of estimates made for the concentration of metsulfuron methyl in ambient water are acute/accidental exposure and longer-term exposure.

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 metsulfuron methyl 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 a 425-fold difference in the upper and lower limits of the exposure assessment. As detailed in worksheet D06, this wide range is attributable primarily to differences in the field dilutions of the commercial formulation (a factor of about 400) rather than differences in the estimated amounts of water that might be consumed (only a factor of about 2.5).

3.2.3.4.2. LONGER-TERM EXPOSURE -- The scenario for chronic exposure to metsulfuron methyl from contaminated water is detailed in worksheet D07. This scenario assumes that an adult (70 kg male) consumes contaminated ambient water for a lifetime.

There are no monitoring studies available on metsulfuron methyl that permit an assessment of concentrations in ambient water associated with ground or aerial applications of the compound over a wide area. Consequently, for this component of the exposure assessment, estimates of levels in ambient water are made based on the GLEAMS model. Details of this assessment are given in Appendix 2. As indicated in this Appendix, the exposure assessments are made for applications to both clay and sand. While there are temporal differences in the concentrations that might be expected, maximum worst-case concentrations for both soil types lead to peak concentrations in ambient water of about 0.006 mg/L at an application rate of 0.02 lbs a.i./acre. This upper range concentration is used in this exposure assessment (worksheet B07). As indicated in Appendix 2, metsulfuron methyl is not likely to accumulate in water with repeated annual applications.

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

The only available study regarding the bioconcentration of metsulfuron methyl is a standardized test that is required as part of the registration process (Han and Anderson 1984). As summarized in Appendix 3, Han and Anderson (1984) exposed bluegill sunfish to phenyl-^{14}C labeled metsulfuron methyl at concentrations of 0.01 and 1.0 mg/L for 28 days and found no indication of bioconcentration. Thus, 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 metsulfuron methyl 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 metsulfuron methyl concentrations in ambient water are based on GLEAMS modeling as indicated in Appendix 2..

3.2.3.6. Oral Exposure from Contaminated Vegetation -- Under normal circumstances and in most types of applications, it is extremely unlikely that humans will consume vegetation contaminated with metsulfuron methyl. 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 metsulfuron methyl (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 metsulfuron methyl 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 and the dissipation on the vegetation is estimated using a foliar half-time of 30 days (Knisel, et al. 1992). Although the duration of exposure appears to be somewhat arbitrarily chosen, it is intended to represent the consumption of contaminated vegetation that might be available over one season. Longer durations could be used for certain kinds of vegetation but would lower the estimated dose (i.e., would result in a less conservative exposure assessment). The central estimate of dose for the longer-term exposure period is taken as the geometric mean of the initial concentration and concentration after 90 days.

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 metsulfuron methyl. 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 and the range of application rates for metsulfuron methyl.

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview. The Office of Pesticide Programs of the U.S. EPA has derived an RfD of 0.3 mg/kg/day for metsulfuron methyl. This is identical to the Agency wide RfD of 0.25 mg/kg/day but rounded to one significant digit. This RfD is based on a chronic rat NOAEL of 500 ppm in the diet with an estimated daily dose of 25 mg/kg/day and an uncertainty factor of 100. In the same study, the LOAEL was 250 mg/kg/day (5000 ppm in the diet) and the only effect noted was a decrease in body weight. No frank signs of toxicity were seen.

3.3.2. Existing Guidelines. The most recent RfD for metsulfuron methyl is 0.3 mg/kg/day, a value derived by the U.S. EPA's Office of Pesticide Programs (U.S. EPA 1998b) and accepted by the U.S. EPA agency work group on RfDs (U.S. EPA 1998a).

This RfD is based on a 52-week dietary exposure study using Sprague-Dawley rats. The rats were given metsulfuron methyl in the diet at concentrations of 0 (control), 5, 25, 500, 2500, or 5000 ppm for 52 weeks (Burns 1984). The investigators observed a statistically significant, treatment related decrease in mean body weight in males (2500 and 5000 ppm) at 13 weeks and in males and females (5000 ppm) at 52 weeks as well as a statistically significant decrease in body weight gain, compared with controls, in males and females (500, 2500, and 5000 ppm) at 13 weeks and in males and females (5000 ppm) at 52 weeks were observed. No overt signs of toxicity were observed at any dose level. As summarized in Appendix 1, there were various changes in relative and absolute organ weights as well as in hematological parameters; however, these effects either were not statistically significant or did not suggest a coherent pattern of toxicity.

In deriving the RfD, the U.S. EPA accepted the 500 ppm exposure group as a NOAEL and estimated the daily intake at 25 mg/kg/day and used an uncertainty factor of 100. The uncertainty factor consists of two components: a factor of 10 for extrapolating from animals to humans and a factor of 10 for extrapolating to sensitive individuals within the human population.

3.3.3. Dose-Severity Relationships. As summarized in section 3.2, all estimated levels of exposure to metsulfuron methyl are substantially less than the RfD, and most estimated levels are are below the RfD by factors of over 100 to nearly 10 billion. Consequently, there is no need to develop elaborate dose-severity relationships to characterize risk. In addition, as shown in Appendix 1, there is no practical basis for developing dose-severity relationships because the available data do not suggest that metsulfuron methyl will cause severe signs of toxicity even at extremely high dose levels relative to reasonable estimates of exposure.

3.4. RISK CHARACTERIZATION

3.4.1. Overview. None of the exposure scenarios for workers or members of the general public result in levels that exceed the RfD. Based on central estimates, the levels of exposure will be below the RfD by factors of 1000 to well over 1 million. Thus, there is no basis for contending that metsulfuron methyl is likely to pose any identifiable risk to human health. This is consistent with the recent evaluation of metsulfuron methyl by the U.S. EPA.

The only reservation associated with this assessment of metsulfuron methyl is the same reservation associated with any risk assessment in which no plausible hazards can be identified: ***Absolute safety cannot be proven and the absence of risk can never be demonstrated***. No chemical, including metsulfuron methyl, is studied for all possible effects. Furthermore, using data from laboratory animals to estimate hazard or the lack of hazard to humans is an uncertain process. 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 metsulfuron methyl in

Forest Service programs does not pose any identifiable hazard to workers or members of the general public.

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

3.4.2. Workers. A quantitative summary of the risk characterization for workers is presented in Table 3-3. 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 0.3 mg/kg/day, as derived in section 3.3.2.

Given the very low hazard quotients for accidental exposure, the risk characterization is reasonably unambiguous. None of the accidental 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 is a factor of more than 1000 lower than the level of concern (i.e., a hazard quotient of 0.0009 as the upper limit for a spill on the lower legs), far more severe and less plausible scenarios are required to suggest a potential for systemic toxic effects. As discussed in section 3.2, confidence in this assessment is diminished by the lack of information regarding the dermal absorption kinetics of metsulfuron methyl 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 1000 or greater in order for the basic characterization of risk to change.

Similarly, the hazard quotients for all of the application methods are below a level of concern by a factor of at least 25 for upper limits and at least 1000 for central estimates. As with the accidental exposures, there are substantial uncertainties in the exposure assessment; however, given the very low hazard quotients, these uncertainties do not have a substantial impact on the characterization of risk.

As discussed in section 3.1.6, metsulfuron methyl can cause irritation 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 metsulfuron methyl. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of the compound.

3.4.3. General Public. The quantitative hazard characterization for the general public is summarized in Table 3-4. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the U.S. EPA RfD of 0.3 mg/kg/day.

None of the longer-term exposure scenarios approach a level of concern. Furthermore, none of the acute/accidental scenarios exceed a level of concern, based on central estimates of exposure, although a hazard index for the consumption of contaminated water after an accidental spill approaches, but remains below, a 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 indices 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 scenario suggesting that the general public will be at substantial risk from longer-term exposure to metsulfuron methyl.

For the acute/accidental scenarios, exposure resulting from the consumption of contaminated water is of greatest concern; exposure resulting from the consumption of contaminated vegetation or fish is of marginal concern. 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 metsulfuron methyl, 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 metsulfuron methyl, such scenarios involve oral rather than dermal exposure.

3.4.4. Sensitive Subgroups. There is limited information to suggest that specific groups or individuals may be especially sensitive to the systemic effects of metsulfuron methyl. As indicated in section 3.1.3, the most sensitive effect of metsulfuron methyl appears to be weight loss; however, there is some suggestion that metsulfuron methyl may influence blood glucose levels and cholesterol regulation. If exposure levels were sufficient to induce decreases in serum glucose, individuals taking medication to lower serum glucose could be at increased risk. Nonetheless, this exposure scenario is highly implausible.

3.4.5. Connected Actions. As discussed in section 3.1.10, metsulfuron methyl may be applied in combination with other herbicides, 2,4-D. There are no animal data to suggest that metsulfuron methyl will interact, either synergistically or antagonistically with 2,4-D or any other herbicide.

3.4.6. Cumulative Effects. This risk assessment specifically considers the effect of repeated exposure in that the chronic RfD is used as an index of acceptable exposure even for acute exposure scenarios. In addition, as indicated in Appendix 2, this risk assessment considers the potential exposures associated with repeated annual applications of metsulfuron methyl.

Consequently, the risk characterizations presented in this risk assessment encompass the potential impact of long-term exposure and cumulative effects.

Table 3-1: Summary of Worker Exposure Scenarios

Scenario	Dose (mg/kg/day or event) Typical	Lower	Upper	Exposure Assessment Worksheet
General Exposures (dose in mg/kg/day)				
Directed ground spray (Backpack)	0.0003	0.000006	0.012	WSC01
Broadcast ground spray (Boom spray)	0.0004	0.000008	0.02	WSC02a
Aerial applications	0.0003	0.000005	0.0016	WSC02b
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	4.40e-09	3.00e-10	7.20e-07	WSC03
Contaminated Gloves, 1 hour	2.64e-07	1.80e-08	4.00e-05	WSC03
Spill on hands, 1 hour	4.00e-07	1.44e-08	1.00e-04	WSC04
Spill on lower legs, 1 hour	1.00e-06	3.55e-08	3.00e-04	WSC04

Table 3-2: 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	0.00001	0.0000005	0.004	WSD01
Direct spray, lower legs	Woman	0.000001	0.00000005	0.0004	WSD02
Dermal, contaminated vegetation	Woman	0.00004	0.000003	0.0024	WSD03
Contaminated fruit, acute exposure	Woman	0.0002	0.00013	0.007	WSD04
Contaminated water, acute exposure	Child	0.002	0.0005	0.15	WSD06
Consumption of fish, general public	Man	0.0001	0.00002	0.0031	WSD08
Consumption of fish, subsistence populations	Man	0.0003	0.00011	0.015	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.00005	0.00003	0.003	WSD05
Consumption of water	Man	0.0002	0.0001	0.002	WSD07
Consumption of fish, general public	Man	0.000001	0.000001	0.0001	WSD09
Consumption of fish, subsistence populations	Man	0.00001	0.000004	0.0005	WSD09

Table 3-3: Summary of risk characterization for workers

RfD	0.3	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.0009	0.00002	0.04	WSC01
Broadcast ground spray (Boom spray)	0.001	0.00003	0.08	WSC02a
Aerial applications	0.001	0.00002	0.005	WSC02b
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	0.00000001	0.000000001	0.000002	WSC03
Contaminated Gloves, 1 hour	0.0000009	0.00000006	0.0001	WSC03
Spill on hands, 1 hour	0.000001	0.00000005	0.0003	WSC04
Spill on lower legs, 1 hour	0.000003	0.0000001	0.0009	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 3-1for summary of exposure assessment.

Table 3-4: Summary of risk characterization for the general public [1] .

RfD		0.3	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00001	0.000002	0.01	WSD01
Direct spray, lower legs	Woman	0.000003	0.0000002	0.001	WSD02
Dermal, contaminated vegetation	Woman	0.0001	0.000009	0.008	WSD03
Contaminated fruit, acute exposure	Woman	0.0007	0.0004	0.02	WSD04
Contaminated water, acute exposure	Child	0.007	0.002	0.5	WSD06
Consumption of fish, general public	Man	0.0003	0.0001	0.01	WSD08
Consumption of fish, subsistence populations	Man	0.001	0.0004	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0002	0.0001	0.01	WSD05
Consumption of water	Man	0.001	0.0003	0.01	WSD07
Consumption of fish, general public	Man	0.000003	0.000003	0.0003	WSD09
Consumption of fish, subsistence populations	Man	0.00003	0.00001	0.002	WSD09

[1] Hazard quotient is the level of exposure divided by the RfD then rounded to one significant decimal place or digit. See Table 3-2for summary of exposure assessment.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview. The mammalian toxicity of metsulfuron methyl is relatively well characterized in experimental mammals; however, there is relatively little information regarding non-target wildlife species. It seems reasonable to assume the most sensitive effects in wildlife mammalian species will be the same as those in experimental mammals (i.e., decreased body weight gain). Several acute toxicity studies and two reproduction studies are available on the toxicity of metsulfuron methyl to birds. These studies indicate that birds appear to be no more sensitive than experimental mammals to the toxic effects of metsulfuron methyl, with the major effect again being weight loss. There are also several acute honey bee assays that indicate that bees are no more sensitive than either mammals or birds to metsulfuron methyl. At exposure rates that exceed the highest recommended application rate by about a factor of 3, metsulfuron methyl appears to be somewhat toxic to the Rove beetle, *Aleochara bilineata*, causing a 15% decrease in egg hatching.

The toxicity of metsulfuron methyl to terrestrial plants was studied extensively and is well characterized. Metsulfuron methyl inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids, all of which are essential for plant growth. This effect is considered quantitatively in the dose-response assessment and is one of the primary effects of concern in this risk assessment.

Terrestrial microorganisms also have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. There are laboratory and field studies on the effects of metsulfuron methyl to soil microorganisms. These studies suggest that transient effects on soil bacteria are plausible.

The available data suggest that metsulfuron methyl, like other herbicides, is much more toxic to aquatic plants than to aquatic animals. Frank toxic effects in fish are not likely to be observed at concentrations less than or equal to 1000 mg/L. Aquatic plants are far more sensitive than aquatic animals to the effects of metsulfuron methyl, although there appear to be substantial differences in sensitivity among species of macrophytes and unicellular algae. In general, the macrophytes appear to be more sensitive.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals– As summarized in the human health risk assessment (see section 3.1), the mode of action of metsulfuron methyl in mammals is not well understood. There are several standard toxicity studies in experimental mammals that were conducted as part of the registration process. The most consistent toxic effect observed in mammals after exposure to metsulfuron methyl is body weight loss; furthermore, there is some information suggesting that metsulfuron methyl may influence glucose and cholesterol metabolism. Other than these effects, metsulfuron methyl does not appear to cause specific target organ toxicity in mammals.

The acute toxicity of metsulfuron methyl is relatively low, with an oral LD_{50} of >2000 mg/kg. Nevertheless, the mortality rate was substantial (e.g. 20%) after a dose of 2000 mg/kg and non-lethal signs of toxicity were observed after single oral doses as low as 50 mg/kg.

The subchronic and chronic toxicity studies on metsulfuron methyl were conducted in dogs, mice, and rats. As discussed in section 3.1.3., the most sensitive effects involve changes to blood and decreased body weight gain, with a NOAEL of 500 ppm in the diet or 25 mg/kg bw/day.

4.1.2.2. Birds– As summarized in Appendix 4, there are several acute and subchronic studies available on the toxicity of metsulfuron methyl to birds (Beavers 1984a,b,c; Beavers et al. 1996a,b; Fink et al. 1981a,b). In quail, the acute oral LD_{50} of metsulfuron methyl administered by gavage is >2000 mg/kg (Beavers 1984b), as it is in mammals. The only remarkable non-lethal effect was a decrease in body weight, an effect that is also commonly seen in experimental mammals. Exposure to dietary concentrations of metsulfuron methyl up to 5620 ppm over a 5-day exposure period resulted in no mortality or signs of toxicity other than decreased body weight gain. In the dietary study by Fink et al (1981b), some of the animals in the 5620 ppm exposure group may have been lethargic.

By far the most relevant studies for this risk assessment are the two 23- week feeding studies conducted by Beavers et al. (1996a,b) in bobwhite quail and mallard ducks. In both of these studies, dietary levels of up to 1000 ppm had no effect on body weight, food consumption, or reproductive performance.

4.1.2.3. Terrestrial Invertebrates– As summarized in Appendix 5, several standard bioassays were conducted on the toxicity of metsulfuron methyl to bees (Meade 1984a,b). For the most part, the results are unremarkable indicating that the acute LD_{50} of metsulfuron methyl to bees is greater than 25 μg/bee and possibly greater than 100 μg/bee. Using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993), these values correspond to doses ranging from about 270 to 1075 mg/kg [0.025 mg/0.000093 kg to 0.1 mg/0.000093 kg].

The open literature includes two toxicity studies involving other terrestrial invertebrates exposed to metsulfuron methyl: Oomen et al. (1991) and Samsoe-Petersen (1995). Following the protocols adopted by European community for testing toxicity to beneficial insects, Oomen et al. (1991) summarizes a series of bioassays on the toxicity of several pesticides, including metsulfuron methyl, to the predatory mite, *Phytoseiulus persimilis.* The study classifies the metsulfuron methyl formulation Ally as harmless; however, specific details about the assay and the endpoints measured are not provided in the publication.

Samsoe-Petersen 1995 assayed the toxicity of metsulfuron methyl to the eggs of the Rove beetle, *Aleochara bilineata*. In this study, a 15% decrease in egg hatching but no mortality in adult beetles and no effects on egg production were noted after direct spray of 0.067% product (20% a.i.) at a level of 6 $\mu L/cm^2$.

4.1.2.4. Terrestrial Plants (Macrophytes)–The toxicity of metsulfuron methyl to terrestrial plants was studied extensively and is well characterized (e.g., Anderson et al. 1989; Badon et al. 1990; Brudenell et al. 1995; Fayez et al. 1994; Kotoula-Syka et al. 1993; Pool and De Villiers 1993; Stork and Hannah 1996). Metsulfuron methyl inhibits acetolactate synthase (ALS), an enzyme that catalyzes the biosynthesis of three branched-chain amino acids (valine, leucine, and isoleucine), all of which are essential for plant growth. Other ALS inhibiting herbicides include other sulfonylureas such as sulfometuron methyl as well as imidazolinones, triazolopyrimidines, and pyrimidinylthiobenzoates.

The most relevant laboratory bioassays regarding the toxicity of metsulfuron methyl to terrestrial plants by direct spray are summarized in Appendix 6. The quantitative use of these studies for this risk assessment is discussed in section 4.3. Levels of metsulfuron methyl in soil (James et al. 1995; Kotoula-Syka et al. 1993; Stork and Hannah 1996) or soil leachate (Guenther et al. 1993) were examined in several bioassays involving various plant species. These studies calibrate the response of various plant species to metsulfuron methyl residues in soil and use the responses in plants to measure or estimate unknown concentrations of metsulfuron methyl in soil. As discussed in the dose-response assessment (section 4.3), these studies are used primarily to quantify the potential effects of soil residues on non-target plant species.

The use of bioassays to measure the amount of a chemical in a medium, like soil, is a long-standing and well-studied practice. The method of extending that use to assess the toxicity of a chemical to non-target plant species is less direct because the bioassays may vary from laboratory to laboratory. For example, Streibig et al. (1995) examined variability in greenhouse bioassays of EC_{50} values in *Brassica rapa*. Although most of the laboratories reported EC_{50} values within a factor of 10, EC_{50} values among all of the laboratories varied between 0.05 and 3.9 g a.i./ha, a factor of 78 fold.

Some of this variability noted by Streibig et al. (1995) could be associated with different experimental conditions, specifically a negative correlation with soil pH and a positive correlation with organic matter in soil. The negative correlation of EC_{50} values with soil pH (i.e., lower EC_{50} values or greater toxicity in alkaline or high pH soils) is consistent with bioassays of root growth in corn, sunflowers, lentils, and sugar-beets (James et al. 1995; Pool and De Villiers 1993; Pool and Du Toit 1995). As discussed by Pool and De Villiers (1993), the increase in toxicity may be associated with increased persistence of metsulfuron methyl in soil with a high pH (i.e., lower acid levels and thus lower rates of acid mediated hydrolysis).

The toxicity of metsulfuron methyl may also be influenced by the use of surfactants or other herbicides. Some surfactants, like Silwet L-77, Activator 90, and LI-700 enhance efficacy while others like Bond, appear to retard efficacy (Balneaves 1992a,b,c; Lawrie and Clay 1993; McDonald et al. 1994). A recent study by Holloway et al. (1995) suggests that the MCPA ester may have a synergistic effect with metsulfuron methyl but that the amine salt of MCPA may have an antagonistic action. It is not clear, however, how significant these effects might be in the field because synergism was apparent at the ED90 but not ED50 level. There is additional evidence that metsulfuron methyl inhibits the phytotoxicity of tralkoxydim in *Avena fatua* (Devine and Rashid 1993) as well as the phytotoxicity of 1,8-naphthalic anhydride to corn roots (Milhomme and Bastide 1990). Moreover, the efficacy of metsulfuron methyl was enhanced somewhat by sequential but not concurrent applications with imazapyr (Lawrie and Clay 1993).

4.1.2.5. Terrestrial Microorganisms– Terrestrial microorganisms have an enzyme that is involved in the synthesis of branched chain amino acids, which is functionally equivalent to the target enzyme in terrestrial macrophytes. Metsulfuron methyl at a concentration of 5 ppm in culture inhibited the growth of several strains of *Pseudomonas*. This effect was attributed to ALS inhibition because the bacteria grew normally with excess amounts of valine, leucine, and isoleucine (Boldt and Jackson 1998). The same concentration in soil (i.e., 5 mg/kg) decreased levels of amylase, urease, and protease activity in loamy sand and clay loam soil (Ismail et al. 1998). The reduced amylase and urease levels were apparent for the 28-day observation period; protease activity was reduced on day 7 but recovered by day 14 (Ismail et al. 1998, Figure 1 p. 31). At surface application rates of 0.05-0.075 kg/ha, transient decreases in soil bacteria were apparent for 3 days but reversed completely after 9 days (Ismail et al. 1996).

4.1.3. Aquatic Organisms.

4.1.3.1. Fish– Standard toxicity bioassays to assess the effects of metsulfuron methyl on fish are summarized in Appendix 7. The lowest concentration at which mortality was observed in any species of fish is 100 mg/L (Hall 1984b). At this level, mortality was observed in 3/10 bluegill sunfish over a 96-hour exposure period. No mortality, however, was observed in 10 bluegills exposed to 1000 mg/L (Hall 1984a). Because of the lack of a dose-response relationship, Hall (1984a) asserts that the mortality in the 100 mg/L exposure group was probably incidental rather than treatment related. Given the lack of a dose-response relationship in the Hall (1984a) study as well as the results of all of the other bioassays summarized in Appendix 7, it appears that compound-related mortality after acute exposure is not likely to be observed in fish exposed to concentrations less than or equal to 1000 mg/L.

Kreamer (1996) is the only study available regarding the toxicity of metsulfuron methyl to fish, eggs, or fry. These investigators observed no effects on rainbow trout hatching, larval survival, or larval growth over a 90-day exposure period at a concentration of up to 4.7 mg/L. Concentrations greater than 8 mg/L resulted in small but significant decreases hatching and survival of fry.

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

4.1.3.3. Aquatic Invertebrates– Standard toxicity bioassays to assess the effects of metsulfuron methyl on aquatic invertebrates are summarized in Appendix 8. Metsulfuron methyl appears to be relatively non-toxic to aquatic invertebrates, based on acute bioassays in *Daphnia*, with an acute LC_{50} value for immobility of 720 mg/L and an NOEC for reproduction of 150 mg/L (Appendix 8). The only effect seen in a 21-day Daphnia study was a decrease in growth (Hutton 1989), which was observed at concentrations as low as 5.1 mg/L. At concentrations less than 30 mg/L, the effect was not statistically significant. In aquatic invertebrates, as in birds and mammals, decreased growth appears to be the most sensitive endpoint. Wei et al. (1999) report that neither metsulfuron methyl nor its degradation products are acutely toxic to *Daphnia* at concentrations that approach the solubility of the compounds in water at pH 7. The specific exposure concentrations are not reported in this publication.

4.1.3.4. Aquatic Plants– Standard toxicity bioassays to assess the effects of metsulfuron methyl on aquatic plants were submitted to the U.S. EPA in support of the registration of metsulfuron methyl and are summarized in Appendix 9. As might be expected for a herbicide, aquatic plants are far more sensitive than aquatic animals to the effects of metsulfuron methyl. The available information summarized in Appendix 9 and discussed in section 4.3.3.2 suggest that there may be substantial differences in sensitivity among species of macrophytes and unicellular algae. The macrophytes appear to be generally more sensitive, with EC_{50} values below 0.001 mg/L. While there are substantial differences among algal species, EC_{50} values are above 0.01 mg/L.

Several additional studies in the published literature report substantially higher EC_{50} values. Fahl et al. (1995) found that the EC_{50} value of metsulfuron methyl to *Chlorella fusca*, a freshwater alga, is 1.2 mg/L for effects on cell volume growth and 0.85 mg/L for cell reproduction at pH of 6.5. Unlike the relationship for terrestrial plants, toxicity increases with lower or more acidic pH, most probably because of decreased ionization leading to more rapid uptake. Mystrom and Blanck (1998) report a similar EC_{50}, 1.6 mg/L, for growth inhibition in *Selenastrum capricornutum*, another freshwater algal species, with a NOEL of 0.038 mg/L. As with terrestrial microorganisms, this effect was attributed to ALS inhibition because the growth inhibition was antagonized by addition of branched chain amino acids. At a concentration of 0.003 mg/L, metsulfuron methyl was associated with a 6-16% inhibition (not statistically significant) in algal growth rates for three species but stimulation of growth was observed in *Selenastrum capricornutum* and the aquatic macrophyte, duck weed (Peterson et al. 1994, Table 5, p. 284).

Wei et al. (1998; 1999) assayed the toxicity of metsulfuron methyl degradation products in *Chlorella pyrenoidosa*. Based on 96-hour algae growth inhibition assays, the acute toxicity of the degradation products was about 2-3 times less than that of metsulfuron methyl itself.

In addition to these laboratory studies, there is one field study on the effects of metsulfuron methyl in algal species indicating that concentrations of metsulfuron methyl as high as 1 mg/L are associated with only slight and transient effects on plankton communities in a forest lake (Thompson et al. 1993a,b,c).

4.1.3.5. Other Aquatic Microorganisms– The only information on toxicity to aquatic microorganisms comes from the study by Peterson et al. (1994) in which significant inhibition in growth was noted in three species of cyanobacteria at a concentration of 0.003 mg/L. By analogy to the effects on terrestrial bacteria and aquatic algae, it seems plausible that aquatic bacteria and fungi will be sensitive to the effects of metsulfuron methyl at low concentrations.

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview. Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation. In acute exposure scenarios, the highest exposures for small terrestrial vertebrates will occur after a direct spray and could reach up to about 4 mg/kg under typical exposure conditions and up to about 60 mg/kg under more extreme conditions. Other routes of exposure, like the consumption of contaminated water or contaminated vegetation, generally will lead to much lower levels of exposure. In chronic exposure scenarios, estimated daily doses for a small vertebrate are usually less than 0.5 mg/kg/day; however, daily doses of up to about 4 mg/kg/day are possible from the consumption of contaminated vegetation. Based on general relationships of body size to body volume, larger vertebrates will be exposed to lower doses and smaller animals, like insects, will be exposed to much higher doses under comparable exposure conditions. Because of the apparently low toxicity of metsulfuron methyl to animals, the rather substantial variations in the exposure assessments have little impact on the assessment of risk to terrestrial animals.

The primary hazards to non-target terrestrial plants are associated with unintended direct deposition or spray drift as well as persistence in and migration through soil. Unintended direct spray will result in an exposure level equivalent to the application rate. At least some plants that are sprayed directly with metsulfuron methyl at or near the recommended range of application rates will be damaged. Based on a monitoring study involving a ground application with a hydraulic sprayer, no more than 0.001 of the application rate would be expected to drift 100 m offsite. Based on monitoring studies involving low-flight agricultural applications of various pesticides and employing 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, are approximately 0.03 at 100 feet, 0.002 at 500 feet, 0.0006 at 1000 feet, and 0.0002 at 2500 feet. Estimates of off-site deposition also can be based on Stoke's Law. Using this method and assuming a wind velocity of no more than 5 miles/hour perpendicular to the line of application, 100 µ particles falling from 3 feet above the surface could drift as far as 23 feet. A raindrop or 400 µ particle applied at 6 feet above the surface could drift about 3 feet.

There are major areas of uncertainty and variability in assessing potential levels of exposure in soil. In general, metsulfuron methyl adsorption to a variety of different soil types will increase as the pH decreases (i.e., the soil becomes more acidic). The persistence of metsulfuron methyl in soil is highly variable, and reported soil half-times range from a few days to several months, depending on factors such as temperature, rainfall, pH, organic matter, and soil depth.

In order to encompass a wide range of field conditions, GLEAMS simulations were conducted for both clay and sand at annual rainfall rates from 5 to 250 inches and the typical application rate of 0.02 lb a.i./acre. In sand or clay under arid conditions (i.e., annual rainfall of about 10 inches or less), there is no percolation or runoff and degradation, not dispersion, accounts for the decrease of metsulfuron methyl concentrations in soil. At higher rainfall rates, plausible concentrations in soil range a high as 0.007 ppm and under a variety of conditions concentrations of 0.0005 ppm and greater may be anticipated in the root zone for appreciable periods of time.

Exposures to aquatic species are impacted by the same factors that influence terrestrial plants except the directions of the impact are reversed. In other words, in very arid environments (i.e., the greatest persistence in soil) substantial contamination of water is unlikely. In areas with increasing levels of rainfall, toxicologically significant exposures to aquatic plants are more likely to occur. As summarized in Appendix 2, peak water levels of about 0.003-0.006 mg/L can be anticipated under worst case conditions and concentrations on the order of 0.001 mg/L or more can be anticipated under various conditions when rainfall rates equal 25-50 inches per year after a single application. Water concentrations are not expected to increase as a result of multiple applications per year.

These estimates of persistence in soil and transport to water should be considered crude approximations of plausible levels of exposure. A variety of site-specific factors may have a substantial impact on these assessment. The factors include application rates, microbial activity, soil binding of metsulfuron methyl, the depth of the water table, proximity to open water, rates of flow in and volumes of groundwater, streams, ponds, or lakes, and specific patterns of rainfall. These site-specific considerations result in substantial variations, either upward or downward, from the modeled values.

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

In this exposure assessment, estimates of oral exposure are expressed in the same units as the available toxicity data (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^2 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, **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.

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 metsulfuron methyl, the available information is not adequate to quantify species differences in sensitivity to metsulfuron methyl. 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 F07).

4.2.2.1. Direct Spray – In the broadcast application of any herbicide, wildlife species may be sprayed directly. This scenario is similar to the accidental exposure scenarios for the general public discussed in section 3.2.3.2. In a scenario involving exposure to direct spray, the 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 metsulfuron methyl.

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 metsulfuron methyl per unit body weight, compared with small mammals. Consequently, a third exposure assessment is developed using a body weight of 0.093 g for the honey bee (USDA/APHIS 1993) and the equation above for body surface area proposed by Boxenbaum and D'Souza (1990). Because there is no information regarding the dermal absorption rate of metsulfuron methyl by bees or other invertebrates, this exposure scenario, detailed in worksheet F03, also assumes complete absorption over the first day of exposure.

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

Unlike the human health risk assessment in which transfer rates for humans are available, there are no transfer rates available for wildlife species. As discussed in Durkin et al. (1995), the transfer rates for humans are based on brief (e.g., 0.5- to 1-hour) exposures that measure the transfer from contaminated soil to uncontaminated skin. Species of wildlife are likely to spend longer periods of time, compared to humans, 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 metsulfuron methyl (section 3.2.3.5) as well as its high water solubility and low octanol/water partition coefficient suggest that metsulfuron methyl 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.

4.2.2.3. 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. This estimate is applied as a general value and may overestimate or underestimate exposure in some circumstances. For example, a 20 g herbivore has a caloric requirement of about 13.5 kcal/day. If the diet of the herbivore consists largely of seeds (4.92 kcal/g), the animal would have to consume about 14% of its body weight per day as food [(13.5 kcal/day ÷ 4.92 kcal/g)÷20g = 0.137]. Conversely, if the diet of the herbivore consists largely of vegetation (2.46 kcal/g), the animal would have to consume about 27% of its body weight per day as food [(13.5 kcal/day ÷ 2.46 kcal/g)÷20g = 0.274] (U.S. EPA 1993, pp 3-5 6o 3-6). Modeling such variability would greatly increase the apparent complexity of the risk assessment by adding several additional scenarios involving different species consuming different diets. A less complicated approach is to make the conservative assumption that 100% of the diet is contaminated. In cases where the oral exposure assessment suggests that adverse effects are plausible, more detailed site-specific or species-specific exposure assessments could be justified. As discussed in section 4.4, this is not the case for metsulfuron methyl. 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 based on the same set of assumptions that were used 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.

4.2.2.4. Ingestion of Contaminated Water -- Estimated concentrations of metsulfuron methyl in water are identical to those used in the human health risk assessment (worksheet B07). As discussed in section 3.2.3.4.2, these estimates are probably very conservative (i.e., they tend to overestimate exposure and subsequent risk). The only major differences from the human health risk assessment 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 (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).

4.2.3. Terrestrial Plants. The exposure assessments for non-target terrestrial plants are discussed below and summarized in Table 4.2. Five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion and the use of contaminated irrigation water. Unintended direct spray is expressed simply as the application rates considered in this risk assessment, 0.02 lbs a.i./acre with a range of 0.015-0.15 lbs a.i./acre, and should be regarded as an extreme/accidental form of exposure that is not likely to occur in most Forest Service applications. Spray drift is based on estimates of drift from a review of numerous field studies. The central estimate of drift is taken as the expected drift at 500 feet down wind from the application site with lower and upper estimates based on distances of 2500 feet and 100 feet, respectively. The proportion of the applied amount transported off-site from runoff is based on GLEAMS modeling of clay and sand. The amount of metsulfuron methyl that might be transported off-site from wind erosion is based on estimates of annual soil loss associated with wind erosion and the assumption that the herbicide is incorporated into the top 1 cm of soil. Exposure from the use of contaminated irrigation water is based on the same data used to estimate human exposure from the consumption of contaminated ambient water and involves both monitoring studies as well as GLEAMS modeling. Based on these exposure assessments, nontarget plants may be exposed to functional application rates of 0.000001 lbs a.i./acre (wind erosion) to 0.02 lbs a.i./acre (accidental direct spray at the typical application rate) and to soil levels of 0.0005-0.0035 ppm.

All of these exposure scenarios are dominated by situational variability because the levels of exposure are highly dependent on site-specific conditions. Thus, these estimates given are intended to represent conservative but plausible ranges of exposures that could occur but these ranges may over-estimate or under-estimate actual exposures in some cases. The impact of this situational variability is discussed further in the risk characterization.

4.2.3.1. Direct Spray – Unintended direct spray will result in an exposure level equivalent to the application rate. As summarized in section 2, the typical application rate used in this risk assessment is 0.02 lbs a.i./acre with a range of 0.015-0.15 lbs a.i./acre.

4.2.3.2. Off-Site Drift – The offsite drift of metsulfuron methyl after ground applications was studied by Marrs et al. (1989). Metsulfuron methyl was applied by hydraulic ground sprayer at an application rate of 0.015 g/ha at wind speeds between 2.5 m/second (5.6 miles/hour) and 3.5 m/sec (7.8 miles/hour). At 100 m downwind, no more than 0.1% (prop = 0.001) of applied amount was shown to drift.

Because off-site drift is more or less a physical process that depends on droplet size and meteorological conditions rather than the specific properties of the herbicide, estimates of off-site drift can also 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 0.05 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).

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.

For this risk assessment, the central estimate of offsite drift is taken as 0.001, the proportion measured during a ground application using a hydraulic sprayer (Marrs et al. 1989). The lower and upper limits of drift are taken as 0.0002 and 0.05 from the range of drift estimates during aerial applications at distances of 100 to 2500 feet downwind (Bird 1995, Figure 2, p. 204). This lower limit is likely to encompass well-directed backpack applications in which very little drift is expected. The upper range is most likely to occur only during aerial applications under unfavorable conditions.

4.2.3.3. Soil Contamination – The off-site movement of metsulfuron methyl will be governed by the binding of metsulfuron methyl to soil, the persistence of metsulfuron methyl in soil, as well as site-specific topographical, climatic, and hydrological conditions. Although generic exposure models like GLEAMS cannot reflect all of the potential site-specific and situational variability, such models are useful for identifying conditions under which off-site transfer through runoff is likely to be most important. In order to encompass a wide range of plausible conditions, two types of soil were modeled using GLEAMS: clay and sand. Details regarding the methods used and the results of the GLEAMS modeling are summarized in Appendix 2. All model results were adjusted for the typical application rate of 0.02 lbs a.i./acre.

As summarized in Appendix 2 (see especially Figures A2-4 and A2-5), maximum soil residues in the upper 1 foot of the root zone at an application rate of 0.02 lbs a.i./acre are about 0.0025-0.0035 ppm (mg/kg). The rate at which these concentrations will decrease depends mostly on site-specific conditions, including soil pH, rainfall, and microbial activity. Nonetheless, the modeled estimates are in general agreement with published studies, indicating that metsulfuron methyl may persist in the upper 1 foot of soil at phytotoxic levels for up to 1 year or may move relatively fast through some soils when rainfall rates are high (Sahid and Quirinus 1997; Walker and Welch 1989).

The modeled estimates are also in general agreement with unpublished studies conducted as part of the registration process (Anderson and Harvey 1984, MRID 00147910; Rapisarda and Scott 1986, MRID 42016507). The unpublished studies provide additional information on the formation of metsulfuron methyl metabolites, which may have a major impact on the potential effects of exposure on non-target plants. In some soils, metsulfuron methyl may undergo relatively rapid degradation to relatively non-toxic metabolites, as noted in the study by Anderson and Harvey (1984). In clay soil (40% clay), up to about 20% of the applied metsulfuron methyl may remain as the parent compound after 1 year when cumulative rainfall amounts to more than 90 cm or about 35 inches (Rapisarda and Scott 1986, Figure 9, p. 49 on MRID 42016507). This finding is similar to the modeled estimates for clay soil (50% clay) given in Appendix 2 (Figure A2-4). Thus, while there will be substantial site-specific variations in the levels of metsulfuron methyl in soil, the range of soil concentrations modeled in Appendix 2 appear to be reasonable and consistent with the available published and unpublished monitoring data.

4.2.3.4. Contaminated Irrigation Water – Unintended direct exposure of non-target plant species may occur through the use of contaminated ambient water for irrigation. Although there are no studies in the literature addressing the impact of metsulfuron methyl in contaminated irrigation water, the effects of such exposure scenarios on non-target vegetation have been observed with other herbicides (e.g., Bhandary et al. 1997; Gomez de Barreda et al. 1993). Furthermore, given the mobility of metsulfuron methyl, the contamination of irrigation water is a plausible scenario.

The levels of exposure associated with this scenario will depend on the concentration of metsulfuron methyl in the ambient water used for irrigation and the amount of irrigation water that is applied. As discussed in section 3.2.3.4, metsulfuron methyl is relatively mobile; consequently, contamination of ambient water may be anticipated and can be quantified. As summarized in Appendix 2, peak water levels of approximately 0.003-0.006 mg/L can be anticipated under worst case conditions, and concentrations on the order of 0.001 mg/L or more may occur under various conditions at rainfall rates of 25-50 inches per year.

Climate, soil type, topography, and the plant species under cultivation will determine the amount of irrigation water used. Thus, selecting an irrigation rate is not entirely objective. Typically, plants require 0.1-0.3 inches of water per day (Delaware Cooperative Extension Service 1999). In the absence of any general approach to determining and expressing the variability of irrigation rates, the application of 1 inch of irrigation water is used in this risk assessment. This rate is somewhat higher than the maximum daily irrigation rate for sandy soil (0.75 inches/day) and substantially higher than the maximum daily irrigation rate for clay (0.15 inches/day) (Delaware Cooperative Extension Service 1999). This variability is addressed further in the risk characterization (section 4.4.2.2).

Based on the estimated concentrations of metsulfuron methyl in ambient water and an irrigation rate of 1 inch per day, the estimated functional application rate of metsulfuron methyl to the irrigated area is 0.00016 (0.0001-0.001) lb a.i./acre [see worksheet F08 for details of these calculations].

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

To estimate the potential transport of metsulfuron methyl by wind erosion, this risk assessment uses average soil losses ranging from 1 to 10 tons/ha·year, with a typical value of 5 tons/ha·year. The value of 5 tons/ha·year is equivalent to 500 g/m^2 [1 ton=1000 kg and 1 ha = 10,000 m^2] or 0.05 g/cm^2 [$1m^2$=10,000 cm^2]. Using a soil density of 2 g/cm^3, the depth of soil removed from the surface per year would be 0.025 cm[(0.05 g/cm^2)÷ (2 g/cm^3)]. The average amount per day would be about 0.00007 cm/day [0.025 cm per year ÷ 365 days/year]. This central estimate is based on a typical soil loss rate of 5 tons/ha·year. Since the range of plausible rates of annual soil loss is 1 to 10 tons/ha·year, the range of soil loss per day may be calculated as 0.00001 cm/day [0.00007÷5 = 0.000014] to 0.0001 cm/day [0.00007×2=0.00014] .

The amount of metsulfuron methyl that might be transported by wind erosion depends on several factors, including the application, the depth of incorporation into the soil, the persistence in the soil, the wind speed, and the topographical and surface conditions of the soil. Under desirable conditions, like relatively deep soil incorporation (10 cm), low wind speed, and surface conditions that inhibit wind erosion, it is not likely that wind transport of metsulfuron methyl will be substantial or significant. Since for the purposes of this risk assessment it is assumed that metsulfuron methyl is incorporated into the top 1 cm of soil, daily soil losses expressed as a proportion of applied amount would be 0.00007 with a range of 0.00001 to 0.001.

Wind erosion deposition of soil contaminated with metsulfuron methyl will vary substantially with local conditions. Furthermore, for the purposes of this risk assessment, neither concentration nor dispersion is considered quantitatively. Nonetheless, these factors together with the general and substantial uncertainties in the exposure assessment are considered in the risk characterization (section 4.4).

4.2.4. Aquatic Organisms. The potential for effects on aquatic species are based on estimated concentrations of metsulfuron methyl in water that are identical to those used in the human health risk assessment (worksheet B07) and summarized in Appendix 2. As indicated in Appendix 2, peak water levels of approximately 0.003-0.006 mg/L can be anticipated under worst case conditions and concentrations on the order of 0.001 mg/L or more can be anticipated under various conditions when rainfall rates equal 25-50 inches per year for prolonged periods.

As illustrated in Figure A2-2, modeled concentrations in water at the end of 1 year after a single application of metsulfuron methyl at the typical application rate of 0.02 lbs a.i./acre to clay soil range from approximately 0.001 to a little more than 0.002 mg/L when rainfall rates range from 25 to 250 inches per year. For sandy soil (Figure A2-3), concentrations in water are much lower, ranging from 0.0003 to 0.0005 at rainfall rates of more than 100 inches per year. As summarized in Appendix 2, however, these is no reason to anticipate that metsulfuron methyl concentrations in ambient water will increase when applications are repeated yearly.

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 25 mg/kg/day from a 2-year feeding study in rats). All of the potential longer-term exposures and all but one of the acute exposures of terrestrial mammals to metsulfuron methyl are substantially below the NOAEL of 25 mg/kg/day. Consequently, a dose of 25 mg/kg/day is used to assess the consequences of all exposures. The limited available data suggest that the sensitivity of birds and terrestrial invertebrates to metsulfuron methyl is similar to that of mammals.

The toxicity of metsulfuron methyl to terrestrial plants is very well characterized. Metsulfuron methyl is a potent herbicide that causes adverse effects in a variety of target and non-target plant species. For exposures associated with direct sprays or drift, functional application rates as low as 0.000037 lbs a.i./acre could be associated with growth inhibition in sensitive species and rates as high as 0.015 lbs a.i./acre might be necessary to inhibit growth in more tolerant species like wheat. With respect to soil contamination, soil concentrations as low as 0.00025 ppm might inhibit growth in some relatively sensitive species like maize, lentils, and sugar beets. At soil concentrations of 0.1 ppm, growth inhibition might occur in several species.

Metsulfuron methyl has a low order of toxicity to fish. Mortality is not likely to occur in fish exposed to metsulfuron methyl concentrations less than or equal to1000 mg/L. For longer-term effects (e.g., hatching, larval survival, or larval growth over 90-day exposure period) the NOEC is 4.7 mg/L, with a corresponding effect level of 8 mg/L. Similarly, aquatic invertebrates do not appear to be sensitive to metsulfuron methyl. Available studies indicate that the acute LC_{50} for immobility is 720 mg/L and that the NOEC for reproduction is 150 mg/L.

Aquatic plants are much more sensitive than aquatic animals to the effects of metsulfuron methyl. For macrophytes, the most sensitive species appears to be *Lemna gibba* with a reported EC_{50} value of 0.00036 mg/L and a NOEC value of approximately 0.00016 mg/L. There appears to be substantial variation in the toxicity of metsulfuron methyl to algal species with reported EC_{50} values ranging from about 0.01 to about 1 mg/L.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals– As summarized in the dose-response assessment for the human health risk assessment (see section 3.3.3.), the lowest NOAEL in experimental mammals is 25 mg/kg/day. None of the exposure scenarios approach this NOAEL (see Table 4-1); thus, it is not necessary to elaborate much more on the dose-response assessment. A dose of 25 mg/kg/day is used to assess the consequences of all exposures.

4.3.2.2. Birds – As noted in section 4.1.2.2, oral toxicity studies suggest that birds are no more sensitive than mammals to the effects of metsulfuron methyl. Thus, for exposure scenarios involving the ingestion of metsulfuron methyl from either contaminated vegetation or water, the dose-response relationships for mammals may serve as estimates for avian species. Notwithstanding this approach and as discussed in section 4.1.2.2, the available data on birds are not as extensive or of the same quality as the data on experimental mammals. This limitation adds uncertainty to this risk assessment.

4.3.2.3. Terrestrial Invertebrates–While standard toxicity studies in bees (see section 4.1.2.3.) do not suggest that bees are any more or less sensitive to metsulfuron methyl than experimental mammals, there is one study (Samsoe-Petersen 1995) using the Rove beetle which notes a 15% reduction in egg hatching after direct spray of 0.067% product (20% a.i.) at a level of 6 $\mu L/cm^2$. The 0.067% solution corresponding to a metsulfuron methyl concentration of 0.00134 mg/μL:

$$0.067\% == 0.0067 \bullet 0.2 \text{ g/mL or } 0.2 \text{ mg}/\mu\text{L} = 1.34\ \mu\text{g}/\mu\text{L}$$

and the application of 6 $\mu L/cm^2$ corresponds to an application rate of 0.00804 mg/cm^2:

$$6\ \mu L/cm^2 \bullet 1.34\ \mu g/\mu L = 8.04\ \mu g/cm^2.$$

By comparison, the typical application rate of 0.02 lbs a.i./acre corresponds to an application rate of 0.2242 $\mu g/cm^2$ and the highest labeled application rate of 0.15 lbs a.i./acre corresponds to an application rate of 1.68 $\mu g/cm^2$.

4.3.2.4. Terrestrial Plants (Macrophytes)– Metsulfuron methyl is a herbicide and causes adverse effects in a variety of non-target plant species. The most relevant studies for assessing the effects of direct spray or drift are the series of bioassays conducted by Drake (1988)—additional supplemental information provided by Drake (1989)—and Heldreth and McKelvey (1996).

In this study, summarized in Appendix 6, 10 species of plants were tested by both preemergence and postemergence applications: dicots—soybean, cocklebur, cotton, morningglory, wild buckwheat, and sugar beet—and monocots—corn, barnyardgrass, rice and nutsedge. The most sensitive species was the morningglory, which showed 70% growth inhibition at preemergence applications of 0.25 g/ha, or about 0.00022 lbs a.i./acre. At the same application rate, the cocklebur evidenced 20% growth inhibition and the sugar beet evidenced 40% growth inhibition. Rice was the only monocot to respond (20% inhibition) to the application rate of 0.25 g/ha. At 4 g/ha or about 0.0036 lbs a.i./acre, all of the dicots were sensitive to metsulfuron methyl with growth inhibition of 90% or greater while the monocots showed growth inhibition ranging from 30 to 70%. At 16 g/ha or about 0.014 lbs a.i./acre, approximately equal to the typical application rate used by the Forest Service, all of the plants showed 60 to 100% growth inhibition.

In a more recent study submitted to the U.S. EPA (Heldreth and McKelvey 1996), bioassays were conducted on preemergence and postemergence toxicity to corn, cucumber, onion, pea, rape, sugar beet, sorghum, soybean, tomato, wheat. EC_{25} values for growth inhibition in preemergence applications ranged from 0.00106 oz/acre or 0.000066 lb/acre (onion) to 0.244 oz/acre or 0.015 lb/acre (wheat). For postemergence applications the observed range of EC_{25} was 0.000586 oz/acre or 0.000037 lb/acre (cucumber) to 0.0624 oz/acre or 0.0039 lb/acre (wheat).

For assessing the effects of soil contamination through off-site movement, the most relevant publications are those by James et al. (1995) and Kotoula-Syka et al. (1993). In the study by James et al. (1995), bioassays for growth inhibition (measured as dry shoot weight) were conducted using mustard and sorghum at soil concentrations ranging from 1 to 100 $\mu g/kg$ soil. A soil concentration of 1 $\mu g/kg$ soil is equivalent to 0.001 mg/kg or 0.001 ppm and 100 $\mu g/kg$ soil is equivalent to 0.1 mg/kg or 0.1 ppm. At a concentration of 0.001 ppm, neither plant evidenced significant growth inhibition. At 0.002 ppm, however, growth in mustard was inhibited by about 35%. At the highest concentration tested, 0.1 ppm, all mustard plants died and growth in sorghum was inhibited by 87%.

In the study by Kotoula-Syka et al. (1993), four species of plants were tested—maize, sunflower, lentil, and sugar beet—at soil concentrations ranging from 0.25 to 10 ng/g. These concentrations are equivalent to 0.25-10 μg/kg which in turn is equivalent to 0.00025-0.01 mg/kg or 0.00025-0.01 ppm. At a concentration of 0.00025 ppm, the only plant tolerant to metsulfuron methyl was the sunflower, which evidenced no growth inhibition. Growth in all other species was inhibited by approximately 50% or more (Kotoula-Syka et al. 1993, Figure 2, p. 360).

Thus, for exposures associated with direct sprays or drift, functional application rates as low as 0.000037 lbs a.i./acre could be associated with growth inhibition in sensitive species and rates as high as 0.015 lbs a.i./acre may be required to cause the same effect in more tolerant species like wheat. With respect to soil contamination, soil concentrations as low as 0.00025 ppm could inhibit the growth of some relatively sensitive species like maize, lentils, and sugar beets. At soil concentrations of 0.1 ppm, growth inhibition may affect a large number of species.

4.3.2.5. Terrestrial Microorganisms– As discussed in section 4.1.2.5, the sensitivity of terrestrial microorganisms appears to operate and be governed by the same mechanism involved in plant toxicity. However, even at concentrations in soil that would likely cause adverse effects in a large number of macrophytes (i.e., 5 ppm) effects on soil microorganisms appear to be transient .

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 have a similar sensitivity to metsulfuron methyl. The fish bioassays in Appendix 3 allow for a reasonably unambiguous estimate of exposure, which might be associated with fish mortality. Mortality is not likely to occur in fish exposed to metsulfuron methyl concentrations less than or equal to1000 mg/L. For longer-term effects (e.g., hatching, larval survival, or larval growth over 90-day exposure period) the NOEC is 4.5 mg/L, with a corresponding effect level of 8 mg/L. Similarly, aquatic invertebrates do not appear to be sensitive to metsulfuron methyl with an acute LC_{50} values for immobility of 720 mg/L and an NOEC for reproduction of 150 mg/L (Appendix 8).

4.3.3.2. Aquatic Plants– The relevant data on the toxicity of metsulfuron methyl to aquatic plants is summarized in Appendix 9. For macrophytes, the most sensitive species appears to be *Lemna gibba*, a freshwater macrophyte with a reported EC_{50} value of 0.00036 mg/L, with NOEC values of approximately 0.00016 mg/L (Douglas and Handley 1988). There appears to be substantial variation in the toxicity of metsulfuron methyl to algal species with reported EC_{50} values ranging from about 0.01 to about 1 mg/L.

4.3.3.3. Aquatic Microorganisms– Based on the report by Peterson et al. (1994), the effect level for growth inhibition in three species of cyanobacteria is 0.003 mg/L. By analogy to the effects on terrestrial bacteria and aquatic algae, it seems plausible that aquatic bacteria and fungi will be sensitive to the effects of metsulfuron methyl at concentrations that are substantially higher than those affecting aquatic algae or macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview. As in the human health risk assessment, the weight of evidence suggests that no adverse effects in terrestrial animals are plausible using typical or even very conservative worst case exposure assumptions. For the small mammals, the hazard quotients are based on the long term NOAEL of 25 mg/kg/day that was used in the human health risk assessment for the derivation of the RfD. None of the hazard quotients for the small mammal approach a level of concern, even at the upper limit of exposure. For the honey bee, the hazard quotient is based on the non-lethal acute dose level of 270 mg/kg from a standard bioassay required for pesticide registration. As with the small mammal, there is no basis for contending that adverse effects in bees are plausible. One study reports a reduction in egg hatching in the Rove beetle after direct spray of metsulfuron methyl that corresponds to an application rate of 8.04 $\mu g/cm^2$. This rate is 30 times greater than the typical application and 2 times greater than the highest labeled application. Although these ratios cannot be treated as hazard quotients, they suggest that adverse effects are not likely to occur at the typical application rate. At the highest labeled rate, however, the occurrence of adverse effects in this species is more plausible. Given the large number of terrestrial invertebrates on which no data are available, caution in applying metsulfuron methyl at the highest labeled rate seems warranted. Such applications are not anticipated in any Forest Service programs.

Terrestrial plants may be affected by metsulfuron methyl in some circumstances. Less sensitive plant species are not likely to be impacted substantially by metsulfuron methyl unless they are directly sprayed at the typical application rate of 0.02 lbs a.i./acre or some higher rate. Sensitive plant species will be adversely affected not only by accidental direct spray but also from on-site soil contamination and possibly through the use of irrigation water contaminated with metsulfuron methyl. Notably, the adverse effects associated with soil contamination are likely to be restricted to the application site because most of the offsite movement of metsulfuron methyl will be associated with leaching rather than runoff. So, although the potential for water contamination may be relatively high, the potential for significant runoff to offsite soil is likely to be low. The potential for offsite damage due to wind erosion also is likely to be low.

The characterization of risk to aquatic species parallels that for terrestrial species: there is no plausible basis for contending that aquatic animals will be exposed to toxic levels of metsulfuron methyl. Nonetheless, effects on aquatic plants are plausible and in some cases likely. Under normal and anticipated conditions of use, metsulfuron methyl contamination of water could cause adverse effects (i.e., reduction in growth and biomass) in sensitive aquatic macrophytes. The duration and magnitude of these effects will depend heavily on the dilution rates of the contaminated body of water and on weather conditions.

4.4.2. Terrestrial Organisms

4.4.2.1. Terrestrial Animals– The quantitative risk characterization for terrestrial animals is summarized in Table 4-3. For the small mammals, the hazard quotients are based on the levels of exposure summarized in Table 4-1 and the long term NOAEL of 25 mg/kg/day that was used in the human health risk assessment to derive the RfD. None of the hazard quotients for the small mammal approach a level of concern, even at the upper limit of exposure. As detailed in Section 4.2.2, these exposure scenarios are based on exposure assumptions that are likely but may not always overestimate exposure. For metsulfuron methyl, further refinement of the exposure assessment would have little impact on the risk characterization because the hazard quotients are far below a level of concern.

For the honey bee, the hazard quotient is based on the non-lethal acute dose level of 270 mg/kg from the study by (Meade 1984a,b), and there is no basis for anticipating the occurrence of adverse effects in bees exposed to metsulfuron methyl. As summarized in Section 4.3.2.3, Samsoe-Petersen (1995) report a reduction in egg hatching in the Rove beetle after direct spray of 0.067% product (20% a.i.) at a level of 6 $\mu L/cm^2$, which corresponds to an application rate of 8.04 $\mu g/cm^2$. By comparison, the typical application rate of 0.02 lbs a.i./acre corresponds to an application rate of 0.2242 $\mu g/cm^2$ and the highest labeled application rate of 0.15 lbs a.i./acre corresponds to an application rate of 1.68 $\mu g/cm^2$. Thus, the typical application rate of 0.02 lbs a.i./acre is a factor of about 36 below the effect level [8.04 $\mu g/cm^2 \div 0.22 \mu g/cm^2 = 36.5$] and the maximum labeled application rate is a factor of about five below this effect level [8.04 $\mu g/cm^2 \div 1.68$ $\mu g/cm^2 = 4.6$]. Although these ratios cannot be treated as hazard quotients, they suggest that adverse effects are not likely to occur at the typical application rate. At the highest labeled rate, however, the occurrence of adverse effects in this species is more plausible. Given the large number of terrestrial invertebrates on which no data are available, caution is advised in applying metsulfuron methyl at the highest labeled rate. Such applications are not anticipated in any Forest Service programs.

The simple verbal interpretation of this quantitative risk characterization for terrestrial animals is similar to that of the human health risk assessment: the weight of evidence suggests that no adverse effects in terrestrial animals 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. Metsulfuron methyl 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 can be anticipated in terrestrial animals from the use of this compound in Forest Service programs.

4.4.2.2. Terrestrial Plants– The quantitative risk characterization for terrestrial plants is summarized in Table 4-4. As with the risk characterization for terrestrial animals, the numerical expression of risk is given as a hazard index, the ratio of exposure to some index of toxicity. Unlike the case with terrestrial animals, however, the index of toxicity is taken as growth inhibition rather than a NOAEL. This approach is adopted because the available toxicity data on terrestrial plants, as summarized in section 4.3.2.4, are focused on levels associated with growth inhibition. For direct spray, the EC_{25} is used as a somewhat more conservative index of toxicity compared with the EC_{50}. This approach has little impact on the qualitative expression of risk. Because of the apparent and reasonably substantial differences in the toxicity of metsulfuron methyl to different plant species, toxicity values are given for the 'most sensitive' species as well as more tolerant species, as discussed in section 4.3.2.4. The estimates of exposure are taken directly from Table 4-2.

Based on the hazard quotients given in Table 4-4, less sensitive plant species are not likely to be affected substantially by exposure to metsulfuron methyl unless they are directly sprayed at the typical application rate of 0.02 lbs a.i./acre or some higher rate. Sensitive plant species will be adversely affected not only by accidental direct spray but also from soil contamination and possibly through the use of irrigation water contaminated with metsulfuron methyl. Nonetheless, the adverse effects associated with soil contamination will probably be restricted to the application site. Based on the GLEAMS modeling summarized in Appendix 2, most of the offsite movement of metsulfuron methyl will be associated with leaching rather than runoff. Thus, while the potential for water contamination may be relatively high, the potential for significant runoff to offsite soil appears to be low. The potential for offsite damage due to wind erosion also appears to be low.

4.4.2.3. Terrestrial Microorganisms – Based on the studies by Boldt and Jackson (1998) and Ismail et al. (1998), a soil concentration of 5 ppm may have an adverse if transient impact on soil bacteria. As detailed in Appendix 2, however, peak soil concentrations of metsulfuron methyl are anticipated to be well below this level (i.e., in the range of 0.0035 ppm) at the typical application rate of 0.02 lbs a.i./acre. Even at the maximum labeled rate of 0.15 lbs a.i./acre, soil concentrations would be well below 5 ppm.

4.4.3. Aquatic Organisms. As summarized in Appendix 2, peak water levels of approximately 0.003-0.006 mg/L can be anticipated under worst case conditions and concentrations on the order of 0.001 mg/L or more could be anticipated under a variety of conditions when rainfall rates equal 25-50 inches per year. These concentrations are far below the level that would have any plausible direct toxic effect on fish or aquatic invertebrates. Notwithstanding the above risk characterization, adverse effects on fish and invertebrate populations are plausible, secondary to the toxicity of metsulfuron methyl to aquatic plants that could adversely affect aquatic animals through a decrease in food availability or a change in habitat.

Like terrestrial plants, aquatic plants are much more sensitive than aquatic animals to metsulfuron methyl exposure. The upper range of expected levels of metsulfuron methyl in ambient water associated with a single application of this herbicide as the typical application rate is 0.003-0.006 mg/L. Based on the available data, frank and substantial toxicity to freshwater macrophytes may be expected in the range of 0.00036 mg/L, a factor of 16 below estimated peak of 0.006 mg/L. Longer-term concentrations in ambient water could be on the order of 0.001 mg/L, which is a factor of about 6 above the NOEC of 0.00016 mg/L in aquatic macrophytes. Thus, adverse effects in aquatic macrophytes appear to be plausible at the typical application rate of 0.02 lbs a.i./acre in areas that are near to standing bodies of water and subject to typical to high rainfall rates.

Freshwater algae are much less sensitive than macrophytes, with EC_{50} values of about 0.01 mg/L or greater. Except for transient effects at or near worst case exposure conditions, effects in these species appear to be less plausible. As shown in Appendix 2 (see Figures A2-2 and A2-3) water concentrations ranging from 0.001 to 0.002 mg/L may be apparent 1 year after application. This risk characterization is consistent with the study by Thompson et al. (1993a) in which no or only transient effects were observed in phytoplankton communities in a forest lake at metsulfuron methyl concentrations of up to 1.0 mg/L.

Thus, under normal and anticipated conditions of use, it is plausible that metsulfuron methyl contamination of water will cause adverse effects (i.e., reduction in growth and biomass) in sensitive aquatic macrophytes. The duration and magnitude of these effects will depend heavily on the dilution rates of the contaminated body of water and weather conditions. For less sensitive unicellular algae, the occurrence of adverse effects is far less likely, at least initially. For relatively brief periods shortly after application, a wider range of aquatic plants could be affected.

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	0.001	0.00007	0.05	WSF01
Direct spray, small animal, 100% absorption	0.5	0.3	3.7	WSF02
Direct spray, bee, 100% absorption	3	2	24	WSF03
Consumption of contaminated vegetation, acute exposure	0.11	0.07	2.8	WSF04
Consumption of contaminated water, acute exposure	0.007	0.002	0.38	WSF06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.04	0.02	1	WSF05
Consumption of contaminated water, chronic exposure	0.0017	0.001094	0.013	WSF07

Table 4-2: Summary of exposure assessment for nontarget terrestrial plants.			
Organism	Value	Units	Comment (Section in document)
Terrestrial Plants			
Direct spray	0.02	lb/acre	This is the typical application rate (4.2.3.1.).
Off-Site Drift	0.00002	lb/acre	Based on central estimate of drift of 0.001 of applied amount (4.2.3.2).
Soil Contamination	0.0005	ppm soil	Probable long term concentration in soil may be greater or equal to this value (Appendix 2, Figures A2-4 and A2-5).
	0.0035	ppm soil	Upper range of plausible exposures for brief periods (4.2.3.3.).
Irrigation Water	0.00016	lb/acre	Based on central estimate of water concentrations (4.2.3.4. and worksheet F08).
	0.001	lb/acre	Based on upper range of estimated water concentrations (4.2.3.4. and worksheet F08).
Wind Erosion	0.000001	lb/acre	Based on central estimate of 0.00007 of applied amount (4.2.3.5.).
	0.00002	lb/acre	Based on upper range estimate of 0.001 of applied amount (4.2.3.5.).

Table 4-3: 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	0.00004	0.000003	0.002
Direct spray, small animal, 100% absorption	0.02	0.01	0.1
Direct spray, bee, 100% absorption[3]	0.01	0.007	0.09
Consumption of contaminated vegetation, acute exposure	0.004	0.003	0.1
Consumption of contaminated water, acute exposure	0.0003	0.00008	0.02
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.002	0.0008	0.04
Consumption of contaminated water, chronic exposure	0.0001	0.00004	0.001
	Toxicity value for mammal [2]	25	mg/kg/day
	Toxicity value for bee [3]	270	mg/kg

[1] See Table 4-1 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 20 mg/kg/day, the study on which the RfD is based, and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on the reported acute dose level of 25 µg/bee that was not associated with increased mortality. Dose is calculated as body weight of 0.000093 kg/bee - i.e., 25 µg/bee ÷ 0.000093 kg/bee = 268817 µg/kg or about 270 mg/kg.

Table 4-4: Summary of risk characterization for terrestrial plants.

Organism[1]	Exposure		Hazard Quotients	
	Value	Units	Most sensitive	Less sensitive
Direct spray	0.02	lb/acre	91	1.4
Off-Site Drift	0.00002	lb/acre	0.09	0.0014
Soil Contamination	0.0005	ppm soil	2.00	0.005
	0.0035	ppm soil	14.00	0.035
Irrigation Water	0.00016	lb/acre	0.7	0.01
	0.001	lb/acre	5	0.07
Wind Erosion	0.000001	lb/acre	0.005	0.00007
	0.00002	lb/acre	0.09	0.001
Toxicity Values[2]				
Sensitive species	0.00022	lb/acre.	EC_{25} for growth inhibition	
	0.00025	ppm soil	Growth inhibition	
Less sensitive species	0.014	lb/acre.	EC_{25} for growth inhibition	
	0.1	ppm soil	Growth inhibition	

[1] Exposure assessments as summarized in Table 4-2.
[2] See Section 4.3.2.4 for a summary of the dose-response assessment.

5. REFERENCES

Abayo GO; English T; Eplee RE; Kanampiu FK; Ransom JK; Gressel J 1998. Control Of Parasitic Witchweeds (striga Spp.) On Corn (zea Mays) Resistant To Acetolactate Synthase Inhibitors. Weed Science. 46 (4):459-466.

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

Anderson J; Harvey J. 1984. Field Soil Dissipation Study of DPX-T6376 in Delaware, North Carolina, Florida, and Mississippi: Metsulfuron: Document No. AMR-117-83. Unpublished study pre- pared by E. I. du Pont de Nemours and Co., Inc. 28 p. MRID No. 00147910.

Badon R; Bastide J; Sabadie J 1990. Reactivity Of The Herbicide Metsulfuron-methyl: Synthesis Of Degradation Products. Chemosphere. 21 (1-2):289-294.

Balneaves JM 1992a. A Comparison Of Surfactants To Aid Control Of Gorse And Scotch Broom With Herbicides. Plant Protection Quarterly. 7 (3):96-99.

Balneaves JM 1992b. A Comparison Of Surfactants To Aid Control Of Gorse And Scotch Broom With Herbicides. Plant Protection Quarterly. 7 (4):174-177.

Balneaves JM 1992c. Silwet L-77 Enhances Rainfastness Of Glyphosate And Metsulfuron-methyl When Applied To Gorse And Scotch Broom. Plant Protection Quarterly. 7 (3):109-111.

Barefoot A; Cooke L. 1990. Water Solubility of DPX-T6376 Using Continuous Sample Agitation: Lab Project Number: AMR-1661-90. Unpublished study prepared by E. I. du Pont de Nemours and Co. 20 p. MRID No. 42545501.

Baskaran S; Bolan NS; Rahman A; Tillman RW 1996. Pesticide Sorption By Allophanic And Non-allophanic Soils Of New Zealand. New Zealand Journal Of Agricultural Research. 39 (2):297-310.

Bastide J; Badon R; Cambon J-P; Vega D 1994. Transformation Rates Of Ortho-substituted Thiophene And Benzene Carboxylic Esters: Application To Thifensulfuron-methyl And Metsulfuron-methyl Herbicides. Pesticide Science. 40 (4):293-297.

Beavers J; Foster J; Mitchell L et al. 1996a. DPX-T6376-141 (Metsulfuron Methyl): A Reproduction Study with the Northern Bobwhite (Colinus virginianus): (Final Report): Lab Project Number: 112-413: AMR 3412-95: CHR27. Unpublished study prepared by Wildlife International Ltd. 169 p. MRID No. 44115701.

Beavers J; Foster J; Mitchell L; et al. 1996b. DPX-T6376-141 (Metsulfuron Methyl): A Reproduction Study with the Mallard (Anas platyrhynchos): (Final Report): Lab Project Number: 112-414: AMR 3413-95: CHR27. Unpublished study prepared by Wildlife International Ltd. 171 p. MRID No. 44115702.

Beavers J. 1984a. An Acute Oral Toxicity Study in the Bobwhite with H #15,527: Final Report: Wildlife International Ltd. Project No. 112-157. Unpublished Haskell report HLO-568-84 prepared by Wildlife International Ltd. 15 p. MRID No. 00148645.

Beavers J. 1984b. A Dietary LC50 Study in the Mallard with H #15, 527: Final Report: Wildlife International Ltd. Project No. 112- 156. Unpublished Haskell report HLO-569-84 prepared by Wildlife International Ltd. 13 p. MRID No. 00148647.

Beavers J. 1984c. A Dietary LC50 Study in the Bobwhite with H #15, 527: Final Report: Wildlife International Ltd. Project No. 112- 155. Unpublished Haskell report HLO-570-84 prepared by Wildlife International Ltd. 13 p. MRID No. 00148646.

Bentley K. 1993. Assessment of IN T6376-74 in the In vitro Unscheduled DNA Synthesis Assay in Primary Rat Hepatocytes: Lab Project Number: 4581-834: 4581-058: 574-90. Unpublished study prepared by E. I. du Pont de Nemours & Co. 17 p. MRID No. 43035601.

Berger BM; Wolfe NL 1996a. Multiresidue Determination Of Sulfonylurea Herbicides By Capillary Electrophoresis For Hydrolysis Studies In Water And Sediments. Fresenius' Journal Of Analytical Chemistry. 356 (8):508-511.

Berger BM; Wolfe NL 1996b. Hydrolysis And Biodegradation Of Sulfonylurea Herbicides In Aqueous Buffers And Anaerobic Water-sediment Systems: Assessing Fate Pathways Using Molecular Descriptors. Environmental Toxicology And Chemistry. 15 (9):1500-1507.

Berger BM; Janowitz K; Menne HJ; Hoppe H-H 1998. Comparative Study On Microbial And Chemical Transformation Of Eleven Sulfonylurea Herbicides In Soil. Zeitschrift Fuer Pflanzenkrankheiten Und Pflanzenschutz. 105 (6):611.

Bergstrom L; Stenstrom J 1998. Environmental Fate of Chemicals In Soil. Ambio. 27 (1):16-23.

Bergstrom L 1990. Leaching Of Chlorsulfuron And Metsulfuron Methyl In Three Swedish Soils Measured In Field Lysimeters. J Environ Qual. 19 (4):701-706.

Bhandary RM; Whitwell T; Briggs J. 1997. Growth of containerized landscape plants is influenced by herbicide residues in irrigation water. Weed Technology. 11(4):793-797.

Bird SL. 1995. A compilation of aerial spray drift field study data for low-flight agricultural application of pesticides. Chapter 18 in Agrochemical Environmental Fate: State of the Art. ML Leng, EMK Leovey, and PL Zubkoff (eds.), Lewis Publishers, Boca Raton, Florida, pp. 195-07.

Boldt TS; Jackson CS 1998. Different Toxic Effects Of The Sulfonylurea Herbicides Metsulfuron Methyl, Chlorsulfuron And Thifensulfuron Methyl On Fluorescent Pseudomonads Isolated From An Agriculture Soils. Fems Microbiology Letters. 161 (1):29-35.

Boulding JR. 1995. Practical Handbook of Soil, Vadose Zone, and Ground-Water Contamination. Lewis Publishers, Boca Raton, Florida, 948 pp.

Boxenbaum J; D'Souza R. 1990. Interspecies pharmacokinetic scaling, biological design and neoteny. Adv. Drug Res. 19: 139-195.

Brennan D. 1990. Metsulfuron Methyl: Analysis and Certification of Product Ingredients: Determination of F6594: Lab Project Number: AMR-1659-90. Unpublished study prepared by E.I. du Pont de Nemours and Co., Inc. 26 p. MRID No. 41393201.

Brennan D. 1995b. Technical Grade Metsulfuron Methyl: Analysis and Certification of Product Ingredients: Lab Project Number: AMR 2732-93. Unpublished study prepared by DuPont Agricultural Products. 206 p. MRID No. 43672601.

Brock W. 1985. Ninety-day Feeding and One-generation Reproduction Study in Rats with Benzoic Acid, 2-N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylamino-carbonylaminosulfonyl, Methyl Ester (INL-5300): Haskell Laboratory Report No. 413-83. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 316 p. MRID No. 00148638.

Brock W. 1987. Primary Eye Irritation Study with IN T6376-41 in Rabbits: Project ID: 630-87; Medical Research No. 4581-561. Unpublished study prepared by E.I. du Pont de Nemours and Co., Haskell Laboratory. 18 p. MRID No. 40858801.

Brudenell A JP; Baker DA; Grayson BT 1995. Phloem Mobility Of Xenobiotics: Tabular Review Of Physicochemical Properties Governing The Output Of The Kleier Model. Plant Growth Regulation. 16 (3):215-231.

Burdock G; Hamada N. 1985. Chronic Feeding Study with Concur- rent Two-generation Reproduction Study in Rats: Chronic Phase: Final Report: Project No. 201-562. Unpublished study prepared by Hazleton Laboratories America, Inc. 6576 p. MRID No. 00151029.

Burdock G; Burns C; Dudjeck L; et al. 1982. Feeding Study with Concurrent Two-generation Reproduction Study in Rats--H-14453: Project No. 201-562. Thirteen week interim rept. (Unpublished study received Feb 14, 1983 under 352-EX-111; prepared by Hazleton Laboratories America, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071436-A; 071437) MRID No. 00125391.

Burdock G. 1984. A Combined Three-Month And One-Year Feeding Study in Dogs of H-14453: Final Report: Project No. 201-571. Unpublished study prepared by Hazleton Labs. America, Inc. 807 p. MRID No. 00141821.

Burgess B; Kinney L; Nash S. 1983. Inhalation Median Lethal Concentration (LC50) of INT-6376-25 by EPA Protocol: Haskell Laboratory Report No. 784-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071435-E) MRID No. 00125830.

Burnmaster DE. 1998. Lognormal distribution for total water intake and tap water intake by pregnant and lactating women in the United States. Risk Analysis. 18(5): 215-219.

Burns C. 1984. Feeding study with concurrent Two-Generation Reproduction Study in Rats of H-14453: Interim Report: Project No. 201-562. Unpublished study prepared by Hazleton Labs. America, Inc. 3071 p. MRID No. 00145007.

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

C&P Press (Chemical and Pharmaceutical Press). 1999. Greenbook.net. Product Labels, Supplementary Labels, and Material Safety Data Sheets for Ally and Escort. http://www.greenbook.net/

Calabrese EJ; Baldwin LA. 1993. Performing Ecological Risk Assessments. Lewis Publishers, Boca Raton, LA, pp. 12-24.

Cantrell RL; Hyland JR. 1985. Application techniques. In: A Guide to Silvicultural Herbicide Use in the Southern United States. Auburn University School of Forestry, Alabama Agricultural Experiment Station. November 1985. 612 pp.

Chamberlain K; Evans AA; Bromilow RH 1996. 1-octanol/water Partition Coefficient (Kow) And pKa For Ionisable Pesticides Measured by a pH-metric Method. Pesticide Science. 47 (3):265-271.

Charlton R; Bookhart S. 1996. Metabolism of (carbon-14) Metsulfuron Methyl in Laying Hens: Lab Project Number: AMR 3554-95: N001761A. Unpublished study prepared by Dupont Agricultural Products and Battelle. 194 p. MRID No. 44179301.

Christian M; Doll A. 1985. Developmental Toxicity Study of L- 5300 in the Rat: Final Report: Project 104-010. Unpublished Haskell Laboratory report no. HLO 513-85 prepared by Argus Re- search Laboratories, Inc. 198 p. MRID No. 00148640.

Cox C. 1993. Sulfometuron methyl (Oust). J. Pest. Reform. 13 (4): 30-35.

Daly I. 1985. A Three-month Feeding Study in Dogs with H-15527: Final Report: Project No. 84-2864. Unpublished Haskell report HLO-514-85 prepared by Bio/dynamics, Inc. 657 p. MRID No. 00148639.

Delaware Cooperative Extension. 1999. Agronomy Facts Series: AF-03. http://bluehen.ags.udel.edu/deces/af/af-03.htm.

Devine MD; Rashid A 1993. Antagonism Of Tralkoxydim Activity In Avena Fatua By Metsulfuron Methyl. Weed Res. 33 (2):97-104.

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

Douglas M; Handley J. 1988. An Assessment of the Inhibitory Ef- fect of DPX-T6376 Technical on the Growth of Duckweed (Lemna minor): Lab Project Number: DPT 186(B)/881173. Unpublished study prepared by Huntingdon Research Centre Ltd. 20 p. MRID No. 41773902.

Drake D. 1988. Tier Testing of Metsulfuron Methyl on Plants Grown under Greenhouse and Field Conditions: Laboratory Project ID DCD-88-1. Unpublished study prepared by E.I. du Pont de Nemours and Co., Inc. 113 p. MRID No. 40639301.

Drake D. 1989. Tier Testing Evaluation of Metsulfuron Methyl on Plants Grown under Greenhouse and Field Conditions: Project ID DCD-88-1. 10 p. MRID No. 41118001.

Drottar K; Krueger H. 1998. DPX-T6376: A Semi-Static Life-Cycle Toxicity Test with the Cladoceran (Daphnia magna): Final Report: Lab Project Number: 5025-98: 112A-176. Unpublished study prepared by Wildlife International Ltd. 76 p.

Du Pont(E I du Pont de Nemours & Co Inc). 1985a. Metasulfuron Methyl Environmental Fate Data Review. Unpublished study. 41 p. MRID No. 00147907.

Du Pont(E I du Pont de Nemours & Co Inc). 1985b. Product Chemistry Data for DPX-R9674 Herbicide. Unpublished study. 24 p. MRID No. 00155976.

Du Pont(E I du Pont de Nemours & Co Inc). 1985c. Metsulfuron Methyl Product Chemistry Data. Unpublished study. 27 p. MRID No. 00151054.

Durkin PR; Hertzberg RC; Stiteler WS; Mumtaz M. 1995. The Identification and Testing of Interaction Patterns. Toxicology Letters, 79:251-264.

Durkin P; Rubin L; Withey J; Meylan W; Nakatsugawa T. 1998. A reevaluation of methods for assessing dermal absorption. Manuscript under review. Draft dated May 18, 3-5, 3-11, 3-11, WS-14, 1998.

EXTOXNET. 1996. Pestcide Information Profile on Metsulfuron-methyl. Extension Toxicology Network: A Pesticide Information Project of Cooperative Extension Offices of Cornell University, Michigan State University, Oregon State University, and University of California at Davis. Online. Revised October, 1996. 4 pp. http://ace.ace.orst.edu/info/ extoxnet/pips/metsulfu.html.

Fahl GM; Kreft L; Altenburger R; Faust M; Boedeker W; Grimme LH 1995. pH-dependent Sorption, Bioconcentration And Algal Toxicity Of Sulfonylurea Herbicides. Aquatic Toxicology (Amsterdam). 31 (2):175-187.

Fayez KA; Gerken I; Kristen U 1994. Ultrastructural Responses Of Root Caps To The Herbicides Chlorsulfuron And Metsulfuron Methyl. Plant And Soil. 167 (1):127-134.

Feussner E; Christian M; Hoberman A; et al. 1982a. Embryo- fetal Toxicity and Teratogenicity Study of INT-6376 in Crl:COBS CD (SD)BR Rats (Segment II Evaluation): Argus Research Laboratories, Inc. Project 104-002. Final rept. (Unpublished study received Feb 14, 1983 under 352-EX-111; prepared by Argus Research Laboratories, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071435-J) MRID No. 00125835.

Feussner E; Christian M; Hoberman A; et al. 1982b. Teratogenicity Study of INT-6376 in New Zealand White Rabbits (Segment II Evaluation): Argus Research Laboratories, Inc. Project 104-003. Final rept. (Unpublished study received Feb 14, 1983 under 352-EX-111; prepared by Argus Research Laboratories, Inc., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071435-K) MRID No. 00125836.

Fink R; Beavers J; Brown R; et al. 1981c. Eight-day Dietary LC50--Bobwhite Quail: H-14,028: Project No. 112-123; HLO-460-81. Final rept. (Unpublished study received Feb 14, 1983 under 352- EX-111; prepared by Wildlife International Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL: 071434-G) MRID No. 00125821.

Fink R; Beavers J; Brown R; et al. 1981b. Eight-day Dietary LC50--Mallard Duck: H-14,028: Project No. 112-124; HLO-455-81. Final rept. (Unpublished study received Feb 14, 1983 under 352- EX-111; prepared by Wildlife International Ltd., submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL: 071434-F) MRID No. 00125820.

Finlay C. 1996. Primary Dermal Irritation Study with DPX-T6376-126 (Escort Herbicide) in Rabbits: Lab Project Number: 10435-001: HLR 3-96. Unpublished study prepared by Dupont Haskell Labs. 23 p. MRID No. 43945401.

Forbis A. 1987. Acute Toxicity Screen of Metsulfuron Methyl to Selenastrum capricornutum Printz: ABC Final Report #35848. Un- published study prepared by Analytical Bio-Chemistry Laboratories, Inc. 17 p. MRID No. 40639302.

Gargus J. 1985a. H9637-4 Skin Absorption LD50 Test on Rabbits: Hazleton Project No. 201-811. Unpublished study prepared by Hazleton Laboratories America, Inc. 17 p. MRID No. 40622702.

Gargus J. 1985b. Skin Absorption Study in Rabbits: Revised Final Report: Haskell No. 15,643: Project No. 201-816. Unpublished study prepared by Hazleton Laboratories America, Inc. 12 p. MRID No. 00162609.

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

Gomez de Barreda D; Carbonell EA; Cases B; Munoz N. 1993. Use of tomato (Lycopersicon esculentum) seedlings to detect bensulfuron and quinclorac residues in water. Weed Technology. 7(2):376-381.

Guenther P; Pestemer W; Rahman A; Nordmeyer H 1993. A Bioassay Technique To Study The Leaching Behaviour Of Sulfonylurea Herbicides In Different Soils. Weed Res. 33 (2):177-185.

Hall C. 1984a. 96-Hour LC50 to Bluegill Sunfish: Benzoic Acid, 2-N-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylaminoócar- bonylóaminoósulfonyl, Methyl Esteró: Haskell Laboratory Report No. 457-84. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 5 p. MRID No. 00148648.

Hall C. 1984b. 96-Hour LC50 to Rainbow Trout: Benzoic Acid, 2-N-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylaminoócar- bonylóaminoósulfonyl, Methyl Ester: Haskell Laboratory Report No. 545-84. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 5 p. MRID No. 00149672.

Han J; Anderson J. 1984. Residue Studies with Carbon-14 Metsulfuron Methyl in Bluegill Sunfish: Document No. AMR-81-82. Unpublished study prepared by E. I. du Pont de Nemours & Co. 29 p. MRID No. 00149407.

Harris SA; Solomon KR. 1992. Human exposure to 2,4-D following controlled activities on recently sprayed turf. J. Environ. Sci. Health. B27(1): 9-22.

Heldreth K; McKelvey R. 1996. Influence of Metsulfuron Methyl (DPX-T6376) on Seedling Emergence and Early Growth and Vegetative Vigor of Several Terrestrial Plants: Lab Project Number: AMR 3242-94: MR 10180. Unpublished study prepared by E.I. du Pont de Nemours and Co. 413 p. . MRID No. 44050301.

Hicks S. 1997a. DPX-T6376: Influence on Growth and Reproduction of Skeletonema costatum: (Final Report): Lab Project Number: AMR 3840-96: 43306: ABC 43306. Unpublished study prepared by ABC Labs., Inc. 65 p. MRID No. 44244002.

Hicks S. 1997b. DPX-T6376: Influence on Growth and Reproduction of Navicula pelliculosa: Lab Project Number: AMR 3841-96: 43307: ABC 43307. Unpublished study prepared by ABC Laboratories, Inc. 59 p. MRID No. 44420901.

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

Holloway J C; Cole AW; Shaw DR. 1995. Effect Of Soil Type And Liming Rates On Rotational Forage Crop Injury Following Metsulfuron Methyl. Weed Technology. 9 (2):286-293.

Hundley S. 1985. Metabolism of Triazine-2-(carbon 14) Metsulfuron Methyl in the Rat: Report No. AMR-405-85. Unpublished study prepared by E. I. du Pont de Nemours & Co., Inc. 18 p. MRID No. 00146612.

Hutt C. 1985. Inhalation Median Lethal Concentration (LC50) of INL-5300-20 by EPA Protocol: Haskell Laboratory Report No. 431- 85. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 20 p. MRID No. 00148634.

Hutton D. 1989. Chronic Toxicity of DPX-T6376-74 to Daphnia magna: Lab Project Number: 4581-654: 833-88: HLR 833-88. Unpublished study prepared by DuPont Haskell Lab for Toxicology and Industrial Medicine. 39 p. MRID No. 43490601.

ICRP (International Commission on Radiologic Protection). 1975. Report of the Task Group on Reference Man. Recommendations of the International Commission on Radiological Protection (ICRP) Publ. No. 23. Pergamon Press, New York, NY.

Ismail BS; Kalithasan K 1997. Mobility Of Metsulfuron-methyl In Tropical Soils. Australian Journal Of Soil Research. 35 (6):1291-1300.

Ismail BS; Lee HJ 1995. Persistence Of Metsulfuron-methyl In Two Soils. J. Environmental Science and Health Part B. 30 (4):485-497.

Ismail BS; Goh KM; Kader J 1996. Effects Of Metsulfuron-methyl On Microbial Biomass And Populations In Soils. J. Enviorn. Science and Health, Part B. 31 (5):987-999.

Ismail BS; Yapp KF; Omar O 1998. Effects Of Metsulfuron-methyl On Amylase, Urease, And Protease Activities In Two Soils. Australian Journal Of Soil Research. 36 (3):449-456.

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

James TK; Klaffenbach P; Holland PT; Rahman A 1995. Degradation Of Primisulfuron-methyl And Metsulfuron-methyl In Soil. Weed Research. 35 (2):113-120.

Knisel WG; Davis FM; Leonard RA. 1992. GLEAMS Version 2.0 User Manual. U.S. Department of Agriculture, Agricultural Research Service, Southeast Watershed Research Laboratory, Tifton, GA. 202pp.

Kotoula-Syka E; Eleftherohorinos IG; Gagianas AA; Sficas AG 1993. Phytotoxicity And Persistence Of Chlorsulfuron, Metsulfuron-methyl, Triasulfuron And Tribenuron-methyl In Three Soils. Weed Res. 33 (5):355-367.

Kreamer G. 1996. Early Life-Stage Toxicity of DPX-T6376-141 (Metsulfuron Methyl) to Rainbow Trout, (Oncorhynchus mykiss): Lab Project Number: HLR 182-96: 10352: 182-96. Unpublished study prepared by DuPont Haskell Lab for Toxicology and Industrial Medicine. 400 p. MRID No. 44122801.

Lawrie J; Clay V 1993. Effects Of Herbicide Mixtures And Additives On Rhododendron Ponticum. Weed Res. 33 (1):25-34.

Leng ML; Leovey EMK; Zubkoff PL. 1995. Agrochemical Environmental Fate: State of the Art. Lewis Publishers, Boca Raton, Florida, 410 pp.

Levine, TE. 1996. The regulation of inert ingredients in the United States. Chapter 1 in Pesticide Formulation and Adjuvant Technology. CL Foy and DW Pritchard (eds). CRC Press. Boca Raton, Florida. Pp. 1-11.

Manugistics. 1995. Statgraphics Plus for Windows. Version 3. Available from Manugistics, Inc. Rockville, Maryland.

Marrs RH; Williams CT; Frost AJ; Plant RA 1989. Assessment Of The Effects Of Herbicide Spray Drift On A Range Of Plant Species Of Conservation Interest. Environ Pollut. 59 (1):71-86.

Mason RW; Johnson BL. 1987. Ergonomic factors in chemical hazard control. In: Handbook of Human Factors. Salveny, G; ed. John Wiley and Sons, New York, NY. Pp. 772-741.

Mcdonald PM; Abbott CS; Fiddler GO 1994. Response Of Young Ponderosa Pines, Shrubs, And Ferns To Three Release Treatments. Western Journal Of Applied Forestry. 9 (1):24-28.

Meade A. 1984a. Acute Contact LD50 Study In Honey Bees (Apis- Mellifera L.) With INT 6376: Final Report: Project No. ABM-84-4. Unpublished study prepared by E. I. Du Pont De Nemours and Co., Inc. 11 p. MRID No. 00141829.

Meade A. 1984b. Acute Contact LD50 Study in Honey Bees with INL5300-14: Final Report: Project No. ABM-84-10. Unpublished study prepared by E.I. du Pont de Nemours & Co. 6 p. MRID No. 00148650.

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

Mendenhall W; Scheaffer RF. 1973. Mathematical Statistics with Applications. Duxbury Press, North Scituate, Massachusetts. 461 pp. plus appendices.

Milhomme H; Bastide J 1990. Uptake And Phytotoxicity Of The Herbicide Metsulfuron Methyl In Corn Root Tissue In The Presence Of The Safener 1,8-naphthalic Anhydride. Plant Physiol (Bethesda). 93 (2):730-738.

Moore JA. 1964. Physiology of the Amphibia. Academic Press, New York. 654 p. (Cited in USDA 1993)

Muska C; Hall C. 1982. 96-hour LC50 to Rainbow Trout: Haskell Laboratory Report No. 515-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-B) MRID No. 00125816.

Mystrom B; Blanck H 1998. Effects Of The Sulfonylurea Herbicide Metsulfuron Methyl On Growth And Macromolecular Synthesis In The Green Alga Selenastrum Capricornutum. Aquatic Toxicology (amsterdam). 43 (1):25-39.

Nix SJ. 1994. Urban Storm-water Modeling and Simulation. CRC Press, Inc., Boca Raton, Florida, 212 pp.

NRC (National Research Council). 1983. Risk assessment in the Federal government: managing the process. Washington, DC: National Academy Press; 176 p. + app.

O'Flaherty EJ. 1981. Toxicants and Drugs: Kinetics and Dynamics. John Wiley and Sons, New York, NY. 398 pp.

Oomen PA; Romeijn G; Wiegers GL 1991. Side-effects Of 100 Pesticides On The Predatory Mite Phytoseiulus Persimilis, Collected And Evaluated According To The Eppo Guideline. Bull Oepp (Organ Eur Mediterr Prot Plant). 21 (4):701-712.

Pastoor T. 1985. Two-generation, Four-litter Reproduction Study in Rats with Benzoic Acid, 2-(4-Methoxy-6-methyl..., Methyl Ester (INT-6376): Medical Research Proj. No. 4908-001: Final Report on the Reproduction Study Conducted June 23, 1983 through September 7, 1984. Unpublished study prepared by E.I. du Pont de Nemours and Co., Inc. 298 p. MRID No. 00151028.

Peterson HG; Boutin C; Martin PA; Freemark KE; Ruecker NJ; Moody MJ 1994. Aquatic Phytotoxicity Of 23 Pesticides Applied At Expected Environmental Concentrations. Aquatic Toxicology (Amsterdam). 28 (3-4):275-292.

Phillips F; Hall C. 1982a. 48-hour LC50 to Daphnia magna: Haskell Laboratory Report No. 157-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-D) MRID No. 00125818.

Phillips F; Hall C. 1982b. 96-hour LC50 to Bluegill Sunfish: Haskell Laboratory Report No. 154-82. (Unpublished study received Feb 14, 1983 under 352-EX-111; submitted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071434-C) MRID No. 00125817.

Pons N; Barrisuo E 1998. Fate Metsulfuron-methyl In Soils In Relation To Pedo-climate Conditions. Pesticide Science. 53 (4):311-323.

Pool CF; De Villiers BL 1993. Importance Of Certain Soil Properties On The Activity Of Imazamethabenz Methyl And Chlorsulfuron/metsulfuron Methyl. Applied Plant Science. 7 (1):30-34.

Pool CF; Du Toit D 1995. Leaching Depth Of Imazamethabenz Methyl And Chlorsulfuron + Metsulfuron Methyl In Different Soils. Applied Plant Science. 9 (2):43-47.

Prasad O; Rai G. 1987. Hematological abnormalities induced by feeding a common artificial sweetener, saccharin, in ICR Swiss mice. Toxicol. Lett. 36(1): 81-8.

Rapisarda C; Scott M. 1986. Field Soil Dissipation of [Phenyl (U)-Carbon-14]-Metsulfuron Methyl on United States and Canadian Soils: Lab Project Number: AMR-476-86. Unpublished study prepared by E.I. du Pont de Nemours and Co., Inc. 46 p. MRID No. 42016507.

Research Institute for Freshwater Fisheries. 1995. Fish Toxicity Trial of the Herbicide ALLY 10/10 WP: Meth. l Metsulfuron + Ethylchlorimuron). Unpublished study. 9 p. MRID No. 44015401.

Rickard L. 1985. Mutagenicity Evaluation of INL-5300-20 in the CHO/HPRT Assay: Haskell Laboratory Report No. 58-85. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 15 p. MRID No. 00149671.

Rubin L; Mistretta P; Thomas D; Durkin P; Meylan W. 1998. A re-evaluation of methods for assessing occupational exposure in pesticide applicators. Manuscript under review.

Ruffle B; Burmaster DE; Anderson PD; Gordon HD. 1994. Lognormal distributions for fish consumption by the general U.S. population. Risk Analy. 14(4): 395-404.

Sabadie J; Bastide J 1990. Degradation Of Metsulfuron-methyl On Various Minerals. Weed Res. 30 (1):1-8.

Sahid IB; Quirinus L 1997. Activity And Mobility Of Metsulfuron-methyl In Soils. Plant Protection Quarterly. 12 (3):125-127.

Samsoe-Petersen L 1995. Effects Of 67 Herbicides And Plant Growth Regulators On The Rove Beetle Aleochara Bilineata (col.: Staphylinidae) In The Laboratory. Entomophaga. 40 (1):95-104.

Sarver J. 1990. Approximate Lethal Dose of IN F6594 in Rats: Revised: Report No. HLR 96-89: Medical Research No. 4581-689. Unpublished study prepared by E. I. du Pont de Nemours and Co., Inc., Haskell Laboratory for Toxicology and Industrial Medicine. 9 p. MRID No. 41393202.

Sarver J. 1991. Acute Oral Toxicity Study with IN F6594-3 in Male and Female Rats: Lab Project Number: 148-91. Unpublished study prepared by E. I. du Pont de Nemours and Co. 30 p. MRID No. 42545901.

SERA (Syracuse Environmental Research Associates, Inc.). 1998. Methodology for Human Health Risk Assessments, SERA TR 96-21-07-03e, draft dated March 26, 1998. Prepared under USDA/FS Contract 53-3187-5-12, Order No. 43-3187-7-0407. Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

Shriram Institute for Industrial Research. 1995. Two Generation Reproduction Study in Albino Rats: Ally Technical: Lab Project Number: 163691: TOX/1. Unpublished study. 48 p. MRID No. 44163302.

Sloman T; Leva S. 1998. Metsulfuron Methyl 60 DF: Influence on Growth and Growth Rate of the Green Alga Selenastrum Capricornutum: Lab Project Number: AMR 4464-97: MR 12119. Unpublished study prepared by E.I. du Pont de Nemours and Company. 45 p. MRID No. 44650101.

Stadler J. 1984. Ninety-day and Long-term Feeding Study in Mice with Benzoic Acid, 2-(4-Methozy-6-methyl-1,3,5-triazin-2-yl) aminocarbonylaminosulfonyl, Methyl Ester: Haskell Laboratory Report No. 463-84; Medical Research Project No. 4461-001. Unpublished study prepared by E. I. du Pont de Nemours & Co. 1514 P. MRID No. 00151135.

Stork P; Hannah MC 1996. A Bioassay Method For Formulation Testing And Residue Studies Of Sulfonylurea And Sulfonanylide Herbicides. Weed Research. 36 (3):271-281.
Streibig JC; Walker A; Blair AM; Anderson-Taylor G; Eagle DJ; Friedlaender H; Hacker E; Iwanzik W; K 1995. Variability Of Bioassays With Metsulfuron-methyl In Soil. Weed Research. 35 (4):215-224.

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

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

Thompson DG; Macdonald LM; Staznik B 1992. Persistence Of Hexazinone And Metsulfuron-methyl In A Mixed-wood/boreal Forest Lake. J Agric Food Chem. 40 (8):1444-1449.

Thompson DG; Holmes SB; Thomas D; Macdonald L; Solomon KR. 1993a. Impact Of Hexazinone And Metsulfuron Methyl On The Phytoplankton Community Of A Mixed-wood/boreal Forest Lake. Environ Toxicol Chem. 12 (9):1695-1707.

Thompson DG; Holmes SB; Wainio-Keizer K; Macdonald L; Solomon KR. 1993b. Impact Of Hexazinone And Metsulfuron Methyl On The Zooplankton Community Of A Boreal Forest Lake. Environ Toxicol Chem. 12 (9):1709-1717.

Thompson DG; Holmes SB; Thomas D; Wainio-Keizer K; Macdonald L; Solomon KR. 1993c. Impact Of Hexazinone And Metsulfuron Methyl Herbicides On Plankton Communities Of A Forest Lake. Twentieth Annual Aquatic Toxicity Workshop, Quebec City, Quebec, Canada, October 17-21, 1993.

U.S. EPA (U.S. Environmental Protection Agency). 1985. Development of Statistical Distributions or Ranges of Standard Factors Used in Exposure Assessments, Report prepared by GCA Corp., Chapel Hill. Available from NTIS: PB85-242667.

U.S. EPA (U.S. Environmental Protection Agency). 1989. Recommendations for and Documentation of Biological Values for use in Risk Assessment. U.S. EPA, Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Cincinnati, OH. ECAO-CIN-554. [pagination not continuous].

U.S. EPA (U.S. Environmental Protection Agency). 1992. Dermal Exposure Assessment: Principles and Applications. EPA/600/8-91/011B. Interim Report. Exposure Assessment Group, Office of Health and Environmental Assessment, Washington, DC.

U.S. EPA (U.S. Environmental Protection Agency).   1993. Wildlife Exposure Factors Handbook. Volumes 1 and 2. EPA/600/R-93/187a,b. Pagination not continuous. Available NTIS: PB94-174778 and PB94-174779..

U.S. EPA (U.S. Environmental Protection Agency). 1996. Exposure Factors Handbook. Office of Research and Development, National Center for Environmental Assessment, U.S. EPA, Washington, DC. EPA/600/P-95/002Ba-c. Avail. NTIS: PB97-117683, 97-117691, PB97-117709

U.S. EPA (United States Environmental Protection Agency). 1995. Pesticide Regulation (PR) Notice 95-3. Notice to Manufacturers, Producers, Formulators, and Registrants of Agricultural Pesticides. Address:http://www.epa.gov/opppmsd1/PR_Notices /pr95-3.html.

U.S. EPA (United States Environmental Protection Agency). 1998. IRIS Database. IRIS Substance file -Ally. File Last Updated 05/31/98.
Address:http://www.epa.gov/ngispgm3/iris/irisdat/0288.html.

U.S. EPA (U.S. Environmental Protection Agency). 1998. Notice of Filing of Pesticide Petitions. Federal Register. 63(53): 13401-13404.

U.S. Weather Service. 1998. NWS Climate Tables, 1961-1990. Http://www.nws.noaa.gov/climatex.shtml. Files downloaded on January 14, 1999.

USDA (U.S. Department of Agriculture/Forest Service). 1989a. Final Environmental Impact Statement: Vegetation Management in the Coastal Plain/Piedmont, Management Bulletin R8-MB-23, dated January, 1989. 1213 pp.

USDA (U.S. Department of Agriculture/Forest Service). 1989b. Draft Environmental Impact Statement: Vegetation Management in the Ozark/Ouachita Mountains, Management Bulletin R8-MB-23, dated June, 1989. 499 pp.

USDA (U.S. Department of Agriculture/Forest Service). 1989c. Final Environmental Impact Statement: Vegetation Management in the Appalachian Mountains, Management Bulletin R8-MB-38, dated July, 1989. 1104 pp.

USDA (U.S. Department of Agriculture). 1992. Risk Assessment for Herbicide Use in Forest Service Regions 1,2,3,4, and 10 and on Bonneville Power Administration Sites. Report dated September 1992, Prepared for the USDA Forest Service under contract number 53-3187-9-30. Pagination not continuous.

USDA. 1995. Metsulfuron methyl pesticide fact sheet. Prepared for the USDA Forest Service by Information Ventures, Inc., http://infoventures.com/e-hlth/.

USDA/FS (United States Department of Agriculture/Forest Service). 1998. DATAH-FY'97 Use Summary. Provided to SERA, Inc. by Dr. Paul Mistretta, USDA Forest Service, Atlanta GA. 6 p.

USDA. 1993. Metsulfuron-Methyl Pesticide Fact Sheet. Prepared for the U.S. Department of Agriculture, Forest Service by Information Ventures, Inc. Http://infoventures.com/e-hlth/pestcide/metsulf.html. Prepared November 1995.

USDA/APHIS. 1993. Nontarget Risk Assessment for the MEDFLY Cooperative Eradication Program. USDA Animal and Plant Health Inspection Service. February 1993.

USDA/ARS (U.S. Department of Agriculture, Agricultural Research Station). 1995. ARS Pesticide Properties. Http://wizard.arsusda.gov/rsml/testfiles. Metsulfuron methyl listing last updated May 1995

USGS (U.S. Geological Survey). 1998. Data on Pesticides in Surface and Ground Water of the United States., Results of the National Water Quality Assessment Program (NAWQA). Revised Oct. 23, 1998. http://wwwdwatcm.wr.usgs.gov/cppt/pns_data/data.html van Hemmen JJ. 1992. Agricultural pesticide exposure data bases for risk assessment. Rev. Environ. Contam. Toxicol. 126: 1-85.

Vincent D. 1985. Assessment of INL-5300-20 in the in vitro Un- scheduled DNA Synthesis Assay in Primary Rat Hepatocytes: Haskell Laboratory Report No. 565-84. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 15 p. MRID No. 00148643.

Walker A; Welch SJ 1989. The Relative Movement And Persistence In Soil Of Chlorsulfuron Metsulfuron-methyl And Triasulfuron. Weed Res. 29 (5):375-384.

Walker A; Cotterill EG; Welch SJ 1989. Adsorption And Degradation Of Chlorsulfuron And Metsulfuron-methyl In Soils From Different Depths. Weed Res. 29 (4):281-288.

Wei L; Yu H; Sun Y; Fen J; Wang L 1998. The Effects Of Three Sulfonylurea Herbicides And Their Degradation Products On The Green Algae Chlorella Pyrenoidosa. Chemosphere. 37 (4):747-751.

Wei L; Yu H; Cao J; Sun Y; Fen J; Wang L 1999. Determination And Prediction Of Partition Coefficient And Toxicity For Sulfonylurea Herbicides And Their Degradation Products. Chemosphere. 38 (7):1713-1719.
Wetzel J. 1984. 48-Hour EC50 to Daphnia magna: Benzoic Acid, 2- N-(4-Methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylaminoócar- bonylóaminoósulfonyl, Methyl Ester: Haskell Laboratory Report No. 461-84. Unpublished study prepared by Haskell Laboratory for Toxicology and Industrial Medicine. 5 p. MRID No. 00148649.

Wiechman B; Lu M; McAlack J; et al. 1982. Ninety-day Feeding and One-generation Reproduction Study with ... (INT-6376) in Rats: Haskell Laboratory Report No. 180-82. Final rept. (Unpublished study received Feb 14, 1983 under 352-EX-111; submit- ted by E.I. du Pont de Nemours & Co., Inc., Wilmington, DE; CDL:071435-I) MRID No. 00125834.

Winegardner DL. 1996. An Introduction to Soils for Environmental Professionals. CRC Press, Boca Raton, Florida. 270 pp.

Wolfram Research. 1997. Mathematica Version 3.0.1. Available from Wolfram Research, Inc. Champaign, IL.

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.

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

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

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

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.

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.

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_{25} -- A concentration that causes 25% inhibition or reduction. As used in this document, this values refers to a 25% inhibition of growth.

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.

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.

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.

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.

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.

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.

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.

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).

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.

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.

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Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Acute - single dose		
Rats, CD, males, ~8 weeks old, 1 rat per dose group	100, 500, 1000, 2000, 4000 mg/kg single gavage administration of test material in corn oil; 14-day post exposure observation period.	At 1000 mg/kg, the rat (initial bw = 270 g) exhibited yellow stained perineum and had a severe weight loss (13% of initial body weight) 1 day after dosing. Mortality occurred in the two high dose groups 1 day after dosing. Initial bw of rats = 276 g (2000 mg/kg dose) and 243 g (4000 mg/kg dose) No other effects of treatment were observed during the 15-day study.	Sarver 1990 MRID 41393202
Rats, CD, 10 males and 10 females per dose group, fasted ~24 hours	1000, 2000, or 3000 mg/kg bw single gavage administration of test material in corn oil, 14- or 15-day post-exposure observation period.	LD_{50} > 3000 mg/kg Signs of clinical toxicity included lethargy; hunched posture; high carriage; ocular, nasal, or oral discharge; and wet or yellow-stained perineum. Gross pathology indicated stress from acute systemic toxicity but did not indicate specific target organ specificity. Mortality data: 1000 mg/kg: males 2/10 (avg bw = 227 g), females 0/10 (avg bw = 172 g); 2000 mg/kg: males 2/10 (avg bw = 229 g), females 1/10 (avg bw = 172 g); 4000 mg/kg: males 1/10 (avg bw = 232 g), females 4/10 (avg bw = 175 g) This study has an appendix of tables for individual bw, individual clinical observations, and acute toxicity	Sarver 1991 MRID 42545901 Synthesis difficulties limited the amount of available test material and precluded the determination of an LD_{50}.

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Acute - single dose (continued)		
Rats, Sprague-Dawley, 49 days old, 15 males and 15 females per dose group	0, 50, 500, or 5000 mg/kg single gavage administration; groups of 5 males and 5 females sacrificed 6, 24, or 48 hrs later for bone marrow sampling. Negative controls received corn oil by gavage Positive controls were treated with cyclophosamide.	Clinical signs of toxicity included red discharge from eyes, nose, or mouth in two females at 50 mg/kg, one female at 500 mg/kg, and five males and eight females at 5000 mg/kg; red, orange, or yellow-stained perineal areas in one male at 50 mg/kg and four males and six females at 5000 mg/kg; other sporadically occurring clinical signs of toxicity included wheezing (one mid- and one high-dose male), lethargy (one high-dose male), hunched back (one high-dose female), sensitivity to touch (two high-dose females), one closed eye (one high-dose female). Diarrhea observed in several treated and control rats was attributed to corn oil vehicle. At 24-hours, decreased weight gain was evident in males in the mid-dose group and was statistically significant ($p < 0.001$) in males and females in the high-dose group; at 48 hours, weight gain was significantly decreased ($p < 0.01$) in males and females in the mid-dose group and males and females in the high dose group ($p < 0.001$).	Ullman 1985a MRID 00148642 This is an in vivo mutagenicity study.

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Acute - single dose (continued)		
Mice, CD, 43-days old, 18 males and 18 females	0, or 5000 mg/kg single gavage administration; groups of 6 treated and 5 control males and 6 treated and 5 control females were sacrificed at 24, 48, or 72 hrs later for bone marrow sampling. Negative controls received corn oil by gavage Positive controls were treated with cyclophosamide.	At 4 hrs, there were no clinical signs of toxicity among control or treated mice; at 6 hrs after treatment, tremors, hyperactivity, and hypersensitivity were observed in one treated male; on day after dosing, clinical signs of toxicity included tremors (4/18 males), hyperactivity (2/18 males), moribundity (1/18 males, 1/18 females), diarrhea (1/18 males), decreased activity (1/18 females), hypersensitivity (1/18 males), and death (1/18 females). At 48 hours after treatment, the previously moribund mice were dead and 1/ll remaining treated males was hyperactive. No clinical signs of toxicity were observed in the remaining mice at 72 hours. There was no significant loss in body weight or decreased weight gain among treated mice, compared with negative controls.	Ullman 1985b MRID 00148644 This is an in vivo mutagenicity study.

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Subacute - 13 weeks (91 days) or less		
Rats, CD, 16 rats per dose group per sex	Dietary levels of 0, 100, 1000, or 7500 ppm INT-6376-16 (97% pure) for 90 days. [Average mean daily intake for males (from Table IX, p. 40): 0, 7, 68, or 521 mg/kg/day; average mean daily intake for females (from Table X, p. 41): 0, 8, 84, or 659 mg/kg/day.] Partial scarifice (10/group) at 90 days; other animals allowed to mate.	Females in the 7500 ppm group had an overall body weight gain that was 12% less than that of the control group; male rats in the 100, 1000, and 7500 ppm groups and female rats in the 100 and 1000 ppm groups had comparable or superior mean body weights and weight gains, compared with controls. No effects on food consumption, food efficiency, or intake of the test material at any dose level. No mortalities occurred during the study. Overall fertility was low in the control and test groups, pre-cluding the evaluation of the test substance on fertility. No adverse effects on other indices of reproduction and lactation performance or weanling body weights were observed. Effects not considered treatment related by the authors, include significantly increased total leukocyte counts and 24-hr urine volume in males at 100 ppm; significant increase in GOT activity in females at 100 ppm, but not at higher doses; significantly lower serum protein values in females at 7500 ppm; significantly decreased urine pH in females at 1000 and 7500 ppm not supported by abnormal histopathology; a dose-related statistically significant increase in the incidence of cytoplasmic clearing of heptocytes related to significantly decreased relative liver weights in males and females.	Wiechman et al. 1982 MRID 00125834 90-day feeding and one-generation reproduction study.

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL	Subacute - 13 weeks (91 days) or less (continued)		
Rats, CD, 16 males and 16 females per dose group	0, 100, 1750, or 5000 ppm in the diet for 90 days. Partial sacrifice after 90 days; survivors allowed to mate	NOEL = 100 ppm Mean body weights and mean body weight gains of males and females were significantly lower (~20-50%) than controls throughout the 90 day. At 1750 and 5000 ppm, overall daily food consumption values for male and females were 15-25% lower compared with controls (weeks 0-13); mean food efficiency values were also lower than control values for males and females; an increased incidence of colored nasal discharge was observed in males and considered treatment related; significant decreases in serum glucose, globulin, and total protein concentration were noted in males at the 2- and 3-month evaluations; significantly lower serum glucose and higher serum cholesterol were observed in females at 1- and 3-month evaluations; the same effect was observed in the high dose females at 2 months, but was not statistically significant; absolute heart, liver, and kidney weights of males and females were significantly lower than controls as were the absolute brain weights of the males in the high dose group; significant increases in relative brain, heart, spleen, and kidney weights were observed in males and females; mean relative liver weights were significantly increased in females in the 1750 and 5000 ppm groups and in males in the 5000 ppm group; relative testes weights were significantly increased in males; no gross or histological changes were observed; one female in the high dose group died probably due to compound-related cachexia. No effects on reproduction or lactation performance were observed in the 100 and 1750 ppm groups; in the 5000 ppm groups, 0-4 and 1-4 day viability indices were 15-20% lower than controls; mean pup body weights were decreased significantly at 24-hrs, 4- and 21-day postpartum in the 1750 and 5000 ppm groups; and dam body weights were significantly lower at 1750 and 5000 ppm.	Brock 1985 MRID 00148638 90-Day feeding and 1-generation reproduction study

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Subacute - 13 weeks (91 days) or less		
Rats, CD, ~40 to 60 g, ~21 days old, 20 males and 20 females per dose group	0, 25, 500, or 5000 ppm in the diest for 90 days	No effect on reproduction or lactation performance. Decreased mean body weight of F_0 and F_{1B} male and female rats in the high dose group was the only compound-related effect.	Pastoor 1985 MRID 00151028
Rats, Sprague-Dawley, ~7 weeks old, weighing 192.1 to 262.5 g (males) and 131.0 to 190.5 g (females), 90 rats per sex/group	0, 5, 25, 500, 2500, or 5000 ppm for 13 weeks.	Statistically significant decrease in growth rates in males and females exposed to ≥500 ppm; body weight gain significantly decreased in males exposed to ≥2500 ppm; food consumption was also decreased significantly in high-dose males and females. In addition, the decrease in terminal body weight in high-dose males was statistically significant as was the decrease in absolute liver weights of males exposed to 5000 ppm and females exposed to ≥2500 ppm. In females exposed to ≥2500 ppm, the liver to body weight ratio was decreased significantly. Significant findings that could not be correlated directly with treatment include elevated platelet counts at week 5 in females exposed to ≥2500 ppm and a similar elevation at week 14 in females exposed to 25, 2500, or 5000 ppm). No hepatic histomorphological changes were associated with treatment.	Burdock et al. 1982 MRID 00125391 First 13 weeks of a chroinic oral toxicity and reproduction study.

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Subacute - 13 weeks (91 days) or less		
Dogs, beagles, 24/sex/group	0, 50, 500, or 2500 ppm for 14 weeks.	NOEL = 500 ppm No treatment related effects on mortality, physical condition, food consumption, feed efficiency, clinical chemistry, or urinalyses. In high-dose males, slight decreases in mean body weight progressed throughout the study, reaching almost -6% at termination; mean body weights of mid- and low-dose males and females in all dose groups were comparable to or slightly greater than controls. Hematological changes in high-dose males included a slight decrease in mean corpuscular hemoglobin concentration at month 2 and a slight increase in mean platelet and mean total leukocyte counts at month 3; there were no hematological effects observed in females at any dose level. Mean thyroid/parathyroid weights and thyroid/parathyroid to body weight ratios increased in the high-dose males and females; however, only the increase in thyroid/parathyroid weight in females was statistically significant. Sporadically occurring gross and microscopically postmortem findings were not considered treatment related.	Daly 1985 00148639

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Teratogenicity/Reproduction		
Rats, CD, females, weighing 230 to 288 on day 0 of gestation, 25 rats/group	0, 20, 125 or 500 mg/kg/day by gavage (in aqueous 0.5% Methocel®) on days 6-15 of gestation.	No abortions occurred and no litters were delivered during the study. No mortality was attributed to treatment. Maternal toxicity was expressed as a statistically significant increase in salivation at 500 mg/kg/day, stomach ulcerations in one rat at 500 mg/kg/day, which may be an effect of treatment, statistically significant ($P \leq 0.01$) decreases in body weight gain and food consumption at 125 or 500 mg/kg/day, a significant decrease in average body weight in the high dose group, which persisted despite a significant increase in average food consumption ($p \leq 0.01$) after the treatment period [corrected maternal body weights were significantly decreased ($p \leq 0.01$) at 125 and 500 mg/kg/day], a dose-dependent, significant increase ($p \leq 0.01$) in average liver/body weight ratios at 125 and 500 mg/kg/day, a statistically significant decrease ($p \leq 0.01$) in average uterine weights at 500 mg/kg/day, which is considered to be related to the significantly decreased body weight, low incidence of resorption ($p > 0.05$) and the significant decrease ($p \leq 0.01$) in fetal body weights. The maternally toxic doses of 125 and 500 mg/kg/day resulted in significantly decreased ($p \leq 0.01$) fetal body weights, dose-dependent increases in the litter incidence of incomplete ossification of the thoracic and caudal vertebrae, sternebrae, xidphoid and pubes, which was statistically significant ($p \leq 0.05$ to $p \leq 0.01$) at 500 mg/kg/day [bifid thoracic vertebral centra and unossified caudal vertebrae were significantly increased ($p \leq 0.05$) at 125 mg/kg/day], and at 500 mg/kg/day increased incidences of edema, enlarged fontanelle, unossified suproccipital, altered ossification of the lumbar and sacral vertebrae and unossified metacarpals and metatarsals which were not statistically significant ($p > 0.05$) were considered thought to be treatment related. There were no significant dose-related incidences of other fetal alterations observed by external, soft tissue, or skeletal examination.	Christian and Doll 1985 MRID 00148640

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Teratogenicity/Reproduction (continued)		
Rats, CD, females, weighing 234 to 324 g on day 4 of gestation, 24 rats/group	0, 40, 250, or 1000 mg/kg/day by gavage (corn oil suspension) on days 5 to 14 of gestation.	No teratogenicity or embryo-fetal toxicity. Maternal toxicity observed at ≥250 mg/kg/day, manifested as increased incidence of salivation (significantly higher among 1000 mg/kg/day dose group), significantly decreased body weight at 1000 mg/kg/day days 5-8 ($p = 0.004$) and days 5-14 ($p < 0.1$). Post-administration of test substance, maternal body weight rebounded and weight gain was significantly increased in the 250 and 1000 mg/kg/day dose groups..	Feussner et al. 1982a MRID 00125835 Embryo-fetal toxicity and teratogenicity study in rats.
Rats, Wistar, 10 males and 20 females per dose group, females weighed 160-200 g, males weighed 180-220 g	0, 10, 50 or 250 mg/kg bw (in corn oil) by gavage daily for two generations (approximately 70 days in males during spermatogenic cycle and 14 days in females to cover up to two estrous cycles)	There were no treatment related signs of toxicity or behavioral changes observed. At 10 or 50 mg/kg bw there were no signs of adverse effects on reproductive performance. One male rat in the high dose group died during the premating dose period. A treatment-related, dose-dependent statistically significant decrease in pup growth was observed in all four litters (F_1a, F_1b, F_2a, F_2b) at the high dose and in three litters (F_1b, F_2a and F_2b) at 50 mg/kg bw. There were no malformed pups in any of the treated groups.	Shriram Institute for Industrial Research 1995 MRID 44163302 2-Generation reproduction study

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
ORAL			
	Teratogenicity/Reproduction		
Rabbits, New Zealand, white, ~5 months old, weighing 2.87 to 5.03 kg	0, 25, 100, 300, or 700 mg/kg/day (aqueous 0.5% Methocal suspension) on days 6-18 of gestation	No teratogenicity or embryo-fetal toxicity. Overt maternal toxicity manifested as a statistically significant increase in mortality ($p < 0.001$) at 700 mg/kg/day (12/20 animals); mortality in the 100 mg/kg/day group was 1/19; mortality in the 300 mg/kg/day group was 2/20. Signs of toxicity prior to death included anorexia and red or orange-colored urine (≥100 mg/kg/day), decreased motor activity and impaired righting reflex (≥300 mg/kg/day), and an isolated incident in the 300 mg/kg/day dose group of red or orange exudate found in cage pan. The incidence of abortion was 2/19, 2/20, and 1/20 in the 100, 300, and 700 mg/kg/day dose groups, respectively. Except for 1/19 in the 100 mg/kg/day group, anorexia was observed prior to abortion and all of the rabbits died subsequent to the abortions. Maternal toxicity also manifested as statistically significant decrease in body weight gain on days 6 through 9 in the 100 and 300 mg/kg/day dose groups. NOEL for maternal toxicity = 25 mg/kg/day.	Feussner et al. 1982b MRID 00125836 Teratogenicity study in New Zealand white rabbits.

Animal	Dose/Exposure	Response	Reference/ Comment
	***Chronic* -** > 90 days		
Rats, Sprague-Dawley, 6 groups of 90 males and 90 females, initial weights: 192.1 to 262.5 g (males), 131.0 to 190.5 g (females).	0, 5, 25, 500, 2500 or 5000 ppm in the diet for 52 weeks. Interim sacrifices conducted at 13 and 52 weeks.	Males exposed to 2500 or 5000 ppm had a statistically significant and treatment-related decrease in group mean body weights at 13 weeks, and the same effect was observed at 52 weeks in males and females exposed to 5000 ppm; depressed body weight gain, compared with controls, was observed in males and females exposed to 500, 2500, or 5000 ppm at 13 weeks and again at 52 weeks in males and females exposed to 5000 ppm; initial decreased food consumption for males exposed to 500, 2500, or 5000 ppm and females exposed to 2500 or 5000 ppm, which continued to be depressed throughout the study for males and females in the 5000 ppm dose group was not considered a toxic effect; rough coat may have been related to treatment and secondary to the poor nutritional status of the rats; alopecia (especially in females) was the most frequently noted clinical observation and appeared to be treatment related; sporadically occurring effects on hematology and clinical chemistry, which were statistically significant from controls were not consistent with a dose-related trend or effect; there was a possible relationship of dose with a darker, cloudy appearing urine with slightly decreased pH, notably in males; at 13 weeks, terminal body and absolute liver weights of 5000 ppm males were statistically less than controls as were the absolute and relative liver weights of females in the 2500 and 5000 ppm groups; at 52 weeks there were several remarkable findings regarding significantly increased organ weights, but the toxicological significance is unclear. Feeding study with concurrent 2-generation reproduction study in rats: 52-Week interim report (represents the results of the 1st year of the toxicity and oncogenicity phase of the study; results of the repro-duction study are reported separately.	Burns 1984 MRID 00145007 **On the basis of the data, and assuming that the effect on body weight gain can be attributed to palatability rather than toxicity, the investigators conclude that the NOEL for this study after 52 weeks of treatment is 500 ppm.**

Animal	Dose/Exposure	Response	Reference/ Comment
	***Chronic* -** > 90 days (continued)		
Rats, Sprague-Dawley, ~7-weeks old, body weights: 192.1 to 262.5 (males) and 131.0 to 190.5 (females)	0, 5, 25, 500, 2500, or 5000 ppm in the diet on a continuous basis for 104 weeks. Group 5 (2500 ppm) was sacrificed during weeks 61 and 62. Interim sacrifices were made after 13 and 52 weeks.	NOEL (104 wks) = 500 ppm, assuming that loss of body weight in males and females at 500 ppm is due to palatability and is not a toxic effect. **body weight**: statistically significant, treatment related decrease in mean body weight in males (2500 and 5000 ppm) at 13 weeks and in males and females (5000 ppm) at 52 weeks; statistically significant decrease in body weight gain, compared with controls, in males and females (500, 2500, and 5000 ppm) at 13 weeks and in males and females (5000 ppm) at 52 weeks. **food consumption (as g/week)**: initial decrease in food consumption in males (500, 2500, and 5000 ppm) and in females (2500 and 5000 ppm); decrease through week 26 in females (5000 ppm) thought to be result of small animal size and/or food refusal. **hematology and clinical findings**: sporadic, statistically significant differences from control values for hematology and clinical chemistry not consistent with dose-related trend or effect; trend (especially in males) toward "darker, cloudy appearing urine with slightly increased occult blood and hydrogen ion concentration (decreased pH) may have been dose related. **necropsy**: no remarkable findings **liver weights**: at 13 weeks, statistically significant decrease in terminal body weight and absolute liver weights of males (5000 ppm); at 52 weeks, statistically significant decrease in absolute and relative liver weights in females (2500 and 5000 ppm). **organ weights at 52 weeks**: statistically significant increases in mean absolute brain weights in males (25, 500, 2500, and 5000 ppm) and in females (2500 and 5000 ppm), mean absolute heart weights in males and females (2500 and 5000 ppm), mean kidney weights in males (2500 ppm), relative brain and heart weights of males and females (2500 and 5000 ppm), and relative kidney weights of males males (2500 and 500 ppm). At terminal sacrifice, statistically significant increase in relative brain and relative kidney weights of males.	Burdock and Hamada 1985 MRID 00151029 Chronic feeding study with concurrent 2-generation reproduction study in rats: Chronic phase. **Investigators state that "increases in realtive organ weights, compared with controls, can be explained by decreased body weight of the treated group."**

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
	***Chronic* - >90 days (continued)**		
Mice, CD-1, ~1 month old, weighing 16.6 to 33.9 g (males) and 15.1 to 28.5 g (females), 90 males and 90 females per dose group	0, 5, 25, 500, 2500 or 5000 ppm for 18 months. Partial sacrifice at 90 days; 2500 ppm group sacrificed at 12 months.	**NOEL = 5000 ppm**, assuming that decreased body weights in treated mice were related to dietary intake of test compound. **body weight**: although decreases in mean body weight were observed in all treatment groups and body weights of all treated males and 500 and 5000 ppm females were statistically lower than controls, there was no dose-response relationship between body weight or body weight gain and treatment. **food consumption**: slightly lower than controls, but no evidence of dose-response relationship. **clinical observations and mortality**: no indication of treatment related toxicity. **organ weights**: statistically significant differences were not considered treatment related and no there was no evidence of a dose-response relationship.	Stadler 1984 MRID 00151135 90-Day and 18 month feeding study
Dogs, purebred beagles, 3 groups of 10 males and 10 females, 18-20 weeks old	0, 50, 500, or 5000 ppm in the diet for 1-year. Four beagles per group sacrificed at 13 weeks.	No mortalities occurred during the study. NOEL (males) = 500 ppm NOEL (females) = 5000 ppm Only evidence of a systemic effect was a slight decrease in food consumption in males exposed to 5000 ppm. There was a consistent decrease in serum lactate dehydrogenase in all groups of both sexes at two or more intervals. Nonetheless, since all mean values (control and treated groups) were within historical control range, investigators are uncertain of biological significance of this finding. The authors report several instances of statistically significant changes among the study parameters but acknowledge no evidence that the effects were treatment related.	Burdock 1984 MRID 00141821 Combined 3-month and 1-year feeding study

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
INHALATION			
Rats CD, 10 males (weighing 229 to 260 g) and 10 females (weighing 160 to 182 g) per dose group	0 or 2.3-8.3 (mean 5.3) mg/L for single 4-hour exposure; observation period = 14 days Controls exposed to air only.	All rats (treated and control) exhibited slight red nasal discharge and ocular discharge ruing exposure; faces of treated rats covered with test material; increased incidence of slight weight loss lasting 1 day after exposure in treated rats; "a few" treated rats (male and females) exhibited slight brown nasal discharge on day 1 after exposure. LC_{50} > 5.0 mg/L	Burgess et al. 1983 MRID 00125830 5 mg/L is the limit test specified by EPA Health Effects Test Guidelines
Rats, CD, 10 males and 10 females, 8 weeks old, per dose group	0, 1.3, or 6.7 mg/L for single 4-hour exposure; observation period = 14 days Control (2 groups) exposed to air only.	No mortality; significant adverse clinical signs included mass on the abdomen of one female in 1.3 mg/L group, and hair loss from legs in one female and two males, all during week 2 of recovery; common clinical signs in rats exposed to 6.7 mg/L included wet or stained perineum, nasal or oral discharges, hair loss from face and faces stained by test material; one female at 6.7 mg/L had lung noise; most clinical signs were observed 1 to 3 days after exposure. No pathological abnormalities observed in treated rats at either concentration level. LC_{50} > 5 mg/L	Hutt 1985 MRID 00148634 5 mg/L is the limit test specified by EPA Health Effects Test Guidelines
OCULAR			
Rabbits, New Zealand white, young adult females	50 mg aliquot administered to lower conjuctival sac of left eyes, which remained unwashed; right eyes served as controls; eyes examined 1, 24, 48, and 72 hours after treatment.	Observations included slight corneal opacity in one rabbit; mild conjunctival redness in six rabbits, and slight chemosis in one rabbit. There was no occurrence of corneal injury. Test material classified as a mild eye irritant under the conditions of this study.	Brock 1987 MRID 40858801 This is a primary eye irritation study; it includes individual eye irritation scores.

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
DERMAL			
Rabbits, New Zealand white, 5 males (weighing 2314 to 2765 g) and 5 females (weighing 2253 to 2598 g) per dose group	2000 mg/kg applied to skin abraded with minor incisions and left in contact with skin for 24 hours by means of a rubber damming nonabsorbent binder.	No mortality; LD_{50} > 2000 mg/kg; all rabbits gained weight and appeared normal throughout the study except for three, which had restraining collars in their mouths on days 1 and 3; dermal effects included Grade 2 (well defined) erythema, Grades 1 and 2 (very slight to slight) edema, and thickening in four males and four females on day 1and compound adhering to the skin in all rabbits on days 1 and 3. Erythema and edema could not be scored in one male and one female on day 1 due to the compound adhering to the skin.	Gargus 1985a MRID 00162609
Rabbits, New Zealand white, 5 males (weighing 2342 to 2772 g) and 5 females (weighing 2575 to 2759 g) per dose group	2000 mg/kg applied to abraded skin and occluded for 24 hours	No mortality; LD_{50} > 2000 mg/kg; no dermal effects, anorexia was observed in one rabbit on days 3 and 4 and in another rabbit on day 5; all animals except one gained weight throughout the study.	Gargus 1985b MRID 40622702

Appendix 1: Toxicity of metsulfuron methyl to experimental mammals

Animal	Dose/Exposure	Response	Reference/ Comment
Rabbits, New Zealand white, 6 young adult males	0.5 g Escort® Herbicide applied to a localized shaved test site on back of each rabbit and covered with semi-occlusive dressing for ~4 hours	No clinical signs of toxicity; desquamation, eschar, sloughing, and epidermal scaling observed during the study; by 1 hour after patch removal, erythema (score of 1 or 2) in all rabbits; one rabbit had edema (score of 1); at 24 and 48 hours, erythema (scores of 1, 2, or 3) observed in all rabbits; 5/6 rabbits had edema (scores of 1, 2, or 3); at 72 hours, erythema (scores of 1, 2, 3, or 4) observed in all rabbits; 5/6 rabbits had edema (scores of 1 or 2); by day 10 erythema and edema resolved in all rabbits; all dermal effects resolved by day 13 after treatment. Escort® Herbicide classified as an "IRRITANT" under conditions of this study. Scores: Erythema 1 = very slight; 2 = well defined; 3 = mod to sever; 4 = severe (in depth injuries) Edema 1 = very slight; 2 = slight; 3 = moderate; 4 = severe (extending beyond exposed area)	Finlay 1996 MRID 43945401

Appendix 2: GLEAMS modeling of metsulfuron methyl.

A2.1. General Considerations -- GLEAMS is a root zone model that can be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions (Knisel et al. 1992). 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 the exposure assessments, two types of estimates are needed: off-site (i.e., application site) movement of metsulfuron methyl to estimate potential concentrations of metsulfuron methyl in water or soil and on-site soil residues of metsulfuron methyl to estimate the duration of potential effects on non-target plant species.

A2.2. Runoff from and Percolation Through Soil Layer -- For off-site movement, preliminary model runs indicated that both runoff and percolation could be significant depending on the soil type and estimates of metsulfuron methyl binding to soil (K_d). This impacts one of the key parameters on the GLEAMS model, the depth of the soil horizon being modeled. This is referred to at the routing depth in the GLEAMS documentation (Knisel et al. 1992). The shallower the depth of the horizon, the greater the amount of runoff from and percolation through the soil layer (Knisel et al. 1992, p. 32). For a generic exposure assessment, the selection of the rooting depth is arbitrary. For this part of the modeling, a routing depth of 1 foot is used. Any percolation losses below this layer are assumed to contaminate ground water - i.e., the water table is very shallow. The selection of shallower or deeper routing depths - i.e., shallower or deeper water table - has a great impact on percolation loss and a lesser impact on runoff, depending on the soil type.

The key chemical-specific parameters for metsulfuron methyl are water solubility, $K_{o/c}$, and soil halftime. The water solubility of metsulfuron methyl is dependent on the pH (USDA/ARS 1995; Barefoot and Cooke 1990; Du Pont 1985a,b,c) and soil pH has a substantial impact on the movement of metsulfuron methyl through soil (Pool and DuToit 1995). At a pH of 5, the water solubility of metsulfuron methyl is 1750 mg/L. At a pH of 7, the water solubility of metsulfuron methyl is 9500 mg/L. For this exposure assessment, a pH of 6 is used for sandy soil (USDA/ARS 1995) and the water solubility is estimated at 1236 mg/L, the geometric mean of values at pH 5 and pH 7. For clay, the water solubility is taken as 2790 mg/L for soil at pH 7 (USDA/ARS 1995). This tends to maximize percolation through sand and runoff from clay.

The $K_{o/c}$ is the soil-water distribution coefficient (K_d) based on organic carbon and is typically calculated as:

$$K_{o/c} = K_d \times 100/OC\%$$

or equivalently

$$K_{o/c} = K_d/oc$$

where *oc* is the organic carbon content of the soil (mg organic carbon/mg soil) (Winegardner 1996, p. 116-117) and *OC* is the percent organic carbon in the soil.

The K_d, also by definition, is the ratio of the concentration of a chemical adhered to soil particles to the concentration of the chemical in soil water and is typically expressed in units of mL/g - i.e., µg of chemical/g of soil ÷ µg of chemical/mL of water = mL water/g soil). The actual value of a particular K_d will depend on the physicochemical properties of both the soil as well as the chemical being bound to the soil (Winegardner 1996).

The binding of metsulfuron methyl to soil is highly variable, depending primarily on pH and organic carbon. Based on measured $K_{o/c}$ values ranging from 4 to 29 and measured K_d values ranging from 0.05 to 1.53 in 10 different soils [Table 3, p. 304 in Baskaran et al. 1996], Baskaran et al. (1996) proposed the following relationship for estimating the K_d of metsulfuron methyl:

$$K_d = 1.12 + (0.07\ OC) - (0.16\ pH) \qquad [r^2=0.81]$$

where *OC* is the % organic carbon and *pH* is the soil pH. Walker et al. (1989) measured the binding of metsulfuron methyl in 8 different soil types and noted K_d values ranging from 0.04 to 0.54. While binding was positively correlated with organic matter, the correlation was not statistically significant and the relationship could be described using an exponential model with soil pH as the sole explanatory variable:

$$K_d = \exp(2.56 - 0.73\ \mathrm{pH}) \qquad [r= -0.865,\ r^2=0.74].$$

As part of the registration package of metsulfuron methyl, Du Pont (1985a,b,c) has conducted studies on soil binding in 12 different soil types and noted K_d values ranging from 0.05 to 4.9 and K_{oc} values ranging from 4 to 206 (USDA/ARS 1995).

For the GLEAMS modeling, the data on soil pH and $K_{o/c}$ is taken from the summary provided by USDA/ARS (1995). A $K_{o/c}$ value 207 is used for sand with a pH of 6.1 and an organic matter content of 0.3%. For clay, the $K_{o/c}$ is set at 12 with a soil pH of 5.3 and an organic matter content of 5.3%. These selections are somewhat arbitrary but encompass a reasonable range of values and are consistent with other data in the published literature.

The persistence of metsulfuron methyl in soil is also highly variable. As indicated in Table 2-2, a number of different studies are available on the persistence of metsulfuron methyl in soil and reported halftimes in soil range from about 1 to 180 days. Factors such as temperature, pH, organic matter, and soil depth may all impact the rate of degradation in soil (Bastide et al. 1994; Berger et al. 1998; Ismail and Lee 1995 James et al. 1995; Pons and Barrisuo 1998; Sabadie and Bastide 1990;Sarmah et al. 1998;Walker and Jurado-Exposito 1998;Walker et al. 1989) . While microbial activity also influences the persistence of metsulfuron methyl in soil, the magnitude of the impact is only about a factor of two (Bastide et al. 1994; Berger and Wolfe 1996b), less than factors such as soil pH, temperature, and moisture content (Pons and Barrisuo 1998; Walker et al. 1989).

Soil halftimes of 10 days to 38 days are reported in USDA/ARS (1995) and this range is consistent with other values reported in published studies (Bastide et al. 1994; James et al. 1995). Much longer soil halftimes have been reported in Knisel et al. (1992) and USDA/FS (1995). These longer halftimes are consistent with and may reflect unpublished field studies that were submitted to U.S. EPA as part in support of the registration of metsulfuron methyl (Anderson and Harvey 1984; Rapisarda and Scott 1986). As detailed by Rapisarda and Scott (1986), field soil halftimes have an overall range of 1 month to somewhat over 10 months and degradation tends to be slower when metsulfuron methyl is applied in the fall as opposed to the spring.

For this risk assessment, a value of 10 days is used in sandy soil and 300 days used for clay soil. This approach tends to reduce the impact of degradation and thus increase the off-site transfer of metsulfuron methyl because, as detailed below, metsulfuron methyl may rapidly leach through sandy soil and thus the influence of degradation processes in sand are reduced regardless of the degradation rate in sand. In clay, however, metsulfuron methyl will tend to move more slowly and thus using a higher soil halftime in clay will tend to reduce estimates of total degradation.

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 0.5 - i.e., half of all of the applied metsulfuron methyl reaches the soil surface immediately after application. Foliar wash-off is taken at 0.9 and foliar half-time is set to 30 days. These values are consistent with the high water solubility of metsulfuron methyl and the reported halftime on vegetation given by Knisel et al. (1992).

As indicated above, 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 concentrations of metsulfuron methyl in ambient 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 and inversely related to percolation. As with the parameters used in the pesticide file, the parameters used in these files are set in the mid-range to balance the potential for runoff and percolation.. 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 as well as percolation 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 6 year period, with applications of metsulfuron methyl contaminated herbicide on Julian day 180 of years 2 through 6. The first year of the simulation was used to condition the soil and the average annual rainfall was simply divided equally among each day. In subsequent years, equal amounts of rainfall were generated every tenth day to yield the average annual rainfall. This approach was taken because most runoff and percolation 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 and percolation.

A summary of the results are given in Table A2-1 and illustrated in Figure A2-1. Under conditions of low rainfall (≈10 inches per year or less), neither runoff nor percolation is anticipated under the conditions modeled. Thus, under relatively arid conditions, the loss of metsulfuron methyl from the soil is likely to be due solely to chemical or biological degradation.

At higher annual precipitation rates, the transport of metsulfuron methyl will depend on the characteristics of the soil. For both clay and sand, the primary mode of transport is percolation, with very little off site movement of the compound in runoff. For example, at rainfall rates of 100 inches per year, off-site loss from clay due to runoff is estimated to be about a factor of 45 less than loss from percolation. For sand, no runoff is anticipated and all off-site movement is from percolation.

Given the general rather than site-specific nature of this modeling exercise and the complexities of estimating both the persistence and movement of metsulfuron methyl in soil, these estimates of runoff and percolation should be considered only as crude approximations of environmentally plausible rates.

A2.3. Estimated Concentrations in Water Associate with Runoff from Clay or Percolation from Sand Using a 1 Foot Soil Layer -- While the data presented in the previous section are useful for assessing the types of loss from various sites and the magnitude of yearly losses relative to the amount applied at the treated site, these cannot be used directly to project concentrations in ambient water. By making certain assumptions concerning the persistence of metsulfuron methyl in water and the amounts of metsulfuron methyl that could be transported to surface water, however, such estimates can be made.

These estimated concentrations of metsulfuron methyl in water require estimates of the daily amount of metsulfuron methyl in runoff or percolation that is transported to water, the volume of water into which the metsulfuron methyl is mixed, and the persistence of metsulfuron methyl in the water.

No field studies have been encountered on the fate of metsulfuron methyl in ambient water. Thompson et al. (1992) measured the persistence of metsulfuron methyl experimental enclosures in a forest lake with pH ranging from 6.7 to 7.3 and a water temperatures of 22°C (71.6°F). At water concentrations of 0.01 mg/L, the halftime for metsulfuron methyl was 29 days. At 1.0 mg/L, however, the halftime was 84 days. As summarized in Table 2-1, metsulfuron methyl is chemically stable in neutral water (pH 7) with a hydrolysis rate constant at pH 7 of 0.00105 $days^{-1}$, corresponding to halftime of 660 days [ln(2)÷0.00105 $days^{-1}$](Berger and Wolfe 1996). Nonetheless, metsulfuron methyl undergoes photolysis with a halftime of 16.9 days (USDA/ARS 1995), similar to the more rapid halftime reported by Thompson et al. (1992).

As summarized below, peak metsulfuron methyl water concentrations under worst case conditions are anticipated to be below 0.007 mg/L or less. Thus, for this risk assessment, the halftime in water of 29 days at concentrations of 0.01 mg/L noted by Thompson et al. (1992) is used. This halftime corresponds to a dissipation/degradation rate of about 0.024 $days^{-1}$ [ln(2)÷29 days = 0.0239 $days^{-1}$].

All GLEAMS simulations were conducted at an application rate of 1 lb a.i./acre but all results presented in this section are adjusted for an application rate of 0.02 lb a.i./acre. [This approach is necessary because very low rates of application can lead to erroneous zero estimates in GLEAMS output files because GLEAMS reports runoff and percolation only to 6 places to the right of the decimal in output files.] GLEAMS output files were read for output field 751 (total off-site loss in g/ha).

Based on a 50 foot wide ROW, one hectare (10,760 ft^2) is about 215 feet long [10,760 ft^2÷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:

$$65.532 \text{ m} \times 15.24 \text{ m} \times 1 \text{ m} = 998.70 \text{ m}^3 \approx 1000 \text{ m}^3 \times 1000 \text{ L/m}^3 = 1{,}000{,}000 \text{ L}.$$

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

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

where ä is the amount added at time *t* by runoff or percolation read from the GLEAM output files. The concentration in water at time *t* in units of mg/L is then calculated as:

$$A_{t\ (g/ha)} \times 1000 \text{ mg/g} \div 1{,}000{,}000 \text{ L/ha}.$$

Following this approach, the concentrations in water over a one year period following the application of metsulfuron methyl at a rate of 0.02 lb a.i./acre can be estimated. Peak water concentrations will vary substantially with rainfall rates. Below annual rainfall rates of 10 inches per year, no substantial off site movement by percolation or runoff is anticipated. At annual rainfall rates of 25 to 250 inches per year, peak water concentrations vary from about 0.0033 mg/L for clay and 0.006 mg/L for sand.

It should be noted that the relatively long period to peak water concentrations in clay simply reflects the slower movement in and slower degradation of metsulfuron methyl through clay relative to sand and the halftime of 29 days used for the degradation/dispersion of metsulfuron methyl in water.

The leaching estimates modeled by GLEAMS are generally consistent with estimates from the published literature. In a general review of the literature, Bergstrom and Stenstrom (1998) have suggested that 0-6% of applied metsulfuron methyl may be expected to leach though soil. Based on the GLEAMS modeling, this statement would be correct at rainfall rates of less than 25 inches per year. As noted above, a mean average annual rainfall in the United States is 27.69 inches and at this rainfall rate GLEAMS estimates off-site movement in the range of 0 to 20%. The relatively high upper range of this estimate is based on clay soil and may be considered an extreme if not worst-case assessment.

While elements of the application of the GLEAMS may be considered conservative, the available field and laboratory studies are reasonably consistent with the model results. In a lysimeter study, Bergstrom (1990) noted leaching of about 0.02% to 0.06% of the applied amount of metsulfuron methyl after a cumulative rainfall plus watering of 447 mm or about 17.5 inches. As illustrated in Figure A2-1, this is reasonably consistent with the GLEAMS modeling which indicates little if any leaching or percolation at rainfall rates below 20 inches per year. At higher rates of rainfall - i.e., on the order of 83 inches per year - Ismail and Kalithasan (1997) noted phytotoxic levels of metsulfuron methyl in some soils at depths of 25-30 cm (about 1 foot) after 40 days. This again is consistent with the GLEAMS estimates suggesting that metsulfuron methyl may leach below 12 inches in both clay and sandy soil at relatively high rainfall rates. The study by Pool and DuToit (1995) suggest that in some high pH soils, metsulfuron methyl may leach to a depth of 240 mm (about 9.5 inches) after a single simulated rainfall of 20 mm (2 cm or about 0.78 inches), which corresponds to an annual rainfall rate of about 287 inches. This is also consistent with the GLEAMS modeling that suggests extensive loss at high rainfall rates.

Because of the levels in water one year after application, the potential for accumulation in water with multiple year treatments must be assessed. Based on the plateau principle (e.g., Goldstein et al. 1974; O'Flaherty 1981), the concentration at infinite time (C_∞) associated with treatments given over an interval of time (Ät) relative to the concentration after the first treatment (C_0) may be calculated as:

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

where, k is the elimination rate in units of reciprocal time and Ät is the time interval between treatments. Taking the halftime of 28 days that corresponds to an loss rate of 0.024 $days^{-1}$ [$k = ln(2) \div t_{1/2}$] and assuming an exposure interval of 365 days (yearly application), no substantial accumulation of metsulfuron methyl expected in water:

$$1 \div (1 - e^{-0.024 \times 365 \text{ days}}) = 1.00016.$$

This is consistent with the 5 year GLEAMS models that indicate no accumulation of metsulfuron methyl in water with repeated yearly applications.

A2.4. Persistence in 1 Foot Soil Layer -- For assessing the impact of on-site soil residues, a routing depth of one foot is used and the soil concentration is expressed as the average concentration within the one foot deep soil layer[1]. A depth of one foot was selected as a reasonable routing depth for non-target plant species. Selecting a deeper layer would decrease the average concentration but increase the duration of exposure. Conversely, selecting a shallower layer would increase the average concentration but decrease the duration of exposure. As with any 'generic' application of a model such as GLEAMS, the choice of a specific depth is arbitrary. Except of the change in rooting depth, all of the model parameters where identical to those described in section A2.2 for the 3 foot deep soil layer.

Based on the GLEAM modeling, peak levels in soil are similar for both clay and sand, about 0.0035 mg/kg and the major differences involve the soil halftimes used for clay (35 days) and sand (10 days). The longer soil halftime used for clay along with the slower movement of metsulfuron methyl through clay account for the more gradual decrease in the concentration of metsulfuron methyl in clay relative to metsulfuron methyl in sand.

In an arid environment (annual precipitation of 10 inches per year or less), off-site movement in through percolation or runoff will be negligible and the rate of degradation in soil will depend primarily on degradation. At higher precipitation rates for both clay and sand, percolation increases and is the dominant factor in dissipation at rainfall rates of 50 inches/year or more.

Substantial concentrations of metsulfuron methyl may remain in soil at the end of one year, particularly in arid environments in which the impact of percolation is minimal. As with the above scenario for water, this suggests the potential for accumulation in the case of multiple applications over the course of several year. Using the plateau principle illustrated above for water and taking a halftime of 300 days, [$k = ln(2) \div 300 \text{ days} = 0.0023 \text{ days}^{-1}$], and assuming an exposure interval of 365 days (yearly application), the accumulation of metsulfuron methyl in soil would be expected to be no more than a factor of about 1.8:

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[1]If only a single soil horizon is specified in the input file, as was done in all cases in this exposure assessment, output files from the GLEAMS model still give soil concentrations (parameter 811) for four soil horizons. The first horizon is the effective mixing depth - one cm for surface applications. The next three horizons are equally divided amount the remaining routing depth. Thus, for a 1(30.48 cm) foot routing depth, the first soil horizon is1 cm and the next three horizons are about 9.83 cm deep.

$$1 \div (1 - e^{-0.0023 \times 365\ days}) = 1.76.$$

This approach is actually rather conservative, not only because it uses a halftime at the upper range of measured values but also because it ignores the effect of dissipation. In any event, while there could be some build up of metsulfuron methyl residues over time, the magnitude of the build up would be expected to be less than a factor of two.

As with the modeling results given in the previous section of this appendix, these estimates of persistence in soil should be considered only as crude approximations of environmentally plausible rates. Site-specific considerations - particularly microbial activity and soil binding of metsulfuron methyl - could lead to substantial variations form the modeled values. There are adequate data in the publications cited in this appendix to conducted more precise site-specific exposure assessments.

Table A2-1: Summary of GLEAMS estimates of the annual off-site transport of imazapyr as a proportion of the applied amount.

Annual Rainfall (inches)	Proportion	
	Clay (Runoff)	Sand (Percolation)
5	0.000	0.000
10	0.000	0.000
25	0.190	0.076
50	0.536	0.447
100	0.610	0.691
150	0.627	0.771
200	0.636	0.800
250	0.642	0.818

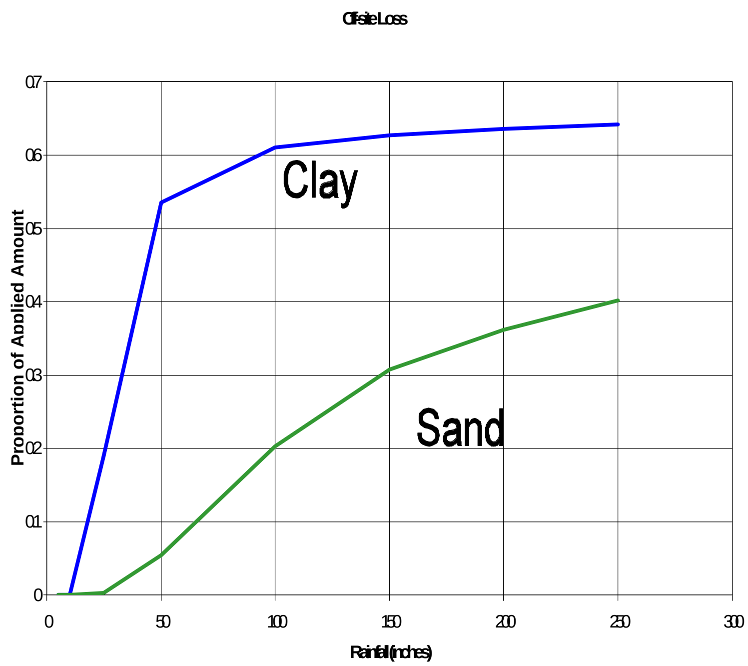

Figure A2-1: Off-site movement of metsulfuron methyl at various rainfall rates from clay and sand.

Appendix 3: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference	Comments
Rainbow trout (*Salmo gairdneri*), 2.8 cm mean length, 0.17 g mean wgt, 10 trout/concentration	0, DMF control, 5, 25, 50, 100, or 150 mg/L for 96 hours, static, no aeration. Higher concentrations not tested due to low water solubility and limited solubility in carrier solvents of test material. DPX-T6376 (purity = 92.9%)	No mortality at concentration up to 150 mg/L during 96-hour exposure period. At 24 hours, 3 fish exposed to 150 mg/L exhibited erratic swimming, rapid breathing and were lying on the bottom of the test container; 2/3 fish recovered completely by 48 hours; the third fish was affected throughout the entire study.	Muska and Hall 1982 MRID 00125816	DMF control = 0.5 mL DMF/L well water
Bluegill sunfish (*Lepomis macrochirus*), 3.6 cm mean length, 0.87 g mean wgt, 10 fish/concentration	0, DMF control, 5, 25, 50, 100, or 150 mg/L for 96 hours, static, no aeration. Higher concentrations not tested due to low water solubility and limited solubility in carrier solvents of test material. DPX-T6376 (purity = 92.9%)	No mortality or acute toxicity at concentrations up to 150 mg/L during 96-hour exposure period.	Phillips and Hall 1982b MRID 00125817	DMF control = 0.5 mL DMF/L well water

Appendix 3: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference	Comments
Bluegill sunfish (*Lepomis macrochirus*), 3.9 (range 3.4 to 4.7) cm mean length, 1.17 g (range 0.78 to 2.00) mean wgt, 10 fish/concentration	0, NaOH control,1, 10, 100, or 1000 mg/L for 96 hours, static, no aeration. pH adjustment (1N NaOH) to accomplish solubility of compound	No mortality or acute toxicity at concentrations up to 1000 mg/L during 96-hour exposure period.	Hall 1984a MRID 00148648	
Bluegill sunfish (*Lepomis macrochirus*), 4-5 cm in length, 2-4 g each, 4 groups of 75 fish	0.01 or 1.0 ppm [phenyl-^{14}C] DPX-T6376 for 4 weeks in dynamic flow through study Exposure phase followed by 14-day depuration phase.	No adverse effects noted in any of the groups of fish, no mortality, and fish behavior appeared normal. The average bioaccumulation factor was <1 for all tissues and dose levels.	Han and Anderson 1984 MRID 00149407	Study designed to measure accumulation of radioactivity in edible tissue, viscera, and liver. Two diluter malfunctions occurred during the study, which increased test concentrations briefly in exposure aquaria.

Appendix 3: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference	Comments
Rainbow trout (*Salmo gairdneri*), 4.1 (range 3.7 to 4.5) cm mean length, 0.82 (range 0.53 to 1.20) g, 10 fish/concentration	0, NaOH control,1, 10, 100, or 1000 mg/L for 96 hours, static, no aeration. pH adjustment (1N NaOH) to implement solubility of compound	Three fish in the 100 mg/L group died (1 at 72 hours; 2 at 96 hour); however, the investigators do not consider this effect significant because there was no mortality at the 1000 mg/L concentration. Clinical signs observed in some fish exposed to ≥100 mg/L include darkening in color, swimming at the surface, lethargy, erratic swimming, rapid respiration and laying at the bottom.	Hall 1984b MRID 00149672	

Appendix 3: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference	Comments
Rainbow trout (*Oncorhynchus mykiss*) 22-hour-old embryos	Nominal test concentrations of 2.4, 4.7, 9.5, 19, 38, 75, or 150 mg/L D{X-T6376 (99.13% ai) for 90 days.	No significant effect on hatch rate, last day of hatching, first day of swim up, survival, abnormalities, or weight of surviving fingerlings. Differences in first day of hatching and surviving fingerling length were small but significant at >8.0 mg/L. NOEC = 4.5 mg/L based on mean measured concentrations, first day of hatching and standard length of surviving fingerlings at 90 days. MATC = 6.0 mg/L LOEC = 8.0 mg/L No meaning estimates of LC_{50} or EC_{50} were calculated because the highest percent affected in any test concentration was <17%.	Kreamer 1996 MRID 44122801	This is a 400 page hard text report with many tables, etc.

Appendix 3: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference	Comments
Common carp (*Cyprinus carpio* LINN) 4.90 (+0.86) cm in length and 4.16 (+0.65) g in wgt and Nile tilapia (*Oreochromis niloticus* PETERS) 4.99 (+0.37) cm in length and 3.23 (+0.54) g in wgt, 20 fish per concentration	5-6 (NOS) concentrations of ALLY 10/10WP were used in standardized static bioassay. Concentrations of the test solutions were not verified by analysis and the results are based on nominal concentrations expressed in ppm.	96-hr LC_{50} for carp = 3320.5 ppm 96-hr LC_{50} for tilapia = 2334.6 ppm	Research Institute for Freshwater Fisheries 1995 MRID 44015401	This study was conducted in Indonesia to meet a registration requirement for an herbicide formulation of 10% metsulfuron methyl and 10% chlorimuron ethyl. This formulation is not registered in the United States and registration action is not pending. The study was submitted because it reports observations in species not previously evaluated.

Appendix 4: Toxicity of metsulfuron methyl to birds.

Animal	Dose	Response	Reference
		ACUTE STUDIES - 1 to 14 days	
Mallard ducks (*Anas platyrhynchos*), 8 days old, 10 ducks/dose group	562, 100, 1780, 3160, or 5620 ppm in diet for 5 days.	No mortalities among treated birds, a dose-related decrease in body weight gain was observed at 3160 and 5620 ppm groups during the exposure period. NOEL = 1780 ppm.	Beavers 1984a MRID 00148647
Bobwhite quail (*Colinus virginianus*), ~6 ½ months old, 5 males and 5 females/dose group	0, 292, 486, 810, 1305, or 2250 mg/kg by gavage for 14 days [vehicle = corn oil]	LD_{50} > 2250 mg/kg (HDT) No treatment-related mortality at any dose group, dose-related effect on body weight observed at ≥292 mg/kg (days 0-3) and slight effect on food consumption in females at ≥486 and possible in males at 2250 mg/kg (days 0-3) NOEL < 292 mg/kg	Beavers 1984b MRID 00148645
Bobwhite quail (*Colinus virginianus*), 10 days old, 10 quail/dose group	0, 562, 1000, 1780, 3160, or 5620 ppm in the diet for 5 days.	No mortality among treated birds, appearance remained normal throughout the study, a decrease in body weight gain was observed in the 3160 and 5620 ppm dose groups. NOEL = 1780 ppm	Beavers 1984c MRID 00148646
Bobwhite quail (*Colinus virginianus*), 14 days old, 10 birds/dose group	0, 562, 1000, 1780, 3160, or 5620 ppm in diet for 5 days, followed by 3-day observation period; [positive controls given 15.9, 25.1, 39.8, 63.1, or 100 ppm technical dieldrin (87% pure)]	LC_{50} > 5620 ppm. No mortality at any dose level; all treated ducks normal in appearance and behavior at all dose levels, except for slight decrease in body weight gain in the 5620 ppm dose group. Postive controls: LC_{50} = 35 ppm	Fink et al. 1981a MRID 00128820

Appendix 4: Toxicity of metsulfuron methyl to birds.

Animal	Dose	Response	Reference
		ACUTE STUDIES - 1 to 14 days *(continued)*	
Mallard ducks (*Anas Platyrhynchos*), 14 days old, 10 birds/dose group	0, 562, 1000, 1780, 3160, or 5620 ppm in diet for 5 days, followed by 3-day observation period; [positive controls given 72, 100, 130, 193, or 269, technical dieldrin (87% pure)]	LC_{50} > 5620 ppm. No mortality at any dose level; all treated ducks normal in appearance and behavior at all dose levels, except for possible lethargy observed in 5620 ppm dose group; only sign toxicity was a slight decrease in food consumption and body weight gain in the 3160 and 5620 ppm dose groups. Postive controls: LC_{50} = 162 ppm	Fink et al. 1981b MRID 00128819
		SUBCHRONIC REPRODUCTION STUDIES - 24 weeks	
Northern bobwhite (*Colinus virginianus*), 19 weeks old, 16 males and 16 females/dose group	0, 40, 200, or 1000 ppm in the diet for 23 weeks.	No mortalities in treated birds at any dose level, no overt signs of toxicity in treated birds, no treat-related effects on body weight or food consumption, no adverse effects on reproductive parameters tested. NOEL = 1000 ppm (HDT)	Beavers et al. 1996a MRID 44115701
Mallard ducks (*Anas platyrhynchos*), 27 weeks old, 16 males and 16 females/dose group	0, 40, 200, or 1000 ppm ai in the diet for 24 weeks	No mortality among treated birds, no treatment related effects on body weight or food consumption, no effects on reproduction at any dose level. NOEL = 1000 ppm (HDT)	Beavers et al. 1996b MRID 44115702

Appendix 5: Toxicity of metsulfuron methyl to honey bees

Animal	Exposure	Response	Reference
Honey bees (*Apis mellifera* L.), two replications of 10 bees each per treatment level, **body weight data not provided**	6.25, 12.5, or 25 μg/bee; in 1 mL acetone; a micropipette was used to apply the dose dorsally to the thorax of immobilized bees. Positive controls (20 bees) received dermal applications of 0.125, 0.25, 0.5, 1, 2, or 4 μg/bee of carbaryl.	48 hr LD_{50} = >25 μg/bee; test material was considered to be relatively nontoxic to the honey bee. Mortality was 20% in the positive control group 48 hr LD_{50} (**carbaryl**) = 0.786 μg/bee These are the results of Test A in this study. No negative control group of untreated bees was used in Test A.	Meade 1984a MRID 00141829
Honey bees (*Apis mellifera* L.), two replications of 10 bees each per treatment level, **body weight data not provided**	0, 3.125, 6.25, 12.5, or 25 μg/bee in 1 mL acetone; a micropipette was used to apply the dose dorsally to the thorax of immobilized bees. Positive controls (20 bees) received dermal applications of 0.125, 0.25, 0.5, 1, 2, or 4 μg/bee of carbaryl.	Mortality in bees treated with test material was 10% at 25 μg/bee, 20% at 12.5 μg/bee, and 15% at 6.25 μg/bee; no mortality occurred at 3.125 μg/bee. 48 hr LD_{50} = >25 μg/bee; test material was considered to be relatively nontoxic to the honey bee. 48 hr LD_{50} (**carbaryl**) = 1.05 μg/bee There was no mortality among negative controls.	Meade 1984a MRID 00141829
Honey bees (*Apis mellifera* L.), four replications of 10 bees each per treatment level, **body weight data not provided**	12.5, 25, 50, or 100 μg/bee in 2 mL acetone; a micropipette was used to apply the dose dorsally to the thorax of immobilized bees. Positive controls received 0.125, 0.25, 0.5, 1, 2, or 4 μg/bee of carbaryl.	There was no mortality among bees treated with the test material even at 100 μg/bee (HDT). 48 hr LD_{50} = >100 μg/bee; test material was considered to be relatively nontoxic to the honey bee. 48 hr LD_{50} (**carbaryl**) = 0.963 μg/bee; 48 hr LD_{90} (**carbaryl**) = 2.287 μg/bee; slope = 3.4127. There was no mortality among untreated bees; mortality in control groups treated with acetone only were 3% at 24 and 48 hours. These are the results of Test B in this study. A negative control group of untreated bees was used in Test B.	Meade 1984b MRID 00148650

Appendix 6: Bioassays of metsulfuron methyl toxicity in terrestrial plants by direct spray.

Plant	Exposure	Response	Reference
Dicots: soybean, cocklebur, cotton, morningglory, wild buckwheat, sugar beet Monocots: corn, barnyardgrass, rice nutsedge	Single application of metsulfuron methyl (technical 99%+); solvent: AGWT containing 8 mL Tween 20, 150 mL glycerine, 160 mL water, and 3000 L acetone. **Preemergence:** at 0.25, 1, 4, 16, 50 or 125 g ai/ha **Postemergence:** at 0.25, 1, 4, 16, 50 or 125 g ai/ha acetone)	50 g ai/ha toxic to all test plants in green-house studies. After 16 days, pre-mergence application caused growth reduction and malformation, while postemergence application resulted in chlorotic (yellowing) and stunted plants. Broadleaf plants highly susceptible to pre-and post-mergence applications of 4 g; monocots more tolerant than dicots. These are the results of the Tier 1 and Tier 2 studies performed under **greenhouse conditions**.	Drake 1988 MRID 40639301
Dicots: soybean, cocklebur Monocots: yellow nutsedge, rice, barnyard-grass, nutsedge Ferns: bracken fern, horsetail, fishtail Conifers: loblolly pine, ponderosa pine	Application at various rates of Ally or Escort herbicides (dry flowable powder) before, during, or after emergence of target plants (weeds).	Ally applied at 14-70 g ai/ha toxic to most dicots tested; monocots tolerated treatment in varying degrees; conifers demonstrated tolerance to Escort applications. These are the results of the Tier 3 studies performed under **field conditions**. There are several tables of raw data. The application rates vary according to crop and must be gleaned from the tables.	Drake 1988 MRID 40639301
See Drake 1988 (Tier 1&2 Studies)	See Drake 1988 (Tier 1&2 Studies)	See Drake 1988 (Tier 1&2 Studies). This fiche contains additional methods and materials information for the Tier 1 & Tier 2 studies conducted by Drake 1988. There are no further results or conclusions.	Drake 1989 MRID 41118001
Corn, cucumber, onion, pea, rape, sugar beet, sorghum, soybean, tomato, wheat	Single application up to 2.40 oz ai/acre Ally® Herbicide (60% dry flowable)	Treatment did not cause a 25% or greater effect on percent emergence for corn, wheat, soybean, tomato, rape and cucumber (90% confidence level); on the other hand, a 25% or greater effect on percent emergence was observed for onion, sorghum, sugar beet, and pea.	Heldreth and McKelvey 1996 MRID 44050301

Appendix 7: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference /Comments
Rainbow trout (*Salmo gairdneri*), 2.8 cm mean length, 0.17 g mean wgt, 10 trout per concentration	0, DMF (dimethyl formamide) positive) control, 5, 25, 50, 100, or 150 mg/L for 96 hours, static, no aeration. Higher concentrations not tested due to low water solubility and limited solubility in carrier solvents of test material. DPX-T6376 (purity = 92.9%)	No mortality at concentration up to 150 mg/L during 96-hour exposure period. At 24 hours, 3 fish exposed to 150 mg/L exhibited erratic swimming, rapid breathing and were lying on the bottom of the test container; 2/3 fish recovered completely by 48 hours; the third fish was affected throughout the entire study.	Muska and Hall 1982 MRID 00125816
Bluegill sunfish (*Lepomis macrochirus*), 3.6 cm mean length, 0.87 g mean wgt, 10 fish per concentration	0, DMF control, 5, 25, 50, 100, or 150 mg/L for 96 hours, static, no aeration. Higher concentrations not tested due to low water solubility and limited solubility in carrier solvents of test material. DPX-T6376 (purity = 92.9%)	No mortality or acute toxicity at concentrations up to 150 mg/L during 96-hour exposure period.	Phillips and Hall 1982a MRID 00125817
Bluegill sunfish (*Lepomis macrochirus*), 3.9 (range 3.4 to 4.7) cm mean length, 1.17 g (range 0.78 to 2.00) mean wgt, 10 fish per concentration	0, NaOH control,1, 10, 100, or 1000 mg/L for 96 hours, static, no aeration. pH adjustment (1N NaOH) to accomplish solubility of compound	No mortality or acute toxicity at concentrations up to 1000 mg/L during 96-hour exposure period.	Hall 1984a MRID 00148648
Bluegill sunfish (*Lepomis macrochirus*), 4-5 cm in length, 2-4 g each, 4 groups of 75 fish	0.01 or 1.0 ppm [phenyl-^{14}C] DPX-T6376 for 4 weeks in dynamic flow through study Exposure phase followed by 14-day depuration phase.	No adverse effects noted in any of the groups of fish, no mortality, and fish behavior appeared normal. The average bioaccumulation factor was <1 for all tissues and dose levels. Two diluter malfunctions occurred during the study, which increased test concentrations briefly in exposure aquaria.	Han and Anderson 1984 MRID 00149407

Appendix 7: Toxicity of metsulfuron methyl to fish.

Species	Exposure	Response	Reference /Comments
Rainbow trout (*Salmo gairdneri*), 4.1 (range 3.7 to 4.5) cm mean length, 0.82 (range 0.53 to 1.20) g, 10 fish per concentration	0, NaOH control,1, 10, 100, or 1000 mg/L for 96 hours, static, no aeration. pH adjustment (1N NaOH) to implement solubility of compound	Three fish in the 100 mg/L group died (1 at 72 hours; 2 at 96 hour); however, the investigators do not consider this effect significant because there was no mortality at the 1000 mg/L concentration. Clinical signs observed in some fish exposed to ≥100 mg/L include darkening in color, swimming at the surface, lethargy, erratic swimming, rapid respiration and laying at the bottom.	Hall 1984b MRID 00149672
Rainbow trout (*Oncorhynchus mykiss*) 22-hour-old embryos	Nominal test concentrations of 2.4, 4.7, 9.5, 19, 38, 75, or 150 mg/L D{X-T6376 (99.13% ai) for 90 days.	No significant effect on hatch rate, last day of hatching, first day of swim up, survival, abnormalities, or weight of surviving fingerlings. Differences in first day of hatching and surviving fingerling length were small but significant at >8.0 mg/L. NOEC = 4.5 mg/L based on mean measured concentrations, first day of hatching and standard length of surviving fingerlings at 90 days. MATC = 6.0 mg/L LOEC = 8.0 mg/L No meaning estimates of LC_{50} or EC_{50} were calculated because the highest percent affected in any test concentration was <17%.	Kreamer 1996 MRID 44122801 This is a 400 page hard text report with many tables, etc. Can be used to elaborate the dose/response assessment
Common carp (*Cyprinus carpio* LINN) 4.90 (+0.86) cm in length and 4.16 (+0.65) g in wgt and Nile tilapia (*Oreochromis niloticus* PETERS) 4.99 (+0.37) cm in length and 3.23 (+0.54) g in wgt, 20 fish per concentration	5-6 (NOS) concentrations of ALLY 10/10WP were used in standardized static bioassay. Concentrations of the test solutions were not verified by analysis and the results are based on nominal concentrations expressed in ppm.	96-hr LC_{50} for carp = 3320.5 ppm 96-hr LC_{50} for tilapia = 2334.6 ppm This study was conducted in Indonesia to meet a registration requirement for an herbicide formulation of 10% metsulfuron methyl and 10% chlorimuron ethyl. This formulation is not registered in the United States and registration action is not pending. The study was submitted because it reports observations in species not previously evaluated.	Research Institute for Freshwater Fisheries 1995 MRID 44015401

Appendix 8: Toxicity of metsulfuron methyl to aquatic invertebrates.

Plant or Animal	Exposure	Response	Reference
Daphnids (*Daphnia magna*), < 24 hours old, 10 daphnids per concentration	0, DMF control, 5, 25, 50, 100, or 150 mg/L for 48 hours, static, no aeration. DPX-T6376 (purity = 92.9%)	No mortality and no acute toxicity.	Phillips and Hall 1982a MRID 00125818
Daphnids (*Daphnia magna*) < 24 hours old, 10 daphnis per concentration	0, NaOH control, 100, 130, 180, 240, 320, 420, 560, 750, or 1000 mg/L metsulfuron methyl for 48 hours, static, no aeration. NaOH solution added to stock solution ot raise the pH to 9.0 to implement solubility	In replicate exposure chambers, exposure to 750 mg/L caused 60% and 80% immobility after 48 hours, while exposure to 1000 mg/L caused 90% and 100% immobility. 48-hr EC_{50} = 720 mg/L (95% CI = 6506 and 780 mg/L)	Wetzel 1984 MRID 00148649

Appendix 8: Toxicity of metsulfuron methyl to aquatic invertebrates.

Plant or Animal	Exposure	Response	Reference
Daphnids (*Daphnia magna*), < 24 hours old, 4 daphnids per concentration, 10 replicates	Nominal concentrations of 5, 10, 19, 38, 75, and 150 mg/L DPX-T6376 for 21 days Measured test concentrations were 5.1, 11, 17, 39, 77, and 150 mg/L	EC_{50} for immobilization > 150 mg/L measured concentration (HCT) The 14- and 21-day survival rates were not significantly different from controls, except for the 77 mg/L group (in replicates 9 & 10, 3/4 daphnids died). But because the 150 mg/L group showed 100% survival, the NOEC for survival is considered to be > 150 mg/L measured concentration. The true LOEC and MATC are considered > 150 mg/L NOEC for reproduction > 150 mg/L The decreased number of daphnids in the 77 mg/L group resulted in statistically significant reduced offspring, but the effect was not seen when reproduction was calculated as offspring/surviving adult. The LOEC for reproduction (offspring/survivng adult) is just above 150 mg/L and the MATC for reproduction is also > 150 mg/L The NOEC, LOEC, and MATC for growth were < 5.1 mg measured concentration/L, the lowest concentration tested. It is not known whether this effect is biologically significant.	Hutton 1989 MRID 43490601 In terms of growth, the differences in daphnid length were within one standard deviation of the control group values, did not demonstrate a dose response below 30 mg/L and were decreased by < 6% from controls
Cladoceran (*Daphnia magna*), < 24 hours old	Negative dilution control, nominal concentrations of 3.1, 6.3, 13, 25, 50, and 100 mg DPX-T6376/L (measured concentrations of 3.0, 6.2, 13, 25, 50, and 100 mg DPX-T6376/L) for 21 days under semi-static test conditions	NOEL = 100 mg/L for survival, reproduction, and growth (based on measured concentrations). No statistically significant differences in survival between controls and treated groups ($p > 0.05$); reproduction not decreased significantly in any treatment group ($p > 0.05$); and no significant differences in growth, compared with controls, in any treatment group.	Drottar and Krueger 1998 MRID 44704901

Appendix 9: Toxicity of metsulfuron methyl to aquatic plants and invertebrates

Plant or Animal	Exposure	Response	Reference
Duckweed (*Lemna minor*), 3 groups of 5 plants (2-3 fronds/plant)	0.04, 0.08, 0.16, 0.32, or 0.64 μg/L DPX-T6376 Technical white powder (99.2% pure) with media renewal 3 times/week one control and one solvent control	14-day EC_{50} = 0.36 μg/L (95% CI = 0.29-0.43 μg/L) NOEL = 0.16 μg/L No adverse effects in control cultures or in treated cultures at 0.04, 0.08, 0.16, or 0.32 μg/L; chlorosis of fronds observed at 0.64 μg/L (day 12); more pronounced chlorosis and blackening of fronds at 0.64 μg/L (day14). After 7-day recovery period, all test and control cultures except 0.64 μg/L showed appreciable increase in frond numbers. Chlorosis and blackening of fronds in the 0.64 μg/L still evident at the end of the "recovery" period.	Douglas and Handley 1988 MRID 41773902
Freshwater filamentous blue-green algae (*Anabaena flos-aquae*)	5-day exposure without media renewal at a single concentration of 110.3 μg ai/L DPX-T6376 (Ally® Herbicide)	DPX-T6376 did not inhibit growth and reproduction parameters of cell density and growth rate for *Anabaena flos-aquae* Inhibition of > 50% not observed at or above the maximum use rate for the *Anabaena flos-aquae* algal species. 120-hr NOEC (cell density) = 95.4 μg ai/L **120-hr NOEC (area under curve) = < 95.4 μg ai/L (significantly different from pooled controls)** 120-hr NOEC (growth rate) = 95.4 μg ai/L 120-hr EC_{25} estimated to be > 95.4 μg ai/L 120-hr EC_{50} estimated to be > 95.4 μg ai/L	Hicks 1997a MRID 44244001 Test concentration represents the expected concentration in a 6"-deep body of water after direct over spray at the maximum labeled use rate of 0.15 lbs ai/acre.
Selenastrum capricornutum	0, 1, 5, 10, or 45 μg/L DPX-T6376 (Ally® Herbicide)	The 45 μg/L nominal test concentration (maximum label application rate) caused a significant inhibition effect on growth, compared with controls, at 120 hours. 120-hr NOEL = 10 μg/L (level of cell inhibition = 37%).	Forbis 1987 MRID 40639302

Appendix 9: Toxicity of metsulfuron methyl to aquatic plants and invertebrates

Plant or Animal	**Exposure**	**Response**	**Reference**
Freshwater, unicellular, non-motile diatom (*Navicula pelliculosa*)	5-day exposure without media renewal at a single concentration of 110.3 µg ai/L DPX-T6376 (Ally® Herbicide)	DPX-T6376 did not inhibit growth or reproduction of *Navicula pelliculosa*. This is a 120-hour static acute algal screen study. It includes a table of measured cell counts at 24, 48, 72, 96, and 120 hours. Inhibition of >50% not observed at or above the maximum use rate for *Novicula pelliculosa*. 120-hr NOEC (cell density) = 95.6 µg ai/L 120-hr NOEC (area under curve) = <95.6 µg ai/L 120-hr NOEC (growth rate) =95.6 µg ai/L 120-hr EC_{50} (cell density) estimated >95.6 µg ai/L 120-hr EC_{50} (area under the curve) estimated >95.6 µg ai/L 120-hr EC_{50} (growth rate) estimated >95.4 µg ai/L	Hicks 1997b MRID 44420901
Freshwater, unicellular, non-motile, green alga (*Selenastrum capricornutum*)	62.5, 125, 250, 500, or 1000 µg metsulfuron methyl 60 DF/L of nutrient medium (ppb) for 72 hours without test medium renewal Trade name = Escort® 60 DF purity = 61.5%	There was a dose-response relationship between increased dose and corresponding decreases in cell density, area under the growth curve, and growth rate. Cell density: EC_{50} = 372 µg/L (95% CI = 312-466 µg/L) NOEC = 125 µg/L Area under the growth curve: EC_{50} = 359 µg/L (95% CI = 306-430 µg/L) NOEC = 125 µg/L Growth rate: EC_{50} = 1307 µg/L (95% CI = 1161-1524 µg/L) NOEC = 125 µg/L In the recovery test, Metsulfuron methyl 60 DF was determined to be algistatic at concentrations 1000 µg/L	Sloman and Leva 1998 MRID 44650101

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Metsulfuron methyl

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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/cm²	lbac_ugcm	11.21
lb/acre to mg/cm²	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	cm²	U.S. EPA 1992c
Surface area of lower legs	LLegs	2070	cm²	U.S. EPA 1992c
Weight of liquid adhering to surface of skin after a spill	Liq	0.008	mg/cm²	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	60		
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 A03c: Aerial Broadcast Sprays (includes pilots, mixers, and loaders) - General Assumptions Used in Worker Exposure Assessments.[AERIAL]

Parameter/Assumption	Code	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		70	acres/hour	USDA 1989a,b,c
Lower estimate		40		
Upper estimate		100		
Acres treated per day				
Central estimate	ACREC	490	acres/day	N/A[1]
Lower estimate	ACREL	240		
Upper estimate	ACREU	800		
Absorbed dose rate				
Central estimate	RATEC	0.00003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	Rubin et al. 1998, Table 5
Lower estimate	RATEL	0.000001		
Upper estimate	RATEU	0.0001		

[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 = ð r^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÷6)× ð × 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:

$$kg = (1 \div 6) \times ð \times d^3 \div 1000$$

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 $\log_{10} k_a$

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

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 $\boldsymbol{a'X'X\, a}$ without using matrix arithmetic.

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

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 1992c). [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 $\boldsymbol{t}_{0.025}$ 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 (1992c), 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 metsulfuron methyl [WSB01]				
Item	Code	Value	Units	Reference/Source
Typical application rate	Typ	0.02	lb a.i./acre	Section 2.4
Lowest application rate	Low	0.0125	lb a.i./acre	Section 2.4
Highest application rate	Hi	0.15	lb a.i./acre	Section 2.4
Lowest dilution	LDil	10	gal./acre	Section 2.4
Highest dilution	Hdil	100	gal./acre	Section 2.4

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.

0.02 lb/acre ÷ [(10 gal/acre + 100 gal/acre)/2] × 119.8 (mg/mL)/(lb/gal) = **0.044 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.

0.0125 lb/acre ÷ 100 gal/acre) × 119.8 (mg/mL)/(lb/gal) = **0.015 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.

0.15 lb/acre ÷ 10 gal/acre × 119.8 (mg/mL)/(lb/gal) = **1.8 mg/mL** [HI_Dr]

Worksheet B02: Summary of central estimate and range of concentrations of metsulfuron methyl in field solutions.				
Parameter	ID	Value	Units	Reference/Source
Typical	TypDR	0.044	mg/mL	See calculations above
Low	LowDR	0.015	mg/mL	
High	Hi_DR	1.8	mg/mL	

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

Parameter	ID	Value	Units	Source/Reference
Molecular weight (acid)	MW	381.4	grams/mole	ARS 1995
Water Solubility, pH 7	WS	2790	mg/L	Barefoot and Cooke 1990
$K_{o/w}$	Kow	0.018	unitless	Du Pont 1984
Foliar half-time ($t_{½}$)	FT12	30	days	[c] Knisel et al. 1992
Half-time on fruit central	FrT12C	30	days	Specific data not available. The central estimate for vegetation is used for all scenarios.
lower	FrT12L	30	days	
upper	FrT12U	30	days	
Bioconcentration factor ($\boldsymbol{BCF}_{(kg\ fish/L)}$)	BCFT	1	kg fish/L	Han and Anderson 1984
EPA/OPP RfD[a]	RfDP	0.3	mg/kg bw/day	U.S. EPA 1998b

[a] This RfD is that derived by EPA/OPP (U.S. EPA 1988b) and is consistent with the U.S. EPA of 0.25 mg/kg/day listed on IRIS (U.S. EPA 1998a) rounded to one significant digit.

Worksheet B04: Calculation of first-order dermal absorption rate (k_a) for metsulfuron methyl.

Parameters	Value	Units	Reference
Molecular weight	381.4	g/mole	
$K_{o/w}$ at pH 7	0.018	unitless	
$\log_{10} K_{o/w}$	-1.74		
Column vector ***a*** for calculating confidence intervals (see Worksheet 08 for definitions.)			
a_1	1		
a_2	381.4		
a_3	-1.74		
Calculation of $\mathbf{a'} \cdot (\mathbf{X'X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07a for details of calculation.			
Term 1	-0.099912446		
Term 2	0.30619412385		
Term 3	0.0741760717		
$\mathbf{a'} \cdot (\mathbf{X'X})^{-1} \cdot \mathbf{a}$	0.2805	calculation verified in Mathematica 3.0.1.1	
$\log_{10} k_a = 0.233255 \log_{10}(\boldsymbol{k_{o/w}}) - 0.005657\, \boldsymbol{MW} - 1.49615$			Worksheet A07a

$\log_{10}$ of first order absorption rate (k_a)

Central estimate	-4.06069621182	±	$t_{0.025}$	×	s	×	$(\mathbf{a'}\cdot(\mathbf{X'X})^{-1}\cdot\mathbf{a})^{0.5}$
Lower limit	-4.91790094213	-	2.0560	×	0.787218	×	0.52962250707
Upper limit	-3.20349148151	+	2.0560	×	0.787218	×	0.52962250707

First order absorption rates (i.e., antilog or 10^x of above values).

Central estimate	0.000087	$hours^{-1}$	
Lower limit	0.0000121	$hours^{-1}$	
Upper limit	0.00062591	$hours^{-1}$	

Worksheet B05: Calculation of dermal permeability rate (K_p) in cm/hour for metsulfuron methyl.							
Parameters	Value	Units					Reference
Molecular weight	381.4	g/mole					
$K_{o/w}$ at pH 7	0.018	unitless					
$\log_{10} K_{o/w}$	-1.7447274949						
Column vector ***a*** for calculating confidence intervals (see Worksheet A07a for definitions.)							
a_1	1						
a_2	381.4						
a_3	-1.7447274949						
Calculation of $\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$ - see Worksheet A07b for details of calculation.							
Term 1	0.0372305202						
Term 2	0.065855538						
Term 3	0.0554012924						
$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}$	0.1585	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	-6.30465959481	±	$t_{0.025}$	×	s	×	$\mathbf{a}' \cdot (\mathbf{X}'\mathbf{X})^{-1} \cdot \mathbf{a}^{0.5}$
Lower limit	-6.87205023924	-	1.9600	×	0.727129	×	0.39812058475
Upper limit	-5.73726895039	+	1.9600	×	0.727129	×	0.39812058475
Dermal permeability							
Central estimate	0.0000005	cm/hour					
Lower limit	0.0000001	cm/hour					
Upper limit	0.000002	cm/hour					

Worksheet B06: Summary of chemical specific dermal absorption values used for metsulfuron methyl dermal absorption. [WSB06]				
Description	Code	Value	Units	Reference/Source
Zero-order absorption (K_p)				
Central estimate	KpC	0.0000005	cm/hour	Worksheet B05, values rounded to two significant figures
Lower limit	KpL	0.0000001	cm/hour	
Upper limit	KpU	0.000002	cm/hour	
First-order absorption rates (k_a)				
Central estimate	AbsC	0.00009	$hour^{-1}$	Worksheet B04, values rounded to two significant figures
Lower limit	AbsL	0.00001	$hour^{-1}$	
Upper limit	AbsU	0.0006	$hour^{-1}$	

Worksheet B07: Estimates of the concentration of metsulfuron methyl 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.i./acre)	ID	WCR[a] (mg/L) ÷ (lb a.i./acre)	Reference
Typical	0.006	0.02	AWT	0.3	Based on GLEAMS modeling. See section 3.2.3.
Low	0.00375	0.0125	AWL	0.3	
High	0.045	0.15	AWU	0.3	

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

WORKER EXPOSURE ASSESSMENTS

Worksheet C01: Worker exposure estimates for directed foliar (backpack) applications of metsulfuron methyl				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	ApplC	0.02	lbs a.i./day	WSB01.TYP
Lower estimate	ApplL	0.0125	lbs a.i./day	WSB01.LOW
Upper estimate	ApplU	0.15	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	0.0875	lb/day	
Lower estimate	HANDLL	0.01875	lb/day	
Upper estimate	HANDLU	1.2	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	0.0003	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000006		
Upper estimate	DOSEU	0.012		

Worksheet C02a: Worker exposure estimates for boom spray (hydraulic ground spray) applications of metsulfuron methyl [WSC01]				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	APPLC	0.02	lbs a.i./day	WSB01.TYP
Lower estimate	APPLL	0.0125	lbs a.i./day	WSB01.LOW
Upper estimate	APPLU	0.15	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	2.24	lb/day	
Lower estimate	HANDLL	0.825	lb/day	
Upper estimate	HANDLU	25.2	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	0.00045	mg/kg bw/day	N/A
Lower estimate	DOSEL	0.000008		
Upper estimate	DOSEU	0.02268		

WSC02b: Worker exposure estimates for aerial applications of metsulfuron methyl [WKAREXP01]				
NOTE: The upper and lower estimates of dose are based on the typical application rate. Variability is encompassed by differences in the number of acres treated and the absorbed dose rate.				
Parameter/Assumption	Code	Value	Units	Source/Designation
Application rates				
Central estimate	WS10C	0.02	lbs a.i./day	APPL.TYP
Lower estimate	WS10L	0.0125	lbs a.i./day	APPL.LOW
Upper estimate	WS10U	0.15	lbs a.i./day	APPL.HI
Acres treated per day				
Central estimate	ACREC	490	acres/day	AERIAL.ACREC
Lower estimate	ACREL	240	acres/day	AERIAL.ACREL
Upper estimate	ACREU	800	acres/day	AERIAL.ACREU
Amount handled per day (product of application rate and acres treated per day)				
Central estimate	HANDLC	9.8	lb/day	N/A[1]
Lower estimate	HANDLL	4.8	lb/day	
Upper estimate	HANDLU	16	lb/day	
Absorbed dose rate				
Central estimate	RATEC	0.00003	(mg agent/kg bw) ÷ (lbs agent handled per day)[2]	AERIAL.RATEC
Lower estimate	RATEL	0.000001		AERIAL.RATEL
Upper estimate	RATEU	0.0001		AERIAL.RATEU
Absorbed dose (product of amount handled and absorbed dose rate)				
Central estimate	DOSEC	0.00029	mg/kg bw	N/A
Lower estimate	DOSEL	0.0000048		
Upper estimate	DOSEU	0.0016		

[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.i. 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.i., etc. - or the units must be converted to some equivalent form in the risk characterization.

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	0.0000005	cm/hour	WSB06.KpC
Lower	0.00000010	cm/hour	WSB06.KpL
Upper	0.0000020	cm/hour	WSB06.KpU
Concentration in solution (*C*) [see Worksheet B02]			
Typical	0.044	mg/mL	WSB02.TypDr
Lower	0.015	mg/mL	WSB02.LowDr
Upper	1.8	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 1992c)

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

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.
0.0000005 cm/hr × 0.044 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 4.40e-09 mg/kg [WZHT1M]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0000001 cm/hr × 0.015 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 3.00e-10 mg/kg [WZHL1M]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0000020 cm/hr × 1.8 mg/cm^3 × 1/60 hr × 840 cm^2 ÷ 70 kg = 0.00000072 mg/kg [WZHU1M]

Wearing Contaminated Gloves for One-Hour

Typical Value: Use typical concentration and central estimate of K_p.
0.0000005 cm/hr × 0.044 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 2.64e-07 mg/kg [WZHT1H]

Lower Estimate: Use lower range of estimated concentration and lower limit of K_p.
0.0000001 cm/hr × 0.015 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.80e-08 mg/kg [WZHL1H]

Upper Estimate: Use upper range of estimated concentration and upper limit of K_p.
0.0000020 cm/hr × 1.8 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 0.00004 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	0.00009	hour^{-1}	`WSB06.ABSC`
Lower limit of range	0.000010	hour^{-1}	`WSB06.ABSL`
Upper limit of range	0.00060	hour^{-1}	`WSB06.ABSU`
Concentration in solution (***C***) [see Worksheet B01]			
Typical	0.044	mg/mL	`TypDr`
Lower	0.015	mg/mL	`LowDr`
Upper	1.8	mg/mL	`HI_Dr`

Details of calculations.

Equation (from Durkin et al. 1995)

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

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]`,
0.0000900 h^{-1} × 0.008 mL/cm^2 × 0.044 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 9.4e-07 mg/kg
Lower range `[WFLL1H]`,
0.0000100 h^{-1} × 0.008 mL/cm^2 × 0.015 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 3.5e-08 mg/kg
Upper range `[WFLU1H]`,
0.0006000 h^{-1} × 0.008 mL/cm^2 × 1.8 mg/cm^3 × 1 hr × 2070 cm^2 ÷ 70 kg = 2.6e-04 mg/kg

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

Typical Value `[WFHT1H]`,
0.0000900 h^{-1} × 0.008 mL/cm^2 × 0.044 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 3.8e-07 mg/kg
Lower range `[WFHL1H]`,
0.0000100 h^{-1} × 0.008 mL/cm^2 × 0.015 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.4e-08 mg/kg
Upper range `[WFHU1H]`,
0.0006000 h^{-1} × 0.008 mL/cm^2 × 1.8 mg/cm^3 × 1 hr × 840 cm^2 ÷ 70 kg = 1.0e-04 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	0.044	mg/mL	WSB02.TYPDR
Low	0.015	mg/mL	WSB02.LOWDR
High	1.8	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00009	$hour^{-1}$	WSB06.AbsC
Low	0.000010	$hour^{-1}$	WSB06.AbsL
High	0.0006	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) ***- see calculations below.***			
Central	0.00001	mg/kg	SPRYC
Low	0.0000005	mg/kg	SPRYL
High	0.004	mg/kg	SPRYH

Details of calculations

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

Central Estimate [SPRYCC]:
0.008 mL/cm^2 × 0.044 mg/mL × 6030 cm^2 × 0.00009 h^{-1} × 1 h ÷ 13.3 kg = 0.00001 mg/kg

Lower Range of Estimate [SPRYCL]:
0.008 mL/cm^2 × 0.015 mg/mL × 6030 cm^2 × 0.00001 h^{-1} × 1 h ÷ 13.3 kg = 0.0000005 mg/kg

Upper Range of Estimate [SPRYCH]:
0.008 mL/cm^2 × 1.8 mg/mL × 6030 cm^2 × 0.0006 h^{-1} × 1 h ÷ 13.3 kg = 0.004 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	0.044	mg/mL	WSB02.TYPDR
Low	0.015	mg/mL	WSB02.LOWDR
High	1.8	mg/mL	WSB02.HI_DR
First-order dermal absorption rate (k_a)			
Central	0.00009	$hour^{-1}$	WSB06.AbsC
Low	0.000010	$hour^{-1}$	WSB06.AbsL
High	0.0006	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) ***- see calculations below.***			
Central	0.000001	mg/kg	SPRYWC
Low	0.000000	mg/kg	SPRYWL
High	0.0004	mg/kg	SPRYWH

Details of calculations

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

Central Estimate [SPRYWC]:
0.008 mL/cm^2 × 0.044 mg/mL × 2915 cm^2 × 0.00009 h^{-1} × 1 h ÷ 64 kg = 0.000001 mg/kg

Lower Range of Estimate [SPRYWL]:
0.008 mL/cm^2 × 0.015 mg/mL × 2915 cm^2 × 0.00001 h^{-1} × 1 h ÷ 64 kg = 0.00000005 mg/kg

Upper Range of Estimate [SPRYWH]:
0.008 mL/cm^2 × 1.8 mg/mL × 2915 cm^2 × 0.0006 h^{-1} × 1 h ÷ 64 kg = 0.0004 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	0.02	lb a.i/acre	WSB01.TYP
Low	0.0125	lb a.i/acre	WSB01.LOW
High	0.15	lb a.i/acre	WSB01.HI
First-order dermal absorption rate (k_a)			
Central	0.00009	$hour^{-1}$	WSB06.AbsC
Low	0.000010	$hour^{-1}$	WSB06.AbsL
High	0.00060	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations on next page.***			
Central	0.000040	mg/kg	VEGDWC
Low	0.000003	mg/kg	VEGDWL
High	0.0024	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 $\mu g/(cm^2 \cdot hr)$) after converting application rate in lb a.i./acre to units of $\mu g/cm^2$:

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

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

Step 2:

Convert Dr from units of $\mu g/(cm^2 \cdot hr)$) to units of $mg/(cm^2 \cdot hr)$) 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 (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:

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

See next page for details of calculations.

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

Central Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}$ (µg/(cm^2·hr)))-0.658 = (1.09 × $\log_{10}$(0.02 ×11.21)) + 0.05 = -0.658 µg/(cm^2·hr)

$\boldsymbol{Dr}$ (µg/(cm^2·hr)) = $10^{-0.658}$ = 0.22 µg/(cm^2·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm^2·hr)) = 0.22 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.00022 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.00022 mg/(cm^2·hr) × 1 hr × 5300 cm^2 = 1.166 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 1.166 mg × 0.00009 hr^{-1} × 24 hours ÷ 64 kg = 0.00004 `[VEGDWC]`

Lower Range of Estimate:

Step 1:

$\log_{10}(\boldsymbol{Dr}$ (µg/(cm^2·hr))) = (1.09 × $\log_{10}$(0.0125 ×11.21)) + 0.05 = -0.88µg/(cm^2·hr)

$\boldsymbol{Dr}$ (µg/(cm^2·hr)) = $10^{-0.88}$ = 0.132 µg/(cm^2·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm^2·hr)) = 0.132 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.000132 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.000132 mg/(cm^2·hr) × 1 hr × 5300 cm^2 =0.7 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 0.7 mg × 0.00001 hr^{-1} × 24 hours ÷ 64 kg = 0.000003 `[VEGDWL]`

Upper Range of Estimate:

0.008Step 1:

$\log_{10}(\boldsymbol{Dr}$ (µg/(cm^2·hr))) = (1.09 × $\log_{10}$(0.15 ×11.21)) + 0.05 = 0.296 µg/(cm^2·hr)

$\boldsymbol{Dr}$ (µg/(cm^2·hr)) = $10^{0.296}$ = 1.98 µg/(cm^2·hr)

Step 2:

$\boldsymbol{Dr}$ (mg/(cm^2·hr)) = 1.98 µg/(cm^2·hr) ÷ 1000 µg/mg = 0.00198 mg/(cm^2·hr)

Step 3:

Amnt(mg) = 0.00198 mg/(cm^2·hr) × 1 hr × 5300 cm^2 = 10.5 mg

Step 4:

$\boldsymbol{D_{Abs}}$ (mg/kg bw) = 10.5 mg × 0.0006 hr^{-1} × 24 hours ÷ 64 kg = 0.0024 `[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	0.02	lb a.i./acre	WSB01.Typ
Lower	0.0125	lb a.i./acre	WSB01.Low
Upper	0.15	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	0.0002	mg/kg bw	VEGCWAT
Lower	0.00013	mg/kg bw	VEGCWAL
Upper	0.007	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 × 0.02 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.0002 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 × 0.0125 lb a.i./acre × 1.5 mg/kg÷lb a.i./acre ÷ 64 kg = 0.00013 mg/kg bw

Upper: Use highest estimated application rate and highest RUD.

D = 0.454 kg × 0.15 lb a.i./acre × 7 mg/kg÷lb a.i./acre ÷ 64 kg = 0.007 mg/kg bw

Worksheet D05: Consumption of contaminated fruit, chronic 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.*			
Parameters/Assumptions	Value	Units	Source/Reference
Halftime on fruit ($t_{½}$) central	30	days	WSB03.FrT12C
lower	30	days	WSB03.FrT12L
upper	30	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	0.02	lb a.i./acre	WSB01.Typ
Lower	0.0125	lb a.i./acre	WSB01.Low
Upper	0.15	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	0.00005	mg/kg bw/day	VEGCWCT
Lower	0.00003	mg/kg bw/day	VEGCWCL
Upper	0.003	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 = 0.02 lb a.i./acre × 1.5 mg/kg veg. = 0.03 mg/kg veg.

Step 2:
k = ln(2) ÷30 days^{-1} = 0.023
C_{90} = 0.03 mg/kg × $e^{-0.023 \times 90}$ = 0.004 mg/kg veg.

Step 3:
D (mg/kg bw/day) = $(0.03 \times 0.004)^{0.5}$ (mg/kg veg.) × 0.0043 kg veg/kg bw = 0.00005 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 = 0.0125 lb a.i./acre × 1.5 mg/kg veg. = 0.01875 mg/kg veg.

Step 2:
k = ln(2) ÷30 days^{-1} = 0.023
C_{90} = 0.01875 mg/kg × $e^{-0.023 \times 90}$ = 0.002 mg/kg veg.

Step 3:
D $_{(mg/kg\ bw)}$ = $(0.01875 \times 0.002)^{0.5}$ $_{(mg/kg\ veg.)}$ × 0.0043 $_{(kg\ veg/kg\ bw)}$ = 0.00003 $_{(mg/kg\ bw)}$

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 = 0.15 lb a.i./acre × 7 mg/kg veg. = 1.05 mg/kg veg.

Step 2:
k = ln(2) ÷30 days^{-1} = 0.023
C_{90} = 1.05 mg/kg × $e^{-0.023 \times 90}$ = 0.1 mg/kg veg.

Step 3:
D $_{(mg/kg\ bw)}$ = $(1.05 \times 0.1)^{0.5}$ $_{(mg/kg\ veg.)}$ × 0.01 $_{(kg\ veg/kg\ bw)}$ = 0.003 $_{(mg/kg\ bw)}$

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
Concentrations in solution ($\boldsymbol{C}_{(mg/L)}$)			
Central	44	mg/L	WSB02.TypDR
Low	15	mg/L	WSB02.LowDR
High	1800	mg/L	WSB02.Hi_DR
Concentrations in ambient water ($\boldsymbol{C}_{(mg/L)}$)			
Central	0.03	mg/L	see calculations on next page
Low	0.011	mg/L	
High	1.36	mg/L	
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
Dose estimates (***D***) - **see details of calculations on next page.**			
Typical	0.002	mg/kg bw	WATCCAT
Lower	0.0005	mg/kg bw	WATCCAL
Upper	0.15	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:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 44_{(mg/L)} \div 1000000_{(liters)} = 0.03_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.03_{(mg/L)} \times 1_{(L)} \div 13.3_{(kg)} = 0.002_{(mg/kg\ bw)}$$ [WATCCAT]

Lower Estimate:

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

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 15_{(mg/L)} \div 1000000_{(liters)} = 0.011_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 0.011_{(mg/L)} \times 0.61_{(L)} \div 13.3_{(kg)} = 0.0005_{(mg/kg\ bw)}$$ [WATCCAL]

Upper Estimate:

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

Step 1:

$$Conc._{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 1800_{(mg/L)} \div 1000000_{(liters)} = 1.36_{(mg/L)}$$

Step 2:

$$D_{(mg/kg\ bw)} = 1.36_{(mg/L)} \times 1.5_{(L)} \div 13.3_{(kg)} = 0.15_{(mg/kg\ bw)}$$ [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 a.i./acre))			
Central	0.02	lb a.i./gal	WSB01.Typ
Low	0.0125		WSB01.Low
High	0.15		WSB01.Hi
Water Contamination Rate (WCR)(***C*** (mg/L)÷***R*** (lb a.i./acre))			
Central	0.3	mg/L/lb a.i./acre	WSB07.AWT
Low	0.3		WSB07.AWL
High	0.3		WSB07.AWU
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	0.0002	mg/kg bw/day	WATCMCT
Lower	0.0001	mg/kg bw/day	WATCMCL
Upper	0.002	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 ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./acre))}}$) 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 ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

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

Central Estimate:

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

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.02_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 2_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0002_{\text{(mg/kg bw)}}$$ [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.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.0125_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 1.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.0001_{\text{(mg/kg bw)}}$$ [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.

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.15_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 2.4_{\text{(L/day)}} \div 70_{\text{(kg bw)}} = 0.002_{\text{(mg/kg bw)}}$$ [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 ($\boldsymbol{C}_{\text{(mg/L)}}$)			
Central	44	mg/L	WSB02.TYPDR×1000
Low	15	mg/L	WSB02.LOWDR×1000
High	1800	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 ($\boldsymbol{BCF}_{\text{(kg fish/L)}}$)	1	kg fish/L	WSB03.BCFT
Dose estimates (***D***) **- see details of calculations on next page.**			
General Population			
Typical	0.0001	mg/kg bw	FISHAMGPT
Lower	0.00002	mg/kg bw	FISHAMGPL
Upper	0.0031	mg/kg bw	FISHAMGPU
Native American subsistence populations			
Typical	0.0003	mg/kg bw	FISHAMNAT
Lower	0.00011	mg/kg bw	FISHAMNAL
Upper	0.015	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.

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

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

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

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:

$\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{L/gal}} \times 44_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 0.03_{\text{(mg/L)}}$

Step 2:

$\text{D}_{\text{(mg/kg bw)}} = 0.03_{\text{(mg/L)}} \times 1_{\text{(L/kg)}} \times 0.158_{\text{(kg fish)}} \div 70_{\text{(kg)}} = 0.0001_{\text{(mg/kg bw)}}$ [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:

$\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{L/gal}} \times 15_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 0.011_{\text{(mg/L)}}$

Step 2:

$\text{D}_{\text{(mg/kg bw)}} = 0.011_{\text{(mg/L)}} \times 1_{\text{(L/kg)}} \times 0.158_{\text{(kg fish)}} \div 70_{\text{(kg)}} = 0.00002_{\text{(mg/kg bw)}}$ [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:

$\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{L/gal}} \times 1800_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 1.36_{\text{(mg/L)}}$

Step 2:

$\text{D}_{\text{(mg/kg bw)}} = 1.36_{\text{(mg/L)}} \times 1_{\text{(L/kg)}} \times 0.158_{\text{(kg fish)}} \div 70_{\text{(kg)}} = 0.0031_{\text{(mg/kg bw)}}$ [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:

$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 44_{(mg/L)} \div 1000000_{(liters)} = 0.03_{(mg/L)}$

Step 2:

$D_{(mg/kg\ bw)} = 0.03_{(mg/L)} \times 1_{(L/kg)} \times 0.77_{(kg\ fish)} \div 70_{(kg)} = 0.0003_{(mg/kg\ bw)}$ [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:

$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 15_{(mg/L)} \div 1000000_{(liters)} = 0.010_{(mg/L)}$

Step 2:

$D_{(mg/kg\ bw)} = 0.01_{(mg/L)} \times 1_{(L/kg)} \times 0.77_{(kg\ fish)} \div 70_{(kg)} = 0.00011_{(mg/kg\ bw)}$ [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:

$\text{Conc.}_{(mg/L)} = 200_{(gal.)} \times 3.785_{L/gal} \times 1800_{(mg/L)} \div 1000000_{(liters)} = 1.360_{(mg/L)}$

Step 2:

$D_{(mg/kg\ bw)} = 1.36_{(mg/L)} \times 1_{(L/kg)} \times 0.77_{(kg\ fish)} \div 70_{(kg)} = 0.015_{(mg/kg\ bw)}$ [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*** $_{\text{(lb a.i./acre)}}$)			
Central	0.02	lb a.i./gal	WSB01.Typ
Low	0.0125		WSB01.Low
High	0.15		WSB01.Hi
Water Contamination Rate (WCR)(***C*** $_{\text{(mg/L)}}$÷***R*** $_{\text{(lb a.i./gal)}}$)			
Central	0.3	mg/L/lb a.i./acre	WSB07.AWT
Low	0.3		WSB07.AWL
High	0.3		WSB07.AWU
Bioconcentration factor (***BCF***$_{\text{(kg fish/L)}}$)	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	0.000001	mg/kg bw/day	FISHMCT
Lower	0.000001	mg/kg bw/day	FISHMCL
Upper	0.0001	mg/kg bw/day	FISHMCU
Native American Subsistence Population			
Typical	0.00001	mg/kg bw/day	FISHNMCT
Lower	0.0000043	mg/kg bw/day	FISHNMCL
Upper	0.0005	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 ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./acre))}}$) 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 ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

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

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.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.02_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 1_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.000001_{\text{(mg/kg bw)}}$ [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.

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.0125_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 1_{\text{(kg fish/L)}} \times 0.01_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.000001_{\text{(mg/kg bw)}}$ [FISHMCL]

Upper Range of Estimate:

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

$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.15_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 1_{\text{(kg fish/L)}} \times 0.158_{\text{(kg fush/day)}} \div 70_{\text{(kg bw)}} = 0.0001_{\text{(mg/kg bw)}}$ [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.

$\boldsymbol{D}_{\text{(mg/kg bw)}}$ = 0.02 $_{\text{(lb a.i./acre)}}$ × 0.3 $_{\text{((mg/L)×(lb a.i./acre))}}$ × 1 $_{\text{(kg fish/L)}}$ × 0.081 $_{\text{(kg fush/day)}}$ ÷ 70 $_{\text{(kg bw)}}$ = 0.00001 $_{\text{(mg/kg bw)}}$ [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.

$\boldsymbol{D}_{\text{(mg/kg bw)}}$ = 0.0125 $_{\text{(lb a.i./acre)}}$ × 0.3 $_{\text{((mg/L)×(lb a.i./acre))}}$ × 1 $_{\text{(kg fish/L)}}$ × 0.081 $_{\text{(kg fush/day)}}$ ÷ 70 $_{\text{(kg bw)}}$ = 4.30e-06 $_{\text{(mg/kg bw)}}$ [FISHNMCL]

Upper Range of Estimate:

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

$\boldsymbol{D}_{\text{(mg/kg bw)}}$ = 0.15 $_{\text{(lb a.i./acre)}}$ × 0.3 $_{\text{((mg/L)×(lb a.i./acre))}}$ × 1 $_{\text{(kg fish/L)}}$ × 0.77 $_{\text{(kg fush/day)}}$ ÷ 70 $_{\text{(kg bw)}}$ = 0.0005 $_{\text{(mg/kg bw)}}$ [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)	0.0003	0.000006	0.012	WSC01
Broadcast ground spray (Boom spray)	0.0004	0.000008	0.02	WSC02a
Aerial applications	0.0003	0.000005	0.0016	WSC02b
Accidental/Incidental Exposures (dose in mg/kg/event)				
Immersion of Hands, 1 minute	4.40e-09	3.00e-10	7.20e-07	WSC03
Contaminated Gloves, 1 hour	2.64e-07	1.80e-08	4.00e-05	WSC03
Spill on hands, 1 hour	4.00e-07	1.44e-08	1.00e-04	WSC04
Spill on lower legs, 1 hour	1.00e-06	3.55e-08	3.00e-04	WSC04

Worksheet E02: Summary of risk characterization for workers				
RfD	0.3	mg/kg/day	Sect. 3.3.3.	
Scenario	Hazard Quotient			Exposure Assessment Worksheet
	Typical	Lower	Upper	
General Exposures				
Directed ground spray (Backpack)	0.0009	0.00002	0.04	WSC01
Broadcast ground spray (Boom spray)	0.001	0.00003	0.08	WSC02a
Aerial applications	0.001	0.00002	0.005	WSC02b
Accidental/Incidental Exposures				
Immersion of Hands, 1 minute	0.00000001	0.000000001	0.000002	WSC03
Contaminated Gloves, 1 hour	0.0000009	0.00000006	0.0001	WSC03
Spill on hands, 1 hour	0.000001	0.00000005	0.0003	WSC04
Spill on lower legs, 1 hour	0.000003	0.0000001	0.0009	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	0.00001	0.0000005	0.004	WSD01
Direct spray, lower legs	Woman	0.000001	0.00000005	0.0004	WSD02
Dermal, contaminated vegetation	Woman	0.00004	0.000003	0.0024	WSD03
Contaminated fruit, acute exposure	Woman	0.0002	0.00013	0.007	WSD04
Contaminated water, acute exposure	Child	0.002	0.0005	0.15	WSD06
Consumption of fish, general public	Man	0.0001	0.00002	0.0031	WSD08
Consumption of fish, subsistence populations	Man	0.0003	0.00011	0.015	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.00005	0.00003	0.003	WSD05
Consumption of water	Man	0.0002	0.0001	0.002	WSD07
Consumption of fish, general public	Man	0.000001	0.000001	0.0001	WSD09
Consumption of fish, subsistence populations	Man	0.00001	0.000004	0.0005	WSD09

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

RfD		0.3	mg/kg/day	Sect. 3.3.3.	
Scenario	Target	Hazard Quotient			Worksheet
		Typical	Lower	Upper	
Acute/Accidental Exposures					
Direct spray, entire body	Child	0.00001	0.000002	0.01	WSD01
Direct spray, lower legs	Woman	0.000003	0.0000002	0.001	WSD02
Dermal, contaminated vegetation	Woman	0.0001	0.000009	0.008	WSD03
Contaminated fruit, acute exposure	Woman	0.0007	0.0004	0.02	WSD04
Contaminated water, acute exposure	Child	0.007	0.002	0.5	WSD06
Consumption of fish, general public	Man	0.0003	0.0001	0.01	WSD08
Consumption of fish, subsistence populations	Man	0.001	0.0004	0.05	WSD08
Chronic/Longer Term Exposures					
Contaminated fruit	Woman	0.0002	0.0001	0.01	WSD05
Consumption of water	Man	0.001	0.0003	0.01	WSD07
Consumption of fish, general public	Man	0.000003	0.000003	0.0003	WSD09
Consumption of fish, subsistence populations	Man	0.00003	0.00001	0.002	WSD09

[1] Hazard quotient is the level of exposure divided by the RfD then rounded to one significant decimal place or digit.

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×BW(kg)$^{0.65}$		Boxenbaum and D'Souza 1990
	87	cm^2	
Application rate (***R***)			
Typical/Central	0.02	lb a.i. /acre	WSB01.TYP
Low	0.0125		WSB01.LOW
High	0.15		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	0.00009	$hour^{-1}$	WSB06.AbsC
Low	0.000010	$hour^{-1}$	WSB06.AbsL
High	0.00060	$hour^{-1}$	WSB06.AbsU
Estimated Absorbed Doses (***D***) - ***see calculations below.***			
Central	0.001	mg/kg	SMDSDC
Low	0.00007	mg/kg	SMDSDL
High	0.05	mg/kg	SMDSDH

Details of calculations on next page.

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

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

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) × 0.02 lb/acre × 87 cm^2
× (1-e$^{-0.00009/h \times 24h}$) ÷ 0.02 kg = 0.001 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) × 0.0125 lb/acre × 87 cm^2
× (1-e$^{-0.00001/h \times 24\ h}$) ÷ 0.02 kg = 0.00007 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) × 0.15 lb/acre × 87 cm^2
× (1-e $^{-0.0006/h \times 24\ h}$) ÷ 0.02 kg = 0.05 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'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	0.02	lb a.i. /acre	WSB01.TYP
Low	0.0125		WSB01.LOW
High	0.15		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	0.5	mg/kg	SMDS2DC
Low	0.3	mg/kg	SMDS2DL
High	3.7	mg/kg	SMDS2DH

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

Equation: *0.5 × F × R × A ÷ 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÷lb/acre) × 0.02 lb/acre × 87 cm^2 ÷ 0.02 kg = 0.5 mg/kg [SMDS2DC]

Lower Range of Estimate [WSE042DL]: Use the lowest anticipated application rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.0125 lb/acre × 87 cm^2 ÷ 0.02 kg = 0.3 mg/kg [SMDS2DL]

Upper Range of Estimate [WSE042DH]: Use the highest anticipated application rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.15 lb/acre × 87 cm^2 ÷ 0.02 kg = 3.7 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'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***)	0.000093	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	0.02	lb a.i. /acre	WSB01.TYP
Low	0.0125		WSB01.LOW
High	0.15		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	3	mg/kg	BEEDS2DC
Low	2	mg/kg	BEEDS2DL
High	24	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÷lb/acre) × 0.02 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 3 mg/kg [BEEDS2DC]

Lower Range of Estimate: Use the lowest anticipated application rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.0125 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 2 mg/kg [BEEDS2DL]

Upper Range of Estimate: Use the highest anticipated application rate,
0.5 × 0.01121 (mg/cm^2÷lb/acre) × 0.15 lb/acre × 2.7 cm^2 ÷ 0.000093 kg = 24 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 1989a
Duration of exposure (***D***)	1	day	N/A
Application rates (***R***)			
Typical	0.02	lb a.i./acre	WSB01.Typ
Lower	0.0125	lb a.i./acre	WSB01.Low
Upper	0.15	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	0.11	mg/kg bw	VGCSMAC
Lower	0.07	mg/kg bw	VGCSMAL
Upper	2.8	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 × 0.02 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 0.11 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 × 0.0125 lb a.i./acre × 35 mg/kg÷lb a.i./acre ÷ 0.02 kg = 0.07 mg/kg bw [VGCSMAL]

Upper: Use highest estimated application rate and highest RUD.

D = 0.003 kg × 0.15 lb a.i./acre × 125 mg/kg÷lb a.i./acre ÷ 0.02 kg = 2.8 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 1989a
kg food consumed per kg bw	0.15	Unitless	0.003/0.02
Application rates (***R***)			
Typical	0.02	lb a.i./acre	WSB01.Typ
Lower	0.0125	lb a.i./acre	WSB01.Low
Upper	0.15	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	0.04	mg/kg bw	VGCSMCT
Lower	0.0200	mg/kg bw	VGCSMCL
Upper	1	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 = 0.02 lb a.i./acre × 35 mg/kg veg. = 0.7 mg/kg veg.

Step 2:

k = ln(2) ÷ 30 $days^{-1}$ = 0.023

C_{90} = 0.7 mg/kg × $e^{-0.023 \times 90}$ = 0.09 mg/kg veg.

Step 3:

D (mg/kg bw/day) = $(0.7 \times 0.09)^{0.5}$ (mg/kg veg.) × 0.15 kg veg/kg bw = 0.04 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 = 0.0125 lb a.i./acre × 35 mg/kg veg. = 0.4375 mg/kg veg.

Step 2:

k = ln(2) ÷30 $days^{-1}$ = 0.023

C_{90} = 0.4375 mg/kg × $e^{-0.023 \times 90}$ = 0.06 mg/kg veg.

Step 3:

$D_{\text{(mg/kg bw)}} = (0.4375 \times 0.06)^{0.5}{}_{\text{(mg/kg veg.)}} \times 0.15_{\text{(kg veg/kg bw)}} = 0.02_{\text{(mg/kg bw)}}$ [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 = 0.15 lb a.i./acre × 125 mg/kg veg. = 18.75 mg/kg veg.

Step 2:

k = ln(2) ÷30 $days^{-1}$ = 0.023

C_{90} = 18.75 mg/kg × $e^{-0.023 \times 90}$ = 2.4 mg/kg veg.

Step 3:

$D_{\text{(mg/kg bw)}} = (18.75 \times 2.4)^{0.5}{}_{\text{(mg/kg veg.)}} \times 0.15_{\text{(kg veg/kg bw)}} = 1_{\text{(mg/kg bw)}}$ [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 ($\boldsymbol{C}_{\text{(mg/L)}}$)			
Central	44	mg/L	WSB02.TYPDR×1000
Low	15	mg/L	WSB02.LOWDR×1000
High	1800	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 1989a
Dose estimates (***D***) **- see details of calculations below.**			
Typical	0.007	mg/kg bw	WTCSMAT
Lower	0.0030	mg/kg bw	WTCSMAL
Upper	0.34	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.

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

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

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

Central Estimate: Use the typical field dilution,

Step 1: $\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{ L/gal}} \times 44_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 0.03_{\text{(mg/L)}}$

Step 2: $\text{D}_{\text{(mg/kg bw)}} = 0.03_{\text{(mg/L)}} \times 0.005_{\text{(L)}} \div 0.02_{\text{(kg)}} = 0.007_{\text{(mg/kg bw)}}$ [WTCSMAT]

Lower Estimate: Use the lowest estimated field dilution,

Step 1: $\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{ L/gal}} \times 15_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 0.011_{\text{(mg/L)}}$

Step 2: $\text{D}_{\text{(mg/kg bw)}} = 0.011_{\text{(mg/L)}} \times 0.005_{\text{(L)}} \div 0.02_{\text{(kg)}} = 0.003_{\text{(mg/kg bw)}}$ [WTCSMAL]

Upper Estimate: Use the highest estimated field concentration,

Step 1: $\text{Conc.}_{\text{(mg/L)}} = 200_{\text{(gal.)}} \times 3.785_{\text{ L/gal}} \times 1800_{\text{(mg/L)}} \div 1000000_{\text{(liters)}} = 1.36_{\text{(mg/L)}}$

Step 2: $\text{D}_{\text{(mg/kg bw)}} = 1.36_{\text{(mg/L)}} \times 0.005_{\text{(L)}} \div 0.02_{\text{(kg)}} = 0.34_{\text{(mg/kg bw)}}$ [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	0.02	lb a.i./gal	WSB01.Typ
Low	0.0125		WSB01.Low
High	0.15		WSB01.Hi
Water Contamination Rate (WCR)($\boldsymbol{C}_{\text{(mg/L)}} \div \boldsymbol{R}_{\text{(lb a.i./gal)}}$)			
Central	0.3	mg/L/lb a.i./acre	WSB07.AWT
Low	0.3		WSB07.AWL
High	0.3		WSB07.AWU
Body weight (***W***)	0.02	kg	U.S. EPA 1989a
Amount of water consumed ($\boldsymbol{A}_{\text{(L/day)}}$)	0.005	L/day	U.S. EPA 1989a
Dose estimates (***D***) **- see details of calculations on next page.**			
Typical	0.0015	mg/kg bw	WTCSMCT
Lower	0.000937	mg/kg bw	WTCSMCL
Upper	0.011	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 ($\boldsymbol{WCR}_{\text{((mg/L)×(lb a.i./acre))}}$) 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 ($\boldsymbol{D}_{\text{(mg/kg bw)}}$).

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

Central Estimate: Use the typical application rate and typical water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.02_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.0015_{\text{(mg/kg bw)}}$$ [WTCSMCT]

Lower Range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.0125_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.000937_{\text{(mg/kg bw)}}$$ [WTCSMCL]

Upper range of Estimate: Use the lowest anticipated application rate and the low end of the range of the water contamination rate (WCR)

$$\boldsymbol{D}_{\text{(mg/kg bw)}} = 0.15_{\text{(lb a.i./acre)}} \times 0.3_{\text{((mg/L)×(lb a.i./acre))}} \times 0.005_{\text{(L/day)}} \div 0.02_{\text{(kg bw)}} = 0.011_{\text{(mg/kg bw)}}$$ [WTCSMCU]

Worksheet F08: Potential exposures of non-target plants through the use of contaminated irrigation water.			
***Verbal Description**: Non-target plants/crops are irrigated with 1 inch of contaminated ambient water. The levels in water are estimated from modeling and/or monitoring data thus dissipation, degradation and other environmental processes are considered.*			
Parameters/Assumptions	Value	Units	Source/Reference
Application Rates ($\boldsymbol{R}$ $_{\text{(lb a.i./acre)}}$)			
Central	0.02	lb a.i./acre	WSB01.Typ
Low	0.0125		WSB01.Low
High	0.15		WSB01.Hi
Water Contamination Rate (WCR)($\boldsymbol{C}$ $_{\text{(mg/L)}}$÷$\boldsymbol{R}$ $_{\text{(lb a.i./arce)}}$)			
Central	0.3	mg/L/lb a.i./acre	WSB07.AWT
Low	0.3		WSB07.AWL
High	0.3		WSB07.AWU
Concentrations in irrigation water ($\boldsymbol{C}_{\text{(mg/L)}}$) ($\boldsymbol{A}$×$\boldsymbol{WRC}$)			
Central	0.006	mg/L	
Low	0.00375	mg/L	
High	0.045	mg/L	
Irrigation rate	1	inch	U.S. EPA 1989a
Liters of water applied per acre ($\boldsymbol{L}$)	10,279	L	see below
Functional Application Rate($\boldsymbol{A}_{\text{lb/acre}}$) ($\boldsymbol{C}$ × $\boldsymbol{L}$ × 0.0000022 lbs/mg ÷ 1 acre)			
Central	0.00014	lb/acre	
Low	0.0001	lb/acre	
High	0.001	lb/acre	

Calculations of constants:

Litters of water applied per acre per inch irrigation water:

1 m^2 = 100 cm × 100 cm = 10,000 cm^2

1 acre = 4047 m^2 = 4047 m^2×10,000 cm^2/m^2 = 4,047,000 cm^2

1 inch = 2.54 cm.

2.54 cm × 4,047,000 cm^2 = 10,279,380 cm^3 = 10,279,380 mL = 10,279 L.

Number of lbs/mg:

1 kg = 2.2 lbs.

1 g = 0.0022 lbs.

1 mg = 0.0000022 lbs.

Worksheet G-01: 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	0.001	0.00007	0.05	WSF01
Direct spray, small animal, 100% absorption	0.5	0.3	3.7	WSF02
Direct spray, bee, 100% absorption	3	2	24	WSF03
Consumption of contaminated vegetation, acute exposure	0.11	0.07	2.8	WSF04
Consumption of contaminated water, acute exposure	0.007	0.003	0.34	WSF06
Longer Term Exposures				
Consumption of contaminated vegetation, chronic exposure	0.04	0.02	1	WSF05
Consumption of contaminated water, chronic exposure	0.0015	0.000937	0.011	WSF07

Worksheet G-02: 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	0.00004	0.000003	0.002
Direct spray, small animal, 100% absorption	0.02	0.01	0.1
Direct spray, bee, 100% absorption[3]	0.01	0.007	0.09
Consumption of contaminated vegetation, acute exposure	0.004	0.003	0.1
Consumption of contaminated water, acute exposure	0.0003	0.00012	0.01
Longer Term Exposures			
Consumption of contaminated vegetation, chronic exposure	0.002	0.0008	0.04
Consumption of contaminated water, chronic exposure	0.0001	0.00004	0.0004
	Toxicity value for mammal [2]	25	mg/kg/day
	Toxicity value for bee [3]	270	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 20 mg/kg/day, the study on which the RfD is based, and then rounded to one significant decimal or digit.
[3] The hazard quotient is based on the reported acute dose level of 25 µg/bee that was not associated with increased mortality. Dose is calculated a body weight of 0.000093 kg/bee - i.e., 25 µg/bee ÷ 0.000093 kg/bee = 268817 µg/kg or about 270 mg/kg.