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Dicamba - Human Health and Ecological Risk Assessment – Final Report

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LIST OF WORKSHEETS

Supplement 1: Dicamba – WordPerfect Worksheets for Human Health and Ecological Risk Assessments, SERA WPWS 04-43-17-06d, Version 2.04d, dated November 24, 2004.

Supplement 2: Dicamba -EXCEL Worksheets for Human Health and Ecological Risk Assessments, SERA EXWS 04-43-17-06d, Version 2.04d, dated November 28, 2004.

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
a.e.	acid equivalents
AEL	adverse-effect level
a.i.	active ingredient
ALS	acetolactate synthase
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
CBI	confidential business information
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
d.f.	degrees of freedom
EC_x	concentration causing X% inhibition of a process
EC_{25}	concentration causing 25% inhibition of a process
EC_{50}	concentration causing 50% inhibition of a process
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FOIA	Freedom of Information Act
FQPA	Food Quality Protection Act
g	gram
ha	hectare
HQ	hazard quotient
IAA	indole-3-acetic acid
IARC	International Agency for Research on Cancer
IRIS	Integrated Risk Information System
k_a	absorption coefficient
k_e	elimination coefficient
kg	kilogram
$K_{o/c}$	organic carbon partition coefficient
$K_{o/w}$	octanol-water partition coefficient
K_p	skin permeability coefficient
L	liter
lb	pound
LC_{50}	lethal concentration, 50% kill
LD_{50}	lethal dose, 50% kill
LOAEL	lowest-observed-adverse-effect level
LOC	level of concern

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

COMMON UNIT CONVERSIONS AND ABBREVIATIONS

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

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

PROGRAM DESCRIPTION

Two commercial formulations of dicamba may be used in Forest Service programs, Vanquish and Banvel. Banvel is the dimethylamine salt of dicamba and Vanquish is the diglycolamine (DGA) salt of dicamba. Both products are recommended for the control of a variety of broadleaf weeds and woody vegetation. Proposed application methods for dicamba include roadside hydraulic spraying, cut-surface treatments, and directed foliar treatments. Aerial and broadcast foliar applications are not planned but are included in this risk assessment in the event that the Forest Service may wish to consider such applications. For Banvel, the labeled application rates range from 0.25 to 2 lbs dicamba a.e. per acre. For Vanquish, the labeled application rates range from 0.25 to 1 lbs dicamba a.e. per acre and the upper limit of the application rate for Vanquish over a single growing season is 2 lbs a.e./acre. For this risk assessment, the typical application rate will be taken as 0.3 lb dicamba a.e./acre. This is the average value of all applications conducted by the Forest Service in 2001. The range of application rates is taken as 0.25 lbs dicamba a.e./acre to 2 lbs dicamba a.e./acre, the range of labeled application rates. Based both on the national use data for dicamba as well as more recent data from California, it appears that the use of dicamba in Forest Service programs is minor relative to the total amount of dicamba used in agriculture and in other non-Forest Service applications.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification – In acute exposures, dicamba is relatively nontoxic by oral administration, with single-dose LD_{50} values ranging from approximately 750 to 3000 mg/kg in rats. There are no clear indications that the dimethylamine salt (e.g., Banvel), sodium salt or methyl ester derivatives differ significantly from the toxicity of dicamba, or that the toxicity of these forms differs significantly between species or sexes. No information was located on the acute toxicity of the diglycolamine salt (e.g., Vanquish). Dicamba is rapidly and extensively absorbed following oral exposure and rapidly excreted predominantly as unmetabolized compound in the urine. Oral studies in rats indicate that there are no significant pharmacokinetic differences in the free acid and amine salt forms of dicamba. Dermal absorption of dicamba has been demonstrated but is less well studied than oral absorption.

A large number of standard subchronic and chronic toxicity studies have been conducted on dicamba with reported NOAELs ranging from about 50 to 500 mg/kg/day depending on the endpoints assayed and species tested. Somewhat lower NOAELs, in the range of 25 to 45 mg/kg/day, have been reported in dietary studies for reproductive toxicity. Dicamba does not appear to be carcinogenic and there is no information indicating species effects on immune or endocrine function. At doses above the chronic or reproductive NOAELs, dicamba may cause neurotoxic effects.

Exposure Assessment – Exposure assessments are conducted for both workers and members of the general public for the typical application rate of 0.3 lb/acre. The consequences of using the

maximum application rate that might be used by the Forest Service, 2 lb/acre, are discussed in the risk characterization.

For workers, three types of application methods are modeled: directed ground, broadcast ground, and aerial. Central estimates of exposure for workers are approximately 0.004 mg/kg/day for aerial and backpack workers and about 0.007 mg/kg/day for broadcast ground spray workers. Upper range of exposures is approximately 0.005 mg/kg/day for directed ground spray workers 0.002 mg/kg/day for backpack and aerial workers. All of the accidental exposure scenarios for workers involve dermal exposures and all of these accidental exposures lead to estimates of doses that are either in the range of or substantially below the general exposure estimates for workers.

For the general public, the range of acute exposures is from approximately 0.0000008 mg/kg to 1 mg/kg. The lower end of this range associated with the lower range for the consumption of contaminated water from a stream by a child. The upper end of the range is associated with the upper range for the consumption of contaminated water by a child following an accidental spill of dicamba into a small pond. High dose estimates are also associated with the direct spray of a child (about 0.17 mg/kg/day at the upper range of exposure). Other acute exposures are lower by about an order of magnitude. For chronic or longer term exposures, the modeled exposures are much lower than for acute exposures, ranging from approximately 0.0000000001 mg/kg/day (one 10 billionth of a mg/kg/day) associated with the lower range for the normal consumption of fish to approximately 0.008 mg/kg/day associated with the upper range for consumption of contaminated fruit.

Dose-Response Assessment – Two RfD values have been derived by U.S. EPA: 0.03 mg/kg/day was set as the Agency wide RfD in 1992 and 0.045 mg/kg/day was derived by U.S. EPA/OPP in 1999 for setting pesticide tolerances. For this risk assessment, the most recent RfD derived by the Office of Pesticides is used to characterize risk. The more recent RfD from the Office of Pesticides is based on the thorough review of the available data and the decision to increase the RfD because of data quality issues in previous RfD is well documented. In addition, Forest Service risk assessments will, in general, defer to the most recent U.S. EPA RfD. For characterizing the risks associated with acute exposures, the 1-day dietary RfD of 0.10 mg/kg/day, also derived by U.S. EPA/OPP is used. The relatively small difference between the acute and chronic RfDs for dicamba is consistent with the relatively small differences in body burdens that would be expected between single and multiple constant doses.

Risk Characterization – At the typical application rate considered in this risk assessment, workers would not be exposed to levels of dicamba that are regarded as unacceptable. At the maximum application, however, worker exposure to dicamba would exceed the level of concern at the upper range of plausible exposures. Members of the general public could be at some risk at the typical application rate only in the event of worst-case exposure assumptions for two accidental exposures involving children. Based on multiple sources of exposure, however, the levels of exposure would modestly exceed the level of concern for adults at the typical

application rate. At the highest application rate that might be used in Forest Service programs, many of the acute exposure scenarios exceed the level of concern at the upper range of exposure. For longer term exposures, no risks are apparent at the typical application rate. The highest application rate, however, the consumption of contaminated vegetation exceeds the level of concern at the upper range of non-accidental and plausible exposures.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification – Dicamba is relatively nontoxic by oral administration, with LD_{50} values ranging from approximately 500 mg/kg to >4600 mg/kg. There is no indication that either the dimethylamine salt or Banvel differs significantly from the toxicity of dicamba. The acute toxicity of dicamba to birds appears generally to be low and consistent with the gavage studies in rats. Very little information is available on the toxicity of dicamba to terrestrial invertebrates. In the honey bee, the acute LD_{50} is greater than 1000 mg/kg bw. Dicamba is an effective auxin herbicide and acts by mimicking the plant hormone indole-3-acetic acid. A large number of phytotoxicity studies are available on dicamba. In pre-emergence assays with standard non-target species, the most sensitive species appears to be soybean, with an LOEC of 0.0022 lb/acre and the least sensitive species appears to cabbage with an NOEC 0.53 lb/acre. In post-emergence applications, the most sensitive species appears to be soybean, with an LOEC of 0.004 lb/acre and the most tolerant species appears to be corn, with an NOEC of 3.9 lb/acre. There is very little indication that dicamba will adversely affect soil microorganisms.

Acute toxicity studies in fish indicate that dicamba is relatively non-toxic, with 24 to 96-hour LC_{50} values in the range of 28–516 mg/L, although salmonids appear to be more sensitive than other freshwater fish to the acute toxicity of dicamba. Amphibians seem to have a sensitivity to dicamba that is similar to that of fish with 24- to 96-hour LC_{50} values in the range of 166 to 220 mg/L. Some aquatic invertebrates appear to be somewhat more sensitive than fish and amphibians to the acute toxicity of dicamba, with lower ranges of EC_{50} values of about 4 to 10 mg/L. Some but not all aquatic plants are much more sensitive to dicamba than aquatic animals, with LC_{50} values of about 0.06 mg/L . Other aquatic plants are much more tolerant, with reported NOEC values of up to 100 mg/L.

Exposure Assessment – Terrestrial animals might be exposed to any applied herbicide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation. In acute exposure scenarios, the highest exposures for small terrestrial vertebrates will occur after a direct spray and could reach up to about 7 mg/kg at an application rate of 0.3 lb/acre. Exposures anticipated from the consumption of contaminated vegetation by terrestrial animals range from central estimates of about 0.4 mg/kg for a small mammal to 8 mg/kg for a large bird with upper ranges of about 0.8 mg/kg for a small mammal and 23 mg/kg for a large bird. The consumption of contaminated water leads to much lower levels of exposure. A similar pattern is seen for chronic exposures. Estimated daily doses for a small mammal from the consumption of contaminated vegetation at the application site are in the range of about 0.003 mg/kg to 0.02 mg/kg. Large birds feeding on contaminated vegetation at the application site could be exposed to much higher concentrations,

ranging from about 0.1 mg/kg/day to 3.3 mg/kg/day. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, which range from about 0.0000002 mg/kg/day to 0.000001 mg/kg/day for a small mammal.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion and the use of contaminated irrigation water. In addition, vapor exposures associated with the volatilization of dicamba are also estimated Unintended direct spray is expressed simply as the application rate considered in this risk assessment, 0.3 lb/acre and should be regarded as an extreme/accidental form of exposure. Estimates for the other routes of exposure are much less. All of these exposure scenarios are dominated by situational variability because the levels of exposure are highly dependent on site-specific conditions. Thus, the exposure estimates are intended to represent conservative but plausible ranges that could occur but these ranges may over-estimate or under-estimate actual exposures in some cases. Spray drift is based on estimates using AgDRIFT. The proportion of the applied amount transported off-site from runoff is based on GLEAMS modeling of clay, loam, and sand. The amount of dicamba that might be transported off-site from wind erosion is based on estimates of annual soil loss associated with wind erosion and the assumption that the herbicide is incorporated into the top 1 cm of soil. Exposure from the use of contaminated irrigation water is based on the same data used to estimate human exposure from the consumption of contaminated ambient water and involves both monitoring studies as well as GLEAMS modeling.

Exposures to aquatic plants and animals are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water. The peak concentrations of dicamba in contaminated water is estimated at 0.003 (0.00006 to 0.01) mg/L per 1 lb/acre applied. For longer-term exposures, average concentrations of dicamba in ambient water associated with the normal application of dicamba is estimated at 0.00001 (0.000005 to 0.00003) mg/L at an application rate of 1 lb/acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application rates considered in this risk assessment.

Dose-Response Assessment – The acute lethal potency of dicamba, expressed as the LD_{50}, is relatively well characterized in several mammalian species and indicates that larger vertebrates are more sensitive to dicamba than smaller vertebrates. This allometric relationship is reasonably consistent over two orders of magnitude in body weight (mice to rabbits). Based on an approximation of the LD_{50} in sheep, the relationships appear to hold over 3 orders of magnitude. Although the allometric relationship can be used to estimate the acute LD_{50} values for nontarget terrestrial species, LD_{50} values are not used directly in this risk assessment to assess potential effects in non-target species. Instead, this risk assessment uses NOAEL values for non-target species. For mammals, a NOAEL of 45 mg/kg/day is used for both acute and chronic exposures. This is consistent with the dose-response assessment for humans and the available pharmacokinetic data in mammals. Although dogs and other canids are typically considered more sensitive than other mammals to weak acids such as dicamba, the available toxicity data on dicamba in dogs does not suggest that dogs are more sensitive to dicamba than other species of

mammals. For birds, the chronic dietary NOAEL in birds of 92 mg/kg/day is used to characterize risks for both acute and chronic exposures. The only data available on terrestrial invertebrates is the standard bioassay in honey bees in which the LD_{50} was about 1000 mg/kg bw.

The toxicity data for terrestrial plants involve standard bioassays for pre-emergent and post-emergent applications. For exposures involving the off-site drift of dicamba, the range of NOAEL values for post-emergence applications is 0.0014 lb/acre for sensitive species and 3.9 lb/acre for the most tolerant species. For exposures involving off-site runoff, the range of NOAEL values for pre-emergence applications is estimated at 0.00016 lb/acre for sensitive species and 0.53 lb/acre for tolerant species. In addition to these two common routes of exposure to herbicides, field studies have demonstrated that dicamba may volatilize from treated vegetation sufficiently rapidly and in sufficiently high concentrations to damage neighboring untreated vegetation. No explicit dose-response relationship is conducted for this route of exposure but damage from dicamba vapor is considered in the risk characterization.

While a relatively large number of toxicity studies are available on dicamba in several aquatic species, the reported values are highly variable, with LC_{50} values in some studies being less than reported NOEC values in the same species from another study. Some of the lowest LC_{50} values are from the older literature and experimental details are sparse. For the current risk assessment, the NOEC values are not used directly and risks are characterized using LC_{50} values. Based solely on LC_{50} values, the most sensitive species appears to be rainbow trout with a 96-hour LC_{50} value of 28 mg/L and the most tolerant species appears to be mosquito fish with a 96-hour LC_{50} value of 465 mg/L. Some species of aquatic invertebrates appear to be more sensitive than fish and an LC_{50} value of 3.8 mg/L is used for sensitive species. The LC_{50} value for tolerant species of aquatic invertebrates is taken as 750 mg/L. No information is available on the chronic toxicity of dicamba to aquatic animals and the available acute toxicity data do not permit reasonable estimates of toxicity values for chronic toxicity. This limits the risk characterization for aquatic animals.

The available toxicity data on aquatic plants are relatively standard. The most sensitive species on which data are available is the freshwater algae, *Anabaene flos-aquae*, with an EC_{50} of 0.061 mg/L and an EC_{10} of 0.0049 mg/L. Other species of freshwater algae are much more tolerant with NOEC values of up to 10 mg/L. Aquatic macrophytes appear to have an intermediate sensitivity and an NOEC of 0.25 mg/L is used to characterize risks to aquatic macrophytes.

Risk Characterization – For terrestrial vertebrates, some acute exposure scenarios but no chronic exposure scenarios exceed the level of concern but only at the highest application rate. At the typical application rate of 0.3 lb/acre, no adverse effects on mammals or birds are plausible for either acute or chronic exposures. At the highest application rate of 2 lb/acre, adverse reproductive effects are plausible in acute exposure scenarios involving mammals and birds consuming contaminated vegetation or contaminated insects. In chronic exposure scenarios at an application rate 2 lb/acre, the hazard quotients associated with the consumption of contaminated vegetation are below the level of concern by factors of 5 to over 16,000.

There is little basis for asserting that adverse effects would be expected in terrestrial insects or soil microorganisms. The very limited data in insects suggest that no lethal effects are likely in a direct spray. There are no data on sublethal effects in insects. At the highest application rate, transient effects might be seen in some populations of soil microorganisms.

Dicamba is an effective herbicide and even some tolerant plants that are directly sprayed with dicamba at normal application rates are likely to be damaged. The greatest risks – i.e., the highest hazard quotients – are associated with runoff but are highly site specific. Some sensitive plant species could be affected by runoff in areas in which runoff is favored – clay soil and surface conditions that are conducive to runoff. Damage associated with off-site drift of dicamba would also depend on local site-specific conditions but would most likely occur within a relatively small distance from the application site – i.e., up to about 100 feet. Vapor exposures to offsite vegetation could also cause damage. While this cannot be well quantified, it is likely that this effect would be less pronounced with Vanquish than with Banvel.

The risk characterization for aquatic animals is extremely limited by the available toxicity data. For the characterization of risk, NOEC values are not used directly and risks are characterized using LC_{50} values. Another very substantial limitation in the risk characterization is that no information is available on the chronic toxicity of dicamba to aquatic animals and the available acute toxicity data do not permit reasonable estimates of toxicity values for chronic toxicity. Within these very serious limitations, there is little basis for asserting that adverse effects in aquatic animals are plausible. This conclusion is consistent with a recent assessment by the U.S. EPA on the impact of dicamba on Pacific anadromous salmonids.

Unlike the risk characterization for aquatic animals, the risk characterization for aquatic plants is based on relatively consistent and standard toxicity data. At the typical application rate, adverse effects in aquatic plants are not likely. At the maximum application rate, peak concentrations in water could be associated with transient effects in sensitive species of algae as well as macrophytes. These concentrations, however, would rapidly diminish to levels substantially below a level of concern.

1. INTRODUCTION

The USDA Forest Service uses the herbicide, dicamba, in its vegetation management programs. Two commercial formulations of dicamba, Banvel and Vanquish, may be used by the Forest Service, primarily in noxious weed control. The present document provides risk assessments for human health effects and ecological effects to support an assessment of the environmental consequences of using dicamba in current and future Forest Service programs. This is an update to the risk assessment conducted for the USDA Forest Service in 1995 (SERA 1995).

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 dicamba, an assessment of potential exposure to this compound, 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 2001). 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. Brief reviews regarding the human health or ecological effects of dicamba have been published and were used in the preparation of this risk assessment (Cox 1994; U.S. EPA 1988; 1992b; 1999). Many of the mammalian toxicology studies and ecotoxicology studies, however, are unpublished reports submitted to the U.S. EPA as part of the registration process for this compound. Because of the preponderance of unpublished relevant data in U.S. EPA files, a complete search of the U.S. EPA files was conducted. Full text copies of relevant studies were kindly provided by the U.S. EPA Office of Pesticide Programs. These studies were reviewed, discussed in Sections 3 and 4 as necessary, and synopses of the most relevant studies are provided in the Appendices 1 through 10 of this risk assessment. 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 (2001).

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 onto 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 dicamba and for most other chemicals, however, this estimation regarding human health must be based on data from experimental animal studies, which cover only a limited number of effects. Generally, judgment is the basis for the methods used to make the assessment. Although the judgments may reflect a consensus (i.e., be used by many groups in a reasonably consistent manner), the resulting estimations of risk cannot be proven analytically. In other words, the estimates regarding risk involve uncertainty. 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. Some of the calculations are relatively simple are included in the body of the document. Some sets of the calculations, however, are cumbersome. For those calculations,

worksheets are included with this risk assessment. The worksheets provide the detail for the estimates cited in the body of the document. Documentation for these worksheets is given in SERA (2003). As detailed in SERA (2003), two versions of the worksheets are available: one in a word processing format (Supplement 1) and one in a spreadsheet format (Supplement 2). The worksheets that are in the spreadsheet format are used only as a check of the worksheets that are in the word processing format. Both sets of worksheets are provided with the hard-text copy of this risk assessment as well as with the electronic version of the risk assessment.

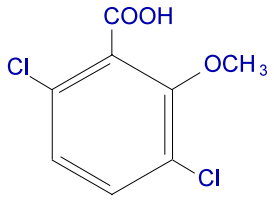
2. PROGRAM DESCRIPTION

2.1. Overview

Two commercial formulations of dicamba may be used in Forest Service programs, Vanquish and Banvel. Banvel is the dimethylamine salt of dicamba and Vanquish is the diglycolamine (DGA) salt of dicamba. Both products are recommended for the control of a variety of broadleaf weeds and woody vegetation. Proposed application methods for dicamba include roadside hydraulic spraying, cut-surface treatments, and directed foliar treatments. Aerial and broadcast foliar applications are not planned but are included in this risk assessment in the event that the Forest Service may wish to consider such applications. For Banvel, the labeled application rates range from 0.25 to 2 lbs dicamba a.e. per acre. For Vanquish, the labeled application rates range from 0.25 to 1 lbs dicamba a.e. per acre and the upper limit of the application rate for Vanquish over a single growing season is 2 lbs a.e./acre. For this risk assessment, the typical application rate will be taken as 0.3 lb dicamba a.e./acre. This is the average value of all applications conducted by the Forest Service in 2001. The range of application rates is taken as 0.25 lbs dicamba a.e./acre to 2 lbs dicamba a.e./acre, the range of labeled application rates. Based both on the national use data for dicamba as well as more recent data from California, it appears that the use of dicamba in Forest Service programs is minor relative to the total amount of dicamba used in agriculture and in other non-Forest Service applications.

2.2. Chemical Description and Commercial Formulations

Dicamba is the common name for 3,6-dichloro-o-anisic acid:



Dicamba

Selected chemical and physical properties of dicamba are summarized in Table 2-1. Selected information used directly in this risk assessment is presented in worksheet B03.

Two commercial formulations of dicamba may be used in Forest Service programs, Vanquish and Banvel. Vanquish is available from Syngenta and Banvel is available from Micro Flo. Banvel is the dimethylamine salt of dicamba and Vanquish is the diglycolamine salt of dicamba. Both Banvel and Vanquish contain dicamba at a concentration of 480 g a.e./L. By weight, Banvel contains 48.2% a.i. (the dimethylamine salt of dicamba) and Vanquish contains 56.8% a.i. (the diglycolamine salt of dicamba). Both products are recommended for the control of a variety of broadleaf weeds and woody vegetation (C&P Press 2003). The Vanquish formulation was originally developed by Sandoz Agro, Inc. (1993) in order to reduce the volatilization rate of

dicamba from the application site. As discussed further in Section 4, the volatilization of dicamba from the application site may cause damage to non-target vegetation.

The identity of the inerts in the dicamba formulations are considered proprietary information; therefore, the manufacturer does not identify the inerts on the general or supplemental product labels or material safety data sheets (C&P Press 2003). This lack of disclosure indicates that none of the inerts present at a concentration of 0.1% or greater is classified as hazardous. The inert ingredients in several herbicides have been obtained by the Northwest Coalition for Alternatives to Pesticides (NCAP) under the Freedom of Information Act (FOIA) and this information is publicly available at http://www.pesticide.org/FOIA/ inertslinks.html. Dicamba, however, is not among the herbicides whose inert ingredients are listed by NCAP. The only inert disclosed publically is ethylene glycol, which is used in some dicamba formulations but the formulations disclosed are different from those covered in this risk assessment (Cox 1994).

The identity of inerts as well as impurities has been disclosed to the U.S. EPA for both Banvel (Velsicol Chemical Corp. 1961,1984) and Vanquish (Bryant 1995a,b). It should be noted that these submissions were made by previous registrants of dicamba but are used to support the current registrations by Syngenta and Micro Flo. This information has been obtained and reviewed in the preparation of this risk assessment. This specific information on the inerts and impurities, however, may not and are not disclosed in this risk assessment. Nonetheless, the potential significance of these inerts can be inferred based on differences in the toxicity of the formulations and technical grade dicamba, as discussed further in Section 3.1.14. In addition, the information in the open literature (Makary et al. 1986 a,b) indicates that the major impurity in technical grade dicamba is 3,5-dichloro-2-methoxy benzoic acid. Further information on this impurity is discussed in Section 3.1.3.1 (Kinetics) and Section 3.1.15 (Impurities and Metabolites).

2.3. Application Methods

Both Banvel and Vanquish are labeled for ground and aerial applications. Proposed application methods for dicamba include roadside hydraulic spraying, cut-surface treatments, and directed foliar treatments. Aerial and broadcast foliar applications are not planned but are included in this risk assessment in the event that the Forest Service may wish to consider such applications.

Roadside hydraulic spraying is used primarily in rights-of-way management. Spray equipment mounted on tractors or trucks is used to apply the herbicide on either side of the roadway. Typically, about 8 acres may be treated in a 45-minute period [approximately 11 acres/hour] with approximately 200 gallons of the herbicide mixture [270 gallons/hour]. Some special truck mounted spray systems may be used to treat up to 12 acres in a 35-minute period with approximately 300 gallons of herbicide mixture [about 21 acres/hour and 510 gallons/hour] (USDA 1989b, p 2-9 to 2-10).

Cut surface treatment methods involve creating a cut surface on the tree by either cutting the tree down [cut stump treatment] or piercing the bark of a standing tree with a hatchet [hack and

squirt] or an injector [injection]. The herbicide is then applied using a backpack sprayer [cut stump], squirt bottle [hack and squirt], or the injector itself [injection].

Direct applications of the herbicide to vegetation without cut surface pretreatment may involve streamline or directed foliar applications. In streamline applications, the herbicide is sprayed directly onto the bark of the lower 2–3 feet of the stem in a horizontal band. In these applications, the herbicide sprayer or container is carried using a backpack. As with cut stump treatments, the nozzle on the wand or gun jet of the backpack sprayer should not be positioned higher than the handlers' waist, reducing the likelihood that the chemical will come into direct contact with the arms, hands, or face. In directed foliar applications, however, crews may treat up to shoulder high brush and chemical contact with the arms, hands, or face is more plausible.

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

2.4. Mixing and Application Rates

For Banvel, the labeled application rates range from 8 fluids ounces (annual weeds) to 64 fluid ounces (some perennials) per acre. This corresponds to about 0.0625 to 0.5 gallons [128 ounces per gallon] of Banvel per acre, which in turn corresponds to about 0.25 to 2 lbs dicamba a.e. per acre [4 lbs a.e. per gallon × 0.0625 to 0.5 gallons/acre]. For Vanquish, the labeled application rates range from 8 fluids ounces (½ pint for small weeds) to 64 fluid ounces (4 pints for stems and roots of woody plant) per acre. This corresponds to about 0.0625 to 0.25 gallons [128 ounces per gallon] of Vanquish per acre, which in turn corresponds to about 0.25 to 1 lbs dicamba a.e. per acre [4 lbs a.e. per gallon × 0.0625 to 0.5 gallons/acre]. The upper limit of the application rate for Vanquish over a single growing season is 2 lbs a.e./acre (C&P Press 2003).

The use of dicamba in Forest Service Programs for fiscal year 2001, the most recent year for which data are available, is summarized in Table 2-2. While not specific in Table 2-2, all of these applications were for noxious weed control (USDA/FS 2002). Based on the total amount used and total number of acres treated, the average application rate is about 0.3 lb/acre, relatively near the low range of the labeled rates.

For this risk assessment, the typical application rate will be taken as 0.3 lb a.e./acre. This is the average value of all applications conducted by the Forest Service in 2001 and somewhat higher than the average application rates used in Forest Service Regions 1 and 4 (Table 2-2). The different regions within the Forest Service are illustrated in Figure 2-1 and discussed further in Section 2.5. The range of application rates will be taken as 0.25 lbs a.e./acre to 2 lbs a.e./acre, the range of application rates recommended for dicamba. All exposure assessments given the worksheets that accompany this risk assessment are based on the typical application rate of 0.3 lb a.e./acre. The consequences of varying application rates within the range of 0.25 lbs a.e./acre to 2 lbs a.e./acre are considered in the risk characterization for human health (Section 3.4) and ecological effects (Section 4.4).

The mixing volumes for Banvel range from 3 to 50 gallons per acre for ground applications. Corresponding mixing volumes for Vanquish range from 10 to 200 gallons per acre. The ranges are dependant on the type of vegetation to be treated as well as the application method (C&P Press 2003). The extent to which a formulation of dicamba 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 dicamba in the applied spray). In all cases, the higher the concentration of dicamba - equivalent to the lower dilution of dicamba - the greater the risk.

For this risk assessment, the lowest dilution is taken as 3 gallons/acre, the minimum recommended for ground applications of Banvel. The highest dilution is based on 200 gallons of water per acre, the highest application volume specifically recommended for ground applications of Vanquish. A typical dilution rate is taken as 25 gallons/acre, the geometric mean of the range. Details regarding the calculation of field dilution rates are given in worksheet B01, and the calculations following this worksheet are summarized in worksheet B02.

It should be noted that the selection of application rates and dilution volumes in this risk assessment is intended to simply reflect typical or central estimates as well as plausible lower and upper ranges. In the assessment of specific program activities, the Forest Service will use program specific application rates in the worksheets that are included with this report to assess any potential risks for a proposed application.

2.5. Use Statistics

The USDA Forest Service (USDA/FS 2002) tracks and reports its use of pesticides by geographical areas referred to as "*Regions*". As illustrated in Figure 2-1, the Forest Service classification divides the U.S. into nine regions designated from Region 1 (Northern) to Region 10 (Alaska). [Note: There is no *Region 7* in the Forest Service system.] As illustrated in Figure 2-1 and detailed further by region in Table 2-2, the use of dicamba by the Forest Service was restricted to the western regions during 2001. The greatest proportion of dicamba used by the Forest Service occurred in Region 4 (Intermountain, 59%) with a lesser proportion used in Region 2 (Rocky Mountain, 17%). Small proportions of the total use occurred in Region 3 (Southwest, 8%) and Region 6 (Pacific Northwest, 11%). The total amount of dicamba used in all regions was about 2,800 lbs (Table 2-2).

Dicamba is used on a number of crops and a summary of the agricultural uses of dicamba is presented in Figure 2-2 (USGS 1998). These use statistics are for 1992, the most recent year for which data are available. As indicated in this figure, about 10,000,000 lbs of dicamba were applied to crops, primarily to corn and pasture (80% of total). Other minor uses include wheat, hay, barley, sorghum, field and grass seed, oats, sod, and prosomillet. The geographic distribution of the agricultural uses of dicamba are broader than those of the Forest Service, covering all Forest Regions with most of the agricultural applications of dicamba occurring in Forest Region 9. The use of dicamba by the Forest Service in 2001 (2,800 lbs) is about 0.028% [or about 1 part in 3600] of the amount used in agriculture in 1992.

More recent data are available on the total amounts of pesticides applied in California in 2001 (California Department of Pesticide Regulation 2002). During 2001, about 29,780 lbs of dicamba was applied in California. While dicamba was not used by the Forest Service in California during 2001, it should be noted that the total use of dicamba by all regions of the Forest Service in 2001 was about 2,800 lbs (Table 2-2), about 10% of the total use of dicamba in California during the same period.

Thus, based both on the national data from 1992 (USGS 1998) as well as the more recent data from California (California Department of Pesticide Regulation 2002), it appears that the use of dicamba in Forest Service programs is minor relative to the total amount of dicamba used in agriculture and in other non-Forest Service applications.

3. HUMAN RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

In acute exposures, dicamba is relatively nontoxic by oral administration, with single-dose LD_{50} values ranging from approximately 750 to 3000 mg/kg in rats. There are no clear indications that the dimethylamine salt (e.g., Banvel), sodium salt or methyl ester derivatives differ significantly from the toxicity of dicamba, or that the toxicity of these forms differs significantly between species or sexes (Appendix 1). No information was located on the acute toxicity of the diglycolamine salt (e.g., Vanquish). Dicamba is rapidly and extensively absorbed following oral exposure and rapidly excreted predominantly as unmetabolized compound in the urine. Oral studies in rats indicate that there are no significant pharmacokinetic differences in the free acid and amine salt forms of dicamba. Dermal absorption of dicamba has been demonstrated but is less well studied than oral absorption.

A large number of standard subchronic and chronic toxicity studies have been conducted on dicamba with reported NOAELs ranging from about 50 to 500 mg/kg/day depending on the endpoints assayed and species tested. Somewhat lower NOAELs, in the range of 25 to 45 mg/kg/day, have been reported in dietary studies for reproductive toxicity. Some early teratology studies involving gavage administration yield a NOAEL of 3 mg/kg/day for both maternal toxicity and reproductive effects. The quality of these studies, however, is questionable. Dicamba does not appear to be carcinogenic and there is no information indicating species effects on immune or endocrine function. At doses above the chronic or reproductive NOAELs, dicamba may cause neurotoxic effects.

3.1.2. Mechanisms of Action

Little information is available regarding mechanisms of toxicity of dicamba in humans or other animals. No data were found on mechanisms of non-cancer effects, and there is no evidence from epidemiological studies and animal bioassays indicating that dicamba is carcinogenic (see Section 3.1.10). Dicamba has been shown to induce hepatic peroxisomal enzymes and activate the peroxisomal proliferator activator receptor (PPAR) in rats, suggesting that it might have liver tumor promoting activity similar to other peroxisomal proliferators (Espandiari et al. 1995, 1998). This hypothesis was not supported by testing with the two-stage hepatocarcinogenesis model in rats, which found that dicamba was inactive as a tumor promoter (Espandiari et al. 1999) (Section 3.1.10).

In plants, dicamba mimics auxin plant growth hormones and causes uncontrolled growth (see Section 4.1.2.4). This hormonal mode of action is specific to plants and does not affect animals.

3.1.3. Kinetics and Metabolism

Information on the kinetics and metabolism of dicamba is available from studies in several laboratory and livestock species. As summarized below, dicamba is rapidly and extensively

absorbed following oral exposure and rapidly excreted predominantly as unmetabolized compound in the urine. Oral studies in rats indicate that there are no significant pharmacokinetic differences in the free acid and amine salt forms of dicamba. Dermal absorption of dicamba has been demonstrated but is less well studied than oral absorption.

3.1.3.1. After Intravenous Administration **–** The pharmacokinetics of dicamba and its 3,5-dichloro-isomer, a primary contaminant in technical dicamba, were compared following intravenous injection or dermal exposure in male Wistar rats (Makary et al. 1986a, 1986b). In the intravenous (i.v.) study (Makary et al. 1986a), single doses of 100 mg/kg dicamba (99.6% pure) and 20 mg/kg of dicamba isomer (99.5% pure) were administered alone or combined as the sodium salts in aqueous solution. The dose levels were based on the ratio of the two chemicals in technical formulation. For the individually administered compounds, disappearance from the blood was best fit by a two-compartment open model. For the combination of chemicals, a one-compartment model best fit dicamba and a two-compartment model best fit the isomer. The half-times for dicamba and isomer were 0.64 and 16.5 hours, respectively, indicating that the isomer was eliminated from the blood more slowly than dicamba. When the compounds were administered together, the rate of dicamba elimination decreased (0.83 hour for dicamba and 13.3 hours for the isomer). *In vitro* testing showed that the isomer had a higher affinity for binding to serum protein (83.3% bound) than dicamba (33.8% bound).

3.1.3.2. Oral Absorption Kinetics **–** The oral absorption of dicamba has been quantified in urinary excretion studies. Tye and Engel (1967) administered a mixture of ^{14}C-labeled dicamba (98% pure) and technical dicamba to Charles River CD rats by a single gavage dose in peanut oil (0.1 and 0.9 g/kg), via diet (10-20,000 ppm) for ≤24 hours, or by a single subcutaneous injection in peanut oil (0.1 g/kg). Following gavage or subcutaneous exposure, approximately 93% and 96% of the administered ^{14}C-dicamba, respectively, was excreted unmetabolized in the urine within 24 hours of dosing. With dietary exposure, urinary and fecal excretion approached 96% and 4% of the rate of intake. Dicamba was excreted unchanged in the urine (20% was conjugated with glucuronic acid). Similarly, following a single oral dose of 100 mg/kg of ^{14}C-dicamba (99% pure) in rats, mice, rabbits and dogs, 67-83% of the radioactivity was eliminated in the urine as parent compound within 48 hours (Atallah and Yu 1980). About 1% of the administered dose was metabolized to 3,6-dichlorosalicylic acid (3,6-DCSA or 3,6-dichloro-2-hydroxybenzoic acid) and another 1% to an unidentified metabolite. These findings are consistent with the results of earlier dicamba studies in rats (Whitacre et al. 1976) and a dog (Velsicol Chemical Corporation 1961), as well as data on amine salts of dicamba in rats as summarized below.

The pharmacokinetics of ^{14}C-dicamba were compared in male CD rats following a single 10 mg/kg gavage dose as the free acid or its dimethylamine, isopropylamine or diglycolamine salt (98.4-99.9% pure) in normal saline (Ekdawi et al. 1994, MRID 43288002). Evaluation for 24 hours following dosing showed that there were no statistically significant differences between dicamba and the three amine salt forms, with 95-97% and 3-5% of the dose excreted in the urine and feces, respectively, and radiocarbon in the blood accounting for about 0.02% of the dose.

Parent dicamba was the major excreted compound, accounting for 92-94% of the urinary radiocarbon and 75-80% of the fecal radiocarbon. 3,6-DSCA was a minor metabolite (0.5-0.6% and 3-4% of the urinary and fecal radiocarbon, respectively), and unidentified metabolites accounted for <1 % of the urinary radiocarbon in the urine. The results of this study indicate that dicamba rapidly dissociated *in vivo* regardless of its form as free acid or an amine salt.

The plasma kinetics of dicamba were investigated in orally-exposed rats (Leibold et al. 1998, MRID 44609801). Wistar and Sprague-Dawley rats of both sexes were pretreated with 900-12,000 ppm non-radiolabeled dicamba (86% pure) in the diet (75-1000 mg/kg/day) for 14 days followed by a single 75-800 mg/kg dose of ^{14}C-dicamba (>95% pure) by gavage. Plasma levels of radioactivity were measured for the next 48 hours. Initial plasma levels and AUC values increased with increasing dose in both strains of rats, indicating that oral absorption was not saturated in the range of tested doses. The increase in plasma AUC was linear with dose up to 150 mg/kg in male Wistar rats, 300 mg/kg in female Wistar rats, 125 male Sprague-Dawley rats, and 250 mg/kg in female Sprague-Dawley rats. Above these dose levels there were disproportionate increases in plasma AUC values, indicating that saturation of renal excretion occurred at the higher doses. This conclusion was supported by another indicator of excretory saturation, plasma initial half-life, which similarly increased at doses above 150 mg/kg in male Wistar rats (to 2.6-5.4 hours), 150 mg/kg in female Wistar rats (to 4.8-6.0 hours), 125 mg/kg in male Sprague-Dawley rats (to 2.8-12.4 hours), and 250 mg/kg in female Sprague-Dawley rats (to 1.7-4.4 hours). This study was conducted to help determine appropriate dose levels for a repeat carcinogenicity study of dicamba that has been requested by U.S. EPA (effect levels above the saturation point would have questionable relevance in human risk assessment).

3.1.3.3. Dermal Absorption Kinetics –As detailed further in Section 3.2.2.2, two types of dermal exposure scenarios are considered in this risk assessment: those involving direct contact with a solution of the herbicide (e.g., immersion) and those associated with accidental spills of the herbicide onto the surface of the skin.

As detailed in SERA (2001b), 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 dicamba is 0.000033 cm/hour with a 95% confidence interval of 0.00000014 to 0.0007 cm/hour. The details of the U.S. EPA (1992) method for estimating K_p based on the molecular weight and octanol-water partition coefficient are given in Worksheet A07b. The application of this method to dicamba is given in Worksheet B04. The estimated K_p is used in all exposure assessments in this document that are based on Fick's first law.

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 SERA (2001), the estimated first-order dermal absorption coefficient is

0.0013 hour^{-1} with 95% confidence intervals of 0.00045 to 0.0039 hour^{-1}. The details of the method specified in SERA (2001) for estimating the first-order dermal absorption coefficient based on the molecular weight and octanol-water partition coefficient are given in Worksheet A07a. The application of this method to dicamba is given in Worksheet B03.

While there are no studies available to evaluate the estimated dermal permeability coefficient for dicamba, the estimated first-order dermal absorption rate in humans can be compared to the first order dermal absorption rate determined in rats in the study by Makery et al. (1986b). In this study, both dicamba and 3,5-dichloro isomer were dissolved in acetone and applied to shaved skin (6 cm^2, 0.8 or 4.1 mg/cm^2), and covered with plastic film. The highest blood concentrations of dicamba and isomer were found at 1 and 9 hours, respectively. Unlike the i.v. study (Section 3.1.3.1), the disappearance of both chemicals from the blood followed first order kinetics, and findings for combined exposure were similar to that for the individual chemicals. The half-times in blood were 0.4 hours for dicamba and 3.6 hours for the isomer, suggesting that dermal absorption was the rate limiting step in urinary elimination of the isomer. As estimated from urinary excretion, 14.1 and 7.5% of the applied dermal doses of dicamba and isomer were absorbed. The absorption rates through the skin were 0.0029 hour^{-1} for dicamba and 0.0012 hour^{-1} for the isomer. The estimated rate for dicamba, 0.0029 hour^{-1}, is in the range of estimates given in Worksheet B03, 0.00045 hour^{-1} to 0.0039 hour^{-1}.

3.1.4. Acute Oral Toxicity

Case studies of human poisonings with dicamba have been reported, but dicamba alone was not the sole cause of toxicity because all cases involved concurrent exposure to one or more other pesticides. Based on poisoning episodes from England and Wales between 1945 and 1987, dicamba in combination with 2,4-D, Mecoprop, Ioxynil and/or MPCA was involved in 10 fatalities, about 1% of the total number of fatal poisonings attributed to pesticides (Casey and Vale 1994). As summarized by Casey and Vale (1994), approximately 70% of all such poisonings are associated with suicide. Flanagan et al. (1990) described a man who ingested 100 mL of an uncharacterized formulation containing 2,4-D and dicamba. Upon admission to a hospital, plasma levels of 2,4-D (0.7 g/L) were higher than for dicamba (0.01 g/L), and signs and symptoms of poisoning included bradycardia, sweating, nausea, vomiting, and tremor. Flanagan et al. (1990) also described a man who vomited after ingesting approximately 100 ml of an unspecified mixture of dicamba and 4-chloro-2-methylphenoxyacetic acid. In another case report (Fraser et al. 1992), a woman consumed an unspecified amount of a formulation containing 2,4-D, mecoprop, and dicamba. Prior to death, the woman's condition was characterized as "comatose and distressed" with heavy breathing and abdominal distension.

Incidents of dicamba poisoning have been recorded in the U.S. EPA Pesticide Incident Monitoring System. From 1966 to 1981, there were reports of 10 incidents with dicamba, six of which involved spray operations (U.S. EPA 1988). Exposed workers developed muscle cramps, dyspnea, nausea, vomiting, skin rashes, loss of voice, or swelling of cervical glands. The other four incidents involved children who had episodes of dizziness (in one child) or coughing. Three children who sucked mint leaves from a ditch bank previously sprayed with dicamba showed no

signs of effects (U.S. EPA 1988). In a program at Oregon State University offering information to members of the public concerned with pesticide exposure, dicamba was a topic in 4 out of approximately 300 queries (Wagner 1990).

Information regarding the acute toxicity of dicamba and dicamba salts in laboratory mammals is summarized in Appendix 1. These data indicate that dicamba is relatively nontoxic by oral administration, with single-dose LD_{50} values ranging from approximately 750 to 3000 mg/kg in rats. Edson and Sanderson (1965) found that "pure" dicamba was less toxic than technical grade dicamba in female rats (LD_{50} of 2560 mg/kg compared to 1414 mg/kg), but interpretation of this finding is complicated by a lack of details on the chemical composition of the two test materials. Gaines and Linder (1986) reported that the acute oral LD_{50} for Technical dicamba was higher in weanling Sherman rats (3294 mg/kg) than in adult males and females (1404 and 1039 mg/kg, respectively); however, no additional information on possible age differences in susceptibility was found. Signs of neurotoxicity (e.g., decreased activity, ataxia, loss of coordination) were the main systemic effects in the LD_{50} assays, although gross pathologic changes (e.g., in liver, kidneys and lungs) have been noted in animals that died.

There are no clear indications that the dimethylamine salt (e.g., Banvel), sodium salt or methyl ester derivatives differ significantly from the toxicity of dicamba, or that the toxicity of these forms differs significantly between species or sexes (Appendix 1). No information was located on the acute toxicity of the diglycolamine salt (e.g., Vanquish). The similar ranges of oral LD_{50} values for the different forms of dicamba are consistent with pharmacokinetic and chemical evidence for toxicological equivalence, i.e., data showing that dicamba rapidly dissociates in aqueous environments regardless of its form as free acid or salt (Ekdawi et al. 1994; U.S. EPA 1984). Intraperitoneal injections appear to be much more hazardous than oral (or inhalation or dermal) exposure (Appendix 1), suggesting that the low acute toxicity by normal exposure routes might be due in part to the kinetics of absorption.

3.1.5. Subchronic and Chronic Toxicity

One study was located that provides some information on the potential toxicity of repeated exposures to dicamba in humans. As summarized in Section 3.1.6, Potter et al. (1993) found that dicamba contributed to an increased incidence of AChE inhibition in farm workers with mixed exposure to dicamba and other herbicides.

Subchronic dietary studies of technical dicamba and dicamba sodium salt were conducted in rats (Edson and Sanderson 1965; Laveglia 1981). As summarized in Appendix 2, the study with technical dicamba was comprehensive in scope and identified NOAELs of 342 mg/kg/day in males and 392 mg/kg/day in females exposed for 13 weeks (Laveglia 1981). Based on small decreases in food consumption (9-11%) and body weight gain (6-8%), and hepatic changes that were likely secondary to the reduced weight gain (increased relative liver weight, histological alterations indicative of reduced glycogen storage), 682 mg/kg/day (males) and 751 mg/kg/day (females) are minimal subchronic LOAELs for dicamba. The dietary study with dicamba sodium salt found dose-related increased absolute and relative liver weights, but no effects on food

consumption, body weight or gross pathology, in rats at the two highest tested dose levels of 67 and 205 mg/kg/day (55.6 and 170 mg/kg/day a.e.) (Edson and Sanderson 1965). No histological examinations were performed. Considering the lack of liver histopathology and other adverse effects in rats at higher dose levels in the subchronic study of technical dicamba (Laveglia 1981), as well as in rats at similar dose levels in a chronic study with technical dicamba (Goldenthal 1985), the increased liver weight caused by dicamba sodium salt is not considered to be adverse. The highest subchronic NOAEL for the sodium salt, 205 mg/kg/day (170 mg/kg/day a.e), is below the subchronic NOAELs for technical dicamba (342/392 in males/females) (Laveglia 1981), indicating that the 392 mg/kg/day NOAEL and 682 mg/kg/day are critical effect levels for subchronic exposure to dicamba.

Chronic dietary studies of dicamba have been performed in rats, mice and dogs (Crome et al. 1987; Davis et al. 1962; Drench 1986; Goldenthal 1985; Laveglia 1981). No information was located on the chronic toxicity of other forms of dicamba. As detailed in Appendix 3, dietary exposure to technical dicamba for approximately two years caused no exposure-related systemic effects, including clinical signs or changes in hematology, blood chemistry, urinalysis endpoints or histopathology, in rats at doses as high as 107 mg/kg/day in males or 127 mg/kg/day in females (Davis et al. 1962; Goldenthal 1985). Higher doses were not tested in the rats, precluding identification of a LOAEL in this species. Mice exposed to dicamba in the diet for up to 89-104 weeks similarly showed no clear effects at doses of $\leq$121 mg/kg/day, although body weight gain was decreased in females at 364 mg/kg/day and there was an equivocal decrease in survival in males at 358 mg/kg/day (Crome et al. 1987).

A two-year study in dogs reported reduced body weight gain, but no exposure-related changes on food consumption or other systemic endpoints, at estimated dietary doses of $\geq$0.75 mg/kg/day (Davis et al. 1962). This finding is questionable considering the very low dose levels and lack of clear corroborating data in a more recent and comprehensive chronic study in dogs exposed to higher dietary levels of technical dicamba (Drench 1986). In particular, dogs exposed to 55 mg/kg/day (females) or 65 mg/kg/day (males) for one year had only slight reductions in body weight gain and food consumption that were transient (only occurred early in the study) and attributed to poor palatability of the test material. There were no exposure-related effects on body weight gain or other systemic endpoints (e.g., food consumption, clinical signs, hematology, blood chemistry, urinalysis, histopathology), indicating that the NOAEL is 65 mg/kg/day and a LOAEL is not identifiable in the one-year dog study. Considering the data in all three species, the NOAEL of 121 mg/kg/day and LOAEL of 358 mg/kg/day for reduced body weight gain in mice (Crome et al. 1987) are critical effect levels for chronic exposure to dicamba.

3.1.6. Effects on Nervous System

One study was located that specifically addresses the potential toxic effects of repeated exposures to dicamba in humans (Potter et al. 1993). These investigators noted an increased incidence of AChE inhibition in farm workers using herbicides, including dicamba, and found that 3,6-dichloro-2-methoxy benzoic acid, the major component in dicamba, causes inhibition of both

plasma and red blood cell (RBC) cholinesterase *in vitro*, using red cells and plasma from human blood samples.

Cohort mortality epidemiology studies of forestry workers exposed to phenoxy herbicides have noted an increase in suicides (Green 1991, Hogstedt and Westerlund 1980). It was speculated that the suicides could possibly be associated with neurotoxic effects of the herbicides (Green 1991), but neither report suggests that suicide is specifically attributable to dicamba.

Clinical signs of neurotoxicity typically occur in humans and animals following acute oral exposure high doses (lethal dose range) of dicamba and its salts. As summarized in Section 3.1.4 and Appendix 1, effects included tremors in cases of acute human poisoning and decreased activity, ataxia and loss of coordination in animal LD_{50} assays.

Neurobehavioral effects of lower dose levels of dicamba were comprehensively evaluated in rats using Functional Observational Battery (FOB) and open-field locomotor activity tests following acute or subchronic exposure (Appendix 4). In the acute study, rats were given a single dose of 300-1200 mg/kg of technical dicamba by gavage and evaluated 1.5 hours after treatment (Minnema, 1993; MRID 42774104). In the subchronic study, rats were tested following dietary exposure to technical dicamba for up to 13 weeks at doses ranging from 200-1000 mg/kg/day (Minnema, 1994; MRID 43245210). Similar effects were observed in both studies, including body tone rigidity in response to handling and touch, abnormal righting reflex, and impaired gait. Other effects included increased salivation and impaired respiration, flattened and/or raised posture, decreased rearing frequency, increased tail flick latency, decreased forelimb grip strength, hypoalterness and decreased locomotor activity in the acute study, and increased latency to first step in the subchronic study. No NOAEL was identified in the single dose study, indicating that the acute neurotoxicity LOAEL is 300 mg/kg. The subchronic study identified a neurotoxicity NOAEL of 472 mg/kg/day and LOAEL of 768 mg/kg/day.

Clinical signs of neurotoxicity, including ataxia, body stiffening and decreased motor activity, occurred in maternal rats treated with 400 mg/kg/day (NOAEL = 160 mg/kg/day) by gavage on days 0-19 of gestation (Smith et al. 1981; MRID 00084024), and rabbits administered $\geq$150 mg/kg/day (NOAEL = 30 mg/kg/day) by capsule on gestation days 6-18 (Hoberman, 1992; MRID 42429401). These LOAELs, like the 300 mg/kg LOAEL in the single dose rat study summarized above (Minnema, 1993), are lower than the subchronic neurotoxicity NOAEL of 472 mg/kg/day and LOAEL of 768 mg/kg/day in rats (Minnema, 1994). The lower neurotoxicity LOAELs in the acute and developmental studies is likely related to the bolus methods of oral exposure (gavage or capsule) compared to diet in the subchronic study.

An avian acute delayed neurotoxicity study found sciatic nerve damage in domestic chickens that were given a single 316 mg/kg oral dose of dicamba in corn oil by gavage. Histological examinations were conducted after an observation period of 21 days (Roberts et al. 1983; MRID 00131290). The birds were unsteady and unable to stand from days 1-19. At the end of the study, nerve damage was observed but was considered likely related to the prolonged

recumbency. Nonetheless, a direct neurotoxic effect of dicamba could not be ruled out. Chickens dosed with 158 mg/kg were recumbent for <1 day and had no histopathological changes in the brain, spinal cord or sciatic nerves, and 79 mg/kg caused no effects.

3.1.7. Effects on Immune System

There is very little direct information on which to assess the immunotoxic potential of dicamba. The only studies specifically related to the effects of dicamba on immune function are skin sensitization studies (Section 3.1.11). While the study by (Kuhn 1998g) indicates that dicamba is not a skin sensitizer, this provides no information useful for directly assessing the potential for dicamba to disrupt immune function.

Nonetheless, the toxicity of dicamba has been examined in numerous acute, subchronic, and chronic bioassays. Although many of these studies did not focus on the immune system, changes in the immune system (which could potentially be manifest as increased susceptibility to infection compared to controls) were not observed in any of the available long-term animal studies (Appendix 3). Typical subchronic or chronic animal bioassays conduct morphological assessments of the major lymphoid tissues, including bone marrow, major lymph nodes, spleen and thymus (thymus weight is usually measured as well), and blood leukocyte counts. These assessments can detect signs of inflammation or injury indicative of a direct toxic effect of the chemical on the lymphoid tissue. Changes in cellularity of lymphoid tissue and blood, indicative of a possible immune system stimulation or suppression, can also be detected (Durkin and Diamond 2002). None of these effects have been noted in any of the longer term toxicity studies (Appendix 3).

3.1.8. Effects on Endocrine Function

In terms of functional effects that have important public health implications, some effects on endocrine function would be expressed as diminished or abnormal reproductive performance. This issue is addressed specifically in the following section (Section 3.1.9). Mechanistic assays are generally used to assess the potential for direct action on the endocrine system (Durkin and Diamond 2002). Dicamba has not been tested for activity as an agonist or antagonist of the major hormone systems (e.g., estrogen, androgen, thyroid hormone), nor have the levels of these circulating hormones been measured following dicamba exposures. Thus, any judgments concerning the potential effect of dicamba on endocrine function must be based on inferences from standard toxicity studies. The major endocrine glands in the body include the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis (Durkin and Diamond 2002). None of the longer term toxicity studies summarized in Appendix 3 or short term toxicity studies summarized in Appendix 1 report effects in any of these organs. As indicated in the following section (Section 3.1.9), extensive data are available on the reproductive performance and development of experimental animals exposed to dicamba. In one study (Masters, 1993), delayed sexual maturation was seen in young male rats at high dietary concentrations – i.e., 5000 ppm. These effects were associated with decreased initial growth rates but it is not clear that the effects were mediated by changes in endocrine function.

3.1.9. Reproductive and Teratogenic Effects

Dicamba has been tested for its ability to cause birth defects (i.e., teratogenicity) as well as its ability to cause reproductive and developmental impairment. Teratogenicity studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Four such studies (each of which is detailed in Appendix 5) were conducted on dicamba: one in rats (Smith et al. 1981) and three in rabbits (Hoberman 1992; Goldenthal et al. 1978; Wazeter et al. 1977). The study by Hoberman (1992) involved administration by capsules rather than gavage. Rabbits were more sensitive to dicamba than rats, with a NOAEL of 3 mg/kg/day for both maternal toxicity and reproductive effects (Goldenthal et al. 1978). The reproductive NOAEL in rats was 400 mg/kg/day, a dose that caused signs of toxicity in dams. As discussed further in Section 3.3, the 3 mg/kg/day NOAEL in rabbits from the study by Goldenthal et al. (1978) is the basis of the Agency wide U.S. EPA RfD on dicamba (U.S. EPA 1992a) but a more recent review of the study by the U.S. EPA/OPP (Rowland 1995) has noted major deficiencies in the quality of this study.

Another type of reproduction study involves exposing more than one generation of the test animal to the compound. Three such studies, all in rats, have been conducted on dicamba and are summarized in Appendix 5 (Davis et al. 1962; Witherup et al. 1966; Masters 1993). The studies by Davis et al. (1962) and Witherup et al. (1966) both report reproductive dietary NOAELs of 500 ppm, corresponding to estimated daily doses of 25 mg/kg/day. The more recent study by Masters (1993) also reports a dietary reproductive NOAEL of 500 ppm, corresponding to 35-44 mg/kg/day based on measured food consumption. The next higher dietary concentration, 1500 ppm (corresponding to doses of 105-135 mg/kg/day), was associated with reduced mean pre-weaning body weight gain. The 500 ppm dietary NOAEL was used by the U.S. EPA Office of Pesticides in setting the chronic RfD used in setting pesticide tolerances for dicamba (U.S. EPA 1999). This is discussed further in Section 3.3.

3.1.10 Carcinogenicity and Mutagenicity

There are no epidemiology studies or case reports that demonstrate or suggest that exposure to dicamba leads to cancer in humans. Morrison et al. (1992) express a general concern with phenoxy acid herbicide exposure and cancer in humans. As reviewed by Green (1991) and Zahm (1997), some case studies and case-control studies have noted an increase in soft tissue sarcomas and non-Hodgkin's lymphomas in individuals exposed to phenoxy herbicides.

A case-control study of multiple myeloma in Iowa men found a statistically insignificant increase in the odds ratio (OR=1.2, 95% CI 0.8–1.7) for 173 farmers compared to 650 non-farmer controls (Brown et al. 1993). Based on the results of a questionnaire survey of these men, there also was no significant association between increased risk of multiple myeloma and use of dicamba (mixing, handling and/or application) (OR=1.3, 95% CI 0.6–2.6).

Dicamba was inactive in the two-stage liver tumor promotion assay in rats (Espandiari et al. 1999). Female Sprague Dawley rats were administered a single oral dose of diethylnitrosamine (150 mg/kg by gavage) as an initiating agent, followed two weeks later by diets containing dicamba (0.75%), phenobarbital (0.05%) (positive control), or both dicamba (0.75%) and

phenobarbital (0.05%) for six months. Dicamba alone did not increase the number or volume of preneoplastic lesions (altered hepatic foci), indicating that it did not have promoting activity. Some significant effects occurred in rats exposed to both dicamba and phenobarbital compared to those receiving phenobarbital alone, suggesting that dicamba in combination with other tumor promoters might have weak promoting activity in the two-stage hepatocarcinogenesis model.

3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes)

As summarized in Appendix 1, mild and transient skin irritation occurred at the application site in some of the studies of the dimethylamine (DMA) and sodium salts after a dermal dose of 5050 mg/kg (Kuhn 1998b,d). One formulation of dicamba, Banvel 480, has been reported to cause severe skin irritation (Budai et al. 1997). The local eye, nasal and skin effects observed in the acute inhalation and dermal studies are consistent with results of skin and eye irritation assays summarized in Appendix 2.

3.1.12. Systemic Toxic Effects from Dermal Exposure

Dermal exposure to dicamba appears to present no substantial acute toxicity. As summarized in Appendix 1, no mortality, clinical signs of toxicity and/or effects on body weight gain were observed in rats and rabbits dermally exposed to dicamba, the dimethylamine (DMA) or Na salts or the methyl ester in single occluded applications of 1000-5050 mg/kg (highest tested dose levels). Mild and transient skin irritation occurred at the application site in some of the studies of the dimethylamine (DMA) and sodium salts.

Subchronic dermal toxicity was studied in rabbits exposed to the dimethylamine (DMA), diglycolamine and IPA salts of dicamba. Skin irritation was induced by the dimethylamine (DMA) salt tested as Banvel. In one study, Banvel technical (86.8%) was applied to the skin on 5 days/week for 3 weeks in dose levels of 0 (vehicle control), 100, 500 or 2500 mg/kg/day (Goldenthal et al., 1979; MRID 00128091). Each dose was mixed with 0.9% saline solution to form a homogeneous paste, spread on clipped skin that was abraded in half the animals, and left uncovered for six hours each day. In another study, Banvel (NOS) was applied undiluted to clipped intact skin in doses of 0 (water), 40, 200 or 1000 mg/kg/day, and covered with an occlusive barrier for 6 hours/day on 5 days/week for 3 weeks (Strouse and Nass, 1986; MRID 40547901). Skin irritation occurred in all exposed groups of both studies, and increased in severity and/or incidence with dose level and duration of exposure. The effects were slight to moderate at the low doses and generally included erythema and edema, with desquammation and fissuring also occurring in some animals in all groups. There were no compound-related changes in behavior and appearance, body weight, hematology, blood chemistry, urinalysis indices, or organ weights in either study. Comprehensive histological examinations were performed that only showed changes in the skin at the application site that were consistent with the dermal irritation.

In contrast to Banvel, repeated dermal exposures to dicamba diglycolamine (DGA) salt (4 lb/gal, 39.7% pure, administered undiluted) or isopropanolamine (IPA) salt (3 lb/gal, 32.3% pure, administered undiluted) caused no skin irritation in rabbits (Blaszcak 1994a, 1994b; MRID

43554206, 43554206). Both dicamba salts were applied to intact skin under a semi-occlusive covering in doses of 0 (sham control), 100, 500 or 2500 mg/kg/day for 6 hours/day, 5 days/week for 3 weeks. There were no clinical signs of toxicity or effects on body weight, hematology, blood chemistry, urinalysis indices, organ weights, or histology in either study.

3.1.13. Inhalation Exposure

As summarized in Appendix 1, rats that were exposed by inhalation to dimethylamine (DMA) salt, sodium salt or methyl ester formulations for 4 hours experienced signs such as decreased activity and indications of eye and nasal irritation, but no effects on body weight gain, gross pathology or survival, at concentrations in the range of 2-5.4 mg/L (Appendix 1). Additionally, no histopathological changes occurred in the lungs, liver or kidneys of rats exposed via inhalation to 5.4 mg/L of a dimethylamine (DMA) salt formulation (Banvel 480) for 4 hours (Collins and Proctor 1984). Inhalation of higher levels (200 mg/L) for 4 hours caused mortality in rats exposed to a methyl ester formulation (Racuza 4 E.C.) (Velsicol Chem. Corp 1979), but not to formulations of dimethylamine (DMA) salt (Technical Banvel or Banvel 310) (Goldenthal et al. 1972). The local eye, nasal and skin effects observed in the acute inhalation studies are consistent with results of skin and eye irritation assays summarized in Appendix 2.

Rats that were exposed by inhalation to dimethylamine (DMA) salt, sodium salt or methyl ester formulations for 4 hours experienced signs such as decreased activity and indications of eye and nasal irritation, but no effects on body weight gain, gross pathology or survival, at concentrations in the range of 2-5.4 mg/L. No histopathological changes occurred in the lungs, liver or kidneys of rats exposed to 5.4 mg/L of a dimethylamine (DMA) salt formulation (Banvel 480) for 4 hours (Collins and Proctor 1984). Inhalation of higher levels (200 mg/L) for 4 hours caused mortality in rats exposed to a methyl ester formulation (Racuza 4 E.C.) (Velsicol Chem. Corp 1979), but not to formulations of dimethylamine (DMA) salt (Technical Banvel or Banvel 310) (Goldenthal et al. 1972).

Subchronic inhalation toxicity was evaluated in rats that were exposed to an aerosol of dicamba dimethylamine (DMA) salt as Banvel 4S (NOS) for 6 hours/day, 5 days/week for 2 weeks (IRDC, 1979; Accession No. 242155). The average exposure concentrations were 0, 0.202, 2.01 and 20.0 mg/L, and the MMAD of the aerosol particles was 4.25 μm (GSD 2.07). Clinical signs, body weight, hematology, blood chemistry, urinalysis indices, organ weights, gross pathology and histopathology were evaluated. Histopathological changes in the lungs (perivascular edema) occurred at $\geq$0.202 mg/L, with gross edema and/or congestion in the lungs and nasal cavity observed in rats that died at 20.0 mg/L. Other effects included pathological changes in the stomach at 2.01 mg/L (hemorrhagic foci in mucosa) and 20.0 mg/L (hemorrhage, necrosis and/or congestion), and spleen at 20.0 mg/L (focal necrosis). Pathological changes in the liver (necrosis) and brain/spinal cord (vacuolation) at 20.0 mg/L were possibly exposure-related. The lung pathology in all exposure groups indicates that the LOAEL is 0.202 mg/L and a NOAEL cannot be identified.

3.1.14. Inerts and Adjuvants

As noted in Section 2.2, the identity of inerts in both Banvel and Vanquish has been disclosed to the U.S. EPA (Velsicol Chemical Corp 1961,1984; Bryant 1995a,b) and this information has been reviewed as part of this risk assessment. This information, however, is protected under FIFRA (Section 10). Other than to state that no apparently hazardous materials have been identified, which is consistent with the MSDS for both Banvel and Vanquish (C&P Press 2003), the information on the inerts in these formulations cannot be detailed.

The potential toxicologic significance of inerts in Banvel can be inferred from a comparison of the toxicity data on Banvel with corresponding toxicity data on dicamba. Comparisons between different bioassays conducted in different laboratories can be misleading because of normal variability in animal responses and because of differences in experimental conditions. Velsicol Chem. Corp. (1979) provides data on the differences between Banvel and the dimethylamine (DMA) salt of dicamba from studies that were conducted at the same time and in the same laboratory. As indicated in Appendix 1, the acute oral LD_{50} value for Banvel in rats is 1028-2629 mg/kg and the corresponding value for the dimethylamine (DMA) salt of dicamba is 1707-2900. The dermal LD_{50} values for both Banvel and the dimethylamine (DMA) salt of dicamba are >2000 mg/kg and the inhalation LC_{50} value for both Banvel and the dimethylamine (DMA) salt of dicamba are >200 mg/L (Velsicol Chem. Corp. 1979). Thus, in terms of acute lethal potency, no substantial differences are apparent between the a.i. in Banvel (the DMA salt of dicamba) and the Banvel formulation. As noted in Appendix 2, however, Banvel causes severe skin irritation (Budai et al. 1997) but the DMA salt of dicamba caused no irritation (Kuhn 1998b) or only slight irritation (Kuhn 1997, 1998a).

For Vanquish, commercial searches of the studies available in the FIFRA CBI files as well as supplemental searches that were kindly provided by the U.S. EPA Office of Pesticides did not identify specific mammalian toxicity studies using Vanquish. Some data are available comparing the toxicity of the IPA salt, the a.i. in Vanquish to other forms of dicamba in birds. As indicated in Appendix 6, the LD_{50} value of a formulation of the IPA salt of dicamba in Bobwhite quail is 1373 mg/kg (95% CI = 1105-1716) (Beavers, 1986) and the corresponding value for dicamba is 216 mg/kg (95% CI = 162-288) (Campbell et al., 1993).

3.1.15. Impurities and Metabolites

Information on impurities in technical grade dicamba have been disclosed to the U.S. EPA (Velsicol Chemical Corp. 1961,1984; Bryant 1995a,b) and this information was obtained and reviewed as part of this risk assessment. Because this information is classified as confidential business information, detail of the information submitted to U.S. EPA cannot be disclosed in this risk assessment.

Some published information, however, is available on the impurities in dicamba. A pharmacokinetics study (Makary et al. 1986 a,b) indicates that the main impurity is 3,5-dichloro-2-methoxy benzoic acid. In a worker exposure study (Draper and Street 1982), analysis of technical grade dicamba (dimethyl amine salt provided by Velsicol) contained the

major (3,6-dichloro) and minor (3,5-dichloro) isomers in a ratio of 5:1. This is comparable to, although somewhat higher than, the ratio of the 3,6-dichloro isomer to the "impurities" in Vanquish [56.8% ÷ 14.2% = 4:1] reported by Sandoz (1993). This information suggests that currently marketed Vanquish probably contains the 3,5-dichloro isomer as the major impurity and that this impurity may be present in Vanquish in lesser amounts than were present in dicamba formulations produced in the 1980s. Alternatively, since no data are available on the variability of the impurities in any dicamba formulations, this apparent difference may be due to simple chance. The synthesis of dicamba involves the reaction of 2,5-dichlorophenol with carbon dioxide to yield 3,6-dichlorosalicylic acid which is then methylated with dimethyl sulfate (Worthing and Hance 1991). It is not clear whether the formation of the 2,5-dichloro isomer of dicamba, the major impurity in the commercial formulation, is attributable to impurities in 2,5-dichlorophenol or some other process.

There is some indication that the impurities in dicamba may be more toxic than dicamba itself. Edson and Sanderson (1965) note that "pure" dicamba was less toxic than technical grade dicamba to female rats. Nonetheless, all of the toxicology studies on dicamba involve technical grade dicamba, which is presumed to be the same as or comparable to the active ingredient in the formulations used by the Forest Service. Thus, if toxic impurities are present in technical dicamba, they are likely to be encompassed by the available toxicity studies using technical grade dicamba.

3.1.16. Toxicologic Interactions

There is very little experimental evidence of interactions between dicamba with other chemical agents. Edson and Sanderson (1965) reported no apparent interactions between dicamba and 4-chloro-2-methyphenozyacetic acid or mecoprop. Details of these interaction studies are not presented in the publication.

In a study designed to assess the effects of various herbicides on liver mixed-function oxidase (MFO) and other drug metabolizing enzymes, mice were given a dose of 250 mg/kg/day dicamba (98% pure) (Moody et al. 1991). Two of four mice died after two intraperitoneal injections. Statistically significant decreases were noted in the level of cytochrome P-450 and aminopyrine N-demethylase activity and epoxide hydrolase activity. The results of this study suggest that dicamba could interact with compounds that are either toxified or detoxified by cytochrome P-450, at least at relatively high or toxic exposure levels.

The toxicity of two herbicide/fertilizer mixtures, both of which contained dicamba, has been assayed in female dogs (Yeary 1984). The doses of dicamba in herbicide mixtures were 0.55 mg/kg/day. Both mixtures also contained urea (623 mg/kg/day), inorganic phosphorus (P_2O_5) (0.24 mg/kg/day), potassium (K_2O) (0.66 mg/kg/day), 2,4-D (6.51 mg/kg/day), and mecoprop (3.26 mg/kg/day). One mixture also contained Bensulide (60.93 mg/kg/day) and the other contained chlorpyrifos (6.77 mg/kg/day). Each of six dogs was used in experiments on both mixtures, with a 3-week recovery period between the two experiments. In both experiments, plasma cholinesterase was inhibited by approximately 50%, compared with individual

pre-exposure baseline values. Because of the experimental design, however, the extent to which dicamba contributed to the plasma cholinesterase inhibition cannot be determined. Some of the agents tested (i.e., Bensulide and chlorpyrifos) are known inhibitors of AChE.

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview. Exposure assessments are conducted for both workers and members of the general public for the typical application rate of 0.3 lb/acre. The consequences of using the maximum application rate that might be used by the Forest Service, 2 lb/acre, are discussed in the risk characterization.

For workers, three types of application methods are modeled: directed ground, broadcast ground, and aerial. Central estimates of exposure for workers are approximately 0.004 mg/kg/day for aerial and backpack workers and about 0.007 mg/kg/day for broadcast ground spray workers. Upper range of exposures is approximately 0.005 mg/kg/day for directed ground spray workers 0.002 mg/kg/day for backpack and aerial workers. All of the accidental exposure scenarios for workers involve dermal exposures and all of these accidental exposures lead to estimates of doses that are either in the range of or substantially below the general exposure estimates for workers.

For the general public, the range of acute exposures is from approximately 0.0000008 mg/kg to 1 mg/kg. The lower end of this range associated with the lower range for the consumption of contaminated water from a stream by a child. The upper end of the range is associated with the upper range for the consumption of contaminated water by a child following an accidental spill of dicamba into a small pond. High dose estimates are also associated with the direct spray of a child (about 0.17 mg/kg/day at the upper range of exposure). Other acute exposures are lower by about an order of magnitude. For chronic or longer term exposures, the modeled exposures are much lower than for acute exposures, ranging from approximately 0.0000000001 mg/kg/day (one 10 billionth of a mg/kg/day) associated with the lower range for the normal consumption of fish to approximately 0.008 mg/kg/day associated with the upper range for consumption of contaminated fruit.

3.2.2. Workers.

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

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

any type of application. The exposure assessments developed in this section as well as other similar assessments for the general public (Section 3.2.3) are based on the typical application rate of 0.3 lbs/acre (Section 2). The consequences of using different application rates in the range considered by the Forest Service are discussed further in the risk characterization (Section 3.4).

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

The specific assumptions used for each application method are detailed in Worksheets C01a (directed foliar), C01b (broadcast foliar), and C01c (aerial). In the worksheets, the central estimate of the amount handled per day is calculated as the product of the central estimates of the acres treated per day and the application rate.

As described in SERA (2001b), worker exposure rates are expressed in units of mg of absorbed dose per kilogram of body weight per pound of chemical handled. These exposure rates are based on worker exposure studies on nine different pesticides with molecular weights ranging from 221 to 416 and log K_{ow} values at pH 7 ranging from -0.75 to 6.50. The estimated exposure rates are based on estimated absorbed doses in workers as well as the amounts of the chemical handled by the workers. As summarized in Table 2-1 of this risk assessment, the molecular weight of dicamba is 221 and the log K_{ow} is -0.56. These values are within the range of the herbicides used in SERA (2001b). As described in SERA (2001b), 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.

One worker exposure study involving dicamba is available (Draper and Street 1982). In this study, workers applied a mixture of 2,4-D and dicamba using a boomspray over a 42 acre pasture. The application involved a mixture of 2,4-D and dicamba at a ratio of 2.5:1 [i.e., 2.5 parts 2,4-D to 1 part dicamba]. Total absorbed doses of both herbicides were estimated from the amounts of both herbicides eliminated in the urine. Two workers were monitored: the driver and the sprayer, who was also responsible for mixing and loading. The estimated absorbed doses for the driver were 40 mg/kg for 2,4-D and 16 mg/kg for dicamba. For the sprayer, the absorbed doses were 160 mg/kg for 2,4-D and 53 mg/kg for the dicamba. The ratios of 2,4-D to dicamba were 2.5:1 for the driver and about 3:1 for the sprayer. Thus, the amounts of each herbicide absorbed per amount of herbicide handled were essentially identical. While this cannot be used directly to validate the worker exposure estimates given in Worksheets C01a, C01b, and C01c (aerial), these estimates are based on the general assumption that worker exposure rates will not

vary among different herbicides and this assumption is supported by the study by Draper and Street (1982).

An estimate of the number of acres treated per hour is needed to apply these worker exposure rates. The typical application rate is taken directly from the program description (see section 2.4). The number of hours worked per day is expressed as a range, the lower end of which is based on an 8-hour work day with 1 hour at each end of the work day spent in activities that do not involve herbicide exposure. The upper end of the range, 8 hours per day, is based on an extended (10-hour) work day, allowing for 1 hour at each end of the work day to be spent in activities that do not involve herbicide exposure.

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

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

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

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

Dicamba can cause mild and transient skin irritation as well as local eye and nasal irritation (Appendix 1). 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, SERA 2001). Two general types of exposure are modeled: those involving direct contact with a solution of the herbicide and those associated with accidental spills of the herbicide onto the surface of the skin. Any number of specific exposure scenarios could be developed for direct contact or accidental spills by varying the amount or concentration of the chemical on or in contact with the surface of the skin and by varying the surface area of the skin that is contaminated.

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

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

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

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

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

Confidence in the exposure assessments based on the assumption of first order dermal absorption is enhanced by the availability of dermal absorption rate data in rats which are consistent with the first order dermal absorption rates estimated in humans (see Section 3.1.3.3). In addition, as summarized in Worksheet E01, comparable exposure scenarios based on both zero-order and first order absorption – i.e., contaminated gloves worn for 1 hour (Worksheet C02b) and a spill onto the skin surface of the hands that is cleaned after 1 hour (Worksheet C03a) – are similar. Thus, 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 dicamba. Nonetheless, any number of exposure scenarios can be constructed for the general public, depending on various assumptions regarding application rates, dispersion, canopy interception, and human activity. Several scenarios are developed for this risk assessment which should tend to over-estimate exposures in general.

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

The exposure scenarios developed for the general public are summarized in Worksheet E03. As with the worker exposure scenarios, details of the assumptions and calculations involved in these exposure assessments are given in the worksheets that accompany this risk assessment (Worksheets D01a to D09b). The remainder of this section focuses on a qualitative description of the rationale for and quality of the data supporting each of the assessments.

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

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

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

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

The accidental spill scenario assumes that a young child consumes contaminated water shortly after an accidental spill into a small pond. The specifics of this scenarios are given in Worksheet D05. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation of dicamba is considered. This scenario is dominated by arbitrary variability and the specific assumptions used will generally overestimate exposure. The actual concentrations in the water would depend heavily on the amount of compound spilled, the size of the water body into which it is spilled, the time at which water consumption occurs relative to the time of the spill, and the amount of contaminated water that is consumed. Based on the spill scenario used in this risk assessment, the concentration of dicamba in a small pond is estimated to range from about 0.15 mg/L to 9 mg/L with a central estimate of about 1 mg/L (Worksheet D05). The highest concentration of dicamba reported in surface water following an accidental spill is 0.517 mg/L (Frank et al. 1990b). Thus, the accidental spill scenario used in this risk assessment appears to be protective – i.e., actual spills or accidental sprays would likely lead to lesser concentrations of dicamba in water.

The other acute exposure scenario for the consumption of contaminated water involves runoff into a small stream. Estimates of these concentrations can be based both on modeling and monitoring data.

Modeling of concentrations in stream water are based solely on GLEAMS (Groundwater Loading Effects of Agricultural Management Systems) modeling. GLEAMS is a root zone model that can

be used to examine the fate of chemicals in various types of soils under different meteorological and hydrogeological conditions (Knisel and Davis 2000). As with many environmental fate and transport models, the input and output files for GLEAMS can be complex. The general application of the GLEAMS model and the use of the output from this model to estimate concentrations in ambient water are detailed in SERA (2004).

For the current risk assessment, the application site was assumed to consist of a 10 acre square area that drained directly into a small pond or stream. The chemical specific values as well as the details of the pond and stream scenarios used in the GLEAMS modeling are summarized in Table 3-1. The GLEAMS modeling yielded estimates runoff, sediment and percolation that were used to estimate concentrations in the stream adjacent to a treated plot, as detailed in Section 6.4 of SERA (2003), included with this risk assessment as Attachment 2. The results of the GLEAMS modeling for the small stream are summarized in Table 3-2 and the corresponding values for the small pond are summarized in Table 3-3. These estimates are expressed as both average and maximum water contamination rates (WCR) - i.e., the concentration of the compound in water in units of mg/L normalized for an application rate of 1 lb a.e./acre.

As indicated in Table 3-2, no stream contamination is estimated in very arid regions for clay and san – i.e., annual rainfall of 10 inches of less. The modeled maximum concentrations in the stream range from about less than 0.01 µg/L to about 0.5 µg/L at annual rainfall rates from 15 to 250 inches per year, with the highest concentrations associated with sandy soil. While not detailed in Table 3-2, the losses from clay are associated primarily with runoff (about 60%), with the remaining amount due almost exclusively with percolation. Losses from sand, on the other hand, are associated exclusively with percolation.

The GLEAMS scenarios do not specifically consider the effects of accidental direct spray. For example, the steam modeled using GLEAMS is about 6 feet wide and it is assumed that the herbicide is applied along a 660 foot length of the stream with a flow rate of 4,420,000 L/day. At an application rate of 1 lb/acre, accidental direct spray onto the surface of the stream would deposit about 41,252,800 µg [1 lb/acre = 112,100 µg/m^2 , 6'x660' = 3960 ft^2 = 368 m^2, 112,100 µg/m^2 × 368 m^2 = 41,252,800 µg]. This would result in a downstream concentration of about 10 µg/L [41,252,800 µg/day ÷ 4,420,000 L/day].

Several monitoring studies of groundwater and surface water have been conducted after ground spray or aerial spray applications of dicamba. Many of the available monitoring studies are summarized by Caux et al. (1993). The following discussion focuses on those studies in which the application of dicamba (amount applied) can be used to assess the GLEAMS modeling.

Dicamba concentrations in runoff water were assayed after mechanical application (small hand sprayer) at a rate of 2 lbs/acre of the dimethyamine salt to sloping (3%–8%) sod plots of clay loam soil (Trichell et al. 1968). Two types of soil cover, sod and fallow, were used. Runoff was induced by the application of 0.5 inches of simulated rain over a 1-hour period 24 hours after application. The level of dicamba in runoff from sod covered soil was 4.81 mg/L. For fallow

covered soil, the concentration of dicamba in runoff water was 1.6 mg/L. Four months after application, dicamba levels in runoff were undetectable for sod covered soil and 0.018 mg/L for fallow covered soil. In terms of the GLEAMS modeling, in which rainfall is simulated on every tenth day, the application of 0.5 inches of simulated rain corresponds to an annual rainfall rate of about 20 inches [0.5 inches × 36.5 events = 18.25 inches]. In the GLEAMS modeling at this rainfall rate, the initial concentration of dicamba in the upper level of soil water was 2.3 mg/L for clay and 2.2 mg/L for loam. Adjusting these concentrations for the application rate of 2 lb/acre, the modeled concentrations would be about 5 mg/L, consistent with the concentrations of 1.6 mg/L to 4.81 mg/L from the study by Trichell et al. (1968).

Waite et al. (1992) conducted a rather extensive survey of herbicide contamination in a 2800 ha area of Canada with predominantly clay soil. Peak concentrations in streams ranged from 0.13 µg/L to 0.22 µg/L, similar to the range of 0.12 to 0.19 µg/L estimated by the GLEAMS modeling for clay over a wide range of rainfall rates (Table 3-2). The maximum modeled concentrations of about 0.5 µg/L for both streams (Tale 3-2) and ponds (Table 3-3) are also consistent with maximum reported concentrations in pond or stream water associated with the local use of dicamba: 0.41 µg/L by Waite et al. (1992), 0.47 µg/L by Frank et al. (1991), and 0.11 to about 1.08 µg/L reported by Gold et al. (1988).

The GLEAMS modeling may also be assessed by comparison to the data collect in the National Water Quality Assessment (NAWQA) of the U.S. Geological Survey (USGS). NAWQA has involved a large scale monitoring effort to characterize pesticides in surface and ground water. A detailed description of the USGS program may be obtained at http://water.usgs.gov/nawqa/. In brief, the USGS has monitored concentrations of a large number of pesticides, including dicamba, in over 50 major river basins and aquifers. The monitoring data are given separately for streams and ground water for three types of sites: agricultural land use areas, urban areas, and major aquifers or large rivers of streams. Detailed data for streams and ground water covering a period from 1992 to 2001 are available at http://ca.water.usgs.gov/pnsp/. A subset of the data covering a period from 1992 to 1996 is available at http://ca.water.usgs.gov/pnsp/allsum/#t1.

A summary of the NAWQA monitoring data for dicamba is presented in Table 3-4. In terms of average concentrations, the NAWQA data is of limited use in assessing the GLEAMS modeling. All average concentrations are below the reporting limits for the various groups – i.e., <0.04 to < 0.11 µg/L. For an average application of 1 lb/acre used in the GLEAMS modeling, average concentrations (0 to about 0.03 µg/L) are also generally less than the reporting limits. In terms of maximum concentrations, the values for agricultural streams (1.14 µg/L) and urban ground water (1.46 µg/L) are above the peak concentrations estimated by GLEAMS by a factor of about 2 to 3 – i.e., a peak concentration of about 0.5 µg/L. While this could be interpreted as an underestimation in the GLEAMS modeling, it would also be consistent with the possible higher application rates of dicamba or the application of dicamba to large areas in a small watershed.

For the current risk assessment, the upper range for the short-term water contamination rate will be taken as 10 µg/L per lb/acre. This is intended to reflect both the direct spray scenario as well

as the possible underestimate of potential dicamba concentrations by the GLEAMS model based on the peak values reported in NAWQA. This value, converted to 0.01 mg/L per lb/acre, is entered into Worksheet B06. The central estimate of the peak concentration will be taken as 0.3 µg/L (0.0003 mg/L). This is about the maximum concentrations modeled for clay and loam at any rainfall rate and about the concentration modeled for sand at an annual rainfall rate of 100 inches. The lower range will be taken as 0.06 µg/L (0.00006 mg/L), a concentration that might be expected in relatively arid regions with clay soil – i.e., annual rainfall of 15 inches.

3.2.3.4.2. LONGER-TERM EXPOSURE – The scenario for chronic exposure to dicamba from contaminated water is detailed in worksheet D07. This scenario assumes that an adult (70 kg male) consumes contaminated ambient water from a contaminated pond for a lifetime. The estimated concentrations in pond water are based both the modeled estimates from GLEAMS, summarized in Table 3-3.

For this risk assessment, the typical WCR is taken as 0.01 µg/L or 0.00001 mg/L per lb/acre. This is about the average concentration that modeled in a pond using GLEAMS in loam over a wide range of rainfall rates. The upper range of the WCR is taken as 0.03 µg/L or 0.00003 mg/L per lb/acre. This is the highest average concentration modeled from clay soil – i.e., at rainfall rates of 100 to 200 inches per year – rounded to one significant digit. The lower range is taken as 0.005 µg/L or 0.000005 mg/L per lb/acre. This selection is somewhat arbitrary but would tend to encompass concentrations that might be found in relatively arid areas.

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

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

Because of its low octanol water partition coefficient, dicamba has a very low potential to bioconcentrate in fish. As discussed by Calabrese Baldwin (1993, p. 17), the bioconcentration factor in edible fish muscle may be estimated from on water solubility:

$$\log BCF_{Muscle} = 0.542 \log K_{ow} + 0.124$$

As noted in Table 2-2, the log K_{ow} for dicamba at pH 7 is -0.56 (Fostiak and Yu 1989). Thus, the estimated log BCF for fish muscle is about -0.18 [0.542 × -0.56 + .124 = -0.179] corresponding to a BCF of 0.66. For whole fish, the relationship is:

$$\log BCF_{\text{Whole Fish}} = 0.76 \log K_{ow} + -0.23$$

Using this equation, the estimated log BCF for whole fish is about 0.66 [0.76 × -0.56 - 0.23] corresponding to a BCF of 0.22. This estimate is very similar to a reported value from a microcosm study by Yu et al. (1975) in which organisms were exposed to dicamba at a concentration of 166 µg/L. Residues in fish were 0.02 µg/g [20 µg/kg], indicating that no bioconcentration occurred over this period – 20 µg/kg ÷ 166 µg/L yields a bioconcentration factor of 0.12 kg/L. The lack of bioconcentration has been reported in two other microcosm studies (Francis et al. 1985, Sanborn 1974).

For this risk assessment, the highest estimated bioconcentration factor – i.e., 0.66 for edible muscle – will be used for all human health and ecological exposure assessments. While this approach is somewhat conservative, this has little impact on the risk assessment (human health or ecological) because of the low concentrations of dicamba estimated in water.

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

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

consumption of contaminated berries after treatment of a right-of-way or some other area in which wild berries grow.

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

For the longer-term exposure scenario (D04), a duration of 90 days is used. The rate of decrease in the residues over time is taken from the vegetation half-time of 9 days (Table 2-1). Although the duration of exposure of 90 days is somewhat arbitrarily chosen, this duration is intended to represent the consumption of contaminated fruit that might be available over one season. Longer durations could be used for certain kinds of vegetation but would lower the estimated dose (i.e., would reduce the estimate of risk).

For the longer-term exposure scenarios, the time-weighted average concentration on fruit is calculated from the equation for first-order dissipation. Assuming a first-order decrease in concentrations in contaminated vegetation, the concentration in the vegetation at time t after spray, C_t, can be calculated based on the initial concentration, C_0, as:

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

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

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

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

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

Two RfD values have been derived by U.S. EPA: 0.03 mg/kg/day was set as the Agency wide RfD in 1992 and 0.045 mg/kg/day was derived by U.S. EPA/OPP in 1999 for setting pesticide tolerances. For this risk assessment, the most recent RfD derived by the Office of Pesticides is used to characterize risk. The more recent RfD from the Office of Pesticides is based on the thorough review of the available data and the decision to increase the RfD because of data quality issues in previous RfD is well documented. In addition, Forest Service risk assessments will, in general, defer to the most recent U.S. EPA RfD. For characterizing the risks associated with acute exposures, the 1-day dietary RfD of 0.10 mg/kg/day, also derived by U.S. EPA/OPP is used. The relatively small difference between the acute and chronic RfDs for dicamba is consistent with the relatively small differences in body burdens that would be expected between single and multiple constant doses.

3.3.2. Chronic RfD

The most recent U.S. EPA RfD for dicamba is 0.045 mg/kg/day. This RfD was derived by the U.S. EPA/OPP (1999) in the re-evaluation of pesticide tolerances for dicamba required by the Food Quality Protection Act (FQPA). While the U.S. EPA/OPP (1999) does not specifically identify the studies used in deriving the RfD of 0.045 mg/kg/day, additional and detailed documentation for the RfD is provide by Rowland (1998). The RfD is based on the two generation reproduction study in rats by Masters (1993). As detailed in Appendix 5, the dietary NOAEL in this study was 500 ppm, corresponding to daily doses of in the range of 35-44 mg/kg/day. The dietary LOAEL, based on significantly decreased pup growth, was 1500 ppm, corresponding to daily doses of 105-135 mg/kg/day. At the highest dietary concentration, 5000 ppm, corresponding to daily doses of about 360 to 460 mg/kg/day, effects included signs of neurotoxicity and delayed sexual maturation in F1 males – i.e., first generation of pups from the original parental (F0) animals. The only effect seen at 5000 ppm in the original parental generation (F0) was an increase in liver weight in females only.

The RfD of 0.045 mg/kg/day proposed by U.S. EPA/OPP (1999) appears to be based on a rounding of the NOAEL to 45 mg/kg/day and the use of an uncertainty factor of 1000, 10 for species to species extrapolation, 10 for sensitive subgroups, and 10 as an FQPA uncertainty factor for the protection of children. It should be noted that FQPA requires the U.S. EPA to use an additional uncertainty factor of 10 to encompasses concerns for exposures involving children unless the available toxicity data indicate that such an uncertainty factor is unnecessary. In an earlier version of the RfD development (Rowland 1998), the U.S. EPA/OPP had used an uncertainty factor of 300. It is unclear why the uncertainty factor was increased to 1000 but this factor will be maintained for consistency with the U.S. EPA/OPP risk assessment and because it is more protective than the uncertainty factor of 300.

Prior to the RfD derived by U.S. EPA/OPP (1999), the U.S. EPA (1992b) had recommended a somewhat lower chronic RfD of 0.03 mg/kg/day. This RfD was based on a NOAEL 3 mg/kg/day in a teratology study in rabbits (Goldenthal et al. 1978). At this dose, no effects were noted in

dams or pups. As the next higher dose, 10 mg/kg/day, slight body loss was noted in both dams and pups. In addition, the dose of 10 mg/kg/day was associated with an increase in number of post-implantation losses/dam, which as 20.0% higher than controls although this difference was not statistically significant. This study is consistent with the earlier teratology study by Wazeter et al. (1977), also in rabbits, in which 3 mg/kg/day was also a NOAEL and doses of 10 mg/kg/day and 20 mg/kg/day were associated with a dose-related increase in mean number of post-implantation losses (250 and 600% more than controls) and decrease in mean number of live fetuses (15.1 and 17.2% less than controls).

In a re-evaluation of the data used by U.S. EPA (1992b), the U.S. EPA/OPP determined that the Goldenthal et al. (1978) study was not scientifically adequate and should not be the basis of the chronic RfD (Rowland 1995c). Deficiencies of Goldenthal et al. (1978) study include the use of unhealthy rabbits, lack of clinical signs and individual necropsy data, inadequate number of pregnancies, lack of analytical data on dosing solutions, and the conduct of the study prior to GLP regulations (Rowland 1995). This re-evaluation of the study by Goldenthal et al. (1978) is supported by a more recent teratology study in rabbits by Hoberman (1992). Hoberman (1992) failed to note any effects in dams or pups at a dose of 30 mg/kg/day. At 150 mg/kg/day, there were signs of maternal toxicity as well as an increase in the number of spontaneous abortions.

The difference between the IRIS RfD of 0.03 mg/kg/day (U.S. EPA 1992b) and the RfD of 0.045 mg/kg/day derived by the Office of Pesticides (U.S. EPA/OPP 1999) is not substantial. There is, however, a substantial difference in the NOAEL and LOAEL values: 3 and 10 mg/kg/day from the early teratology studies (Goldenthal et al. 1978; Wazeter et al. 1977) and 45 and about 120 mg/kg/day from the 2-generation reproduction study by Masters (1993) which is supported by the NOAEL/LOAEL values of 30 mg/kg/day and 150 mg/kg/day from the teratology study by Hoberman (1992).

For this risk assessment, the most recent RfD – i.e., 0.045 mg/kg/day derived by the Office of Pesticides (U.S. EPA/OPP 1999) – will be used to characterize risk. Given the reasonable and well-documented concerns with the earlier teratology studies (Rowland 1995) as well as the appropriate application of the FQPA uncertainty factors in the more recent RfD, the use of the more recent chronic RfD seems justified over the earlier and somewhat lower RfD derived by U.S. EPA (1992b).

3.3.3. Acute RfD

U.S. EPA/OPP (1999) has recommended an acute RfD for 1-day dietary exposures of 0.10 mg/kg/day. This RfD is based on the neurotoxicity study by Minnema (1993), detailed in Appendix 4. At the lowest dose tested, 300 mg/kg/day, a number of gross signs of neurotoxicity, including impaired gait and decreased forelimb grip strength, were apparent within 2.5 hours after dosing. Most effects were transient but decreased forelimb grip strength persisted for 7 days. Thus, 300 mg/kg/day was classified as an LOAEL. The RfD was derived by dividing the LOAEL by and uncertainty factor of 3000: 10 for species to species, 10 for sensitive subgroups, 10 for the use of a LOAEL, 3 for FQPA considerations. The use of the 300 mg/kg/day with an

uncertainty factor of 10 for using the LOAEL functionally estimates the NOAEL at 30 mg/kg/day. This is the NOAEL for neurotoxicity in adult rabbits from the teratology study by Hoberman (1992).

As noted above, the Office Drinking Water (U.S. EPA 1988) used the 3 mg/kg/day NOAEL from teratology study by Wazeter et al. (1977) to derive a 10-day health advisory for drinking water of 0.3 mg/L (U.S. EPA 1988) using an uncertainty factor of 100. This 10-day health advisory was also recommended for 1-day exposures. Thus, this is analogous to a 1-day RfD of 0.03 mg/kg/day, identical to the chronic NOAEL.

Following the approach taken in the previous section for the chronic RfD, the most recent acute RfD of 0.1 mg/kg/day (U.S. EPA/OPP 1999) will be used to characterize the risks from acute exposures.

It will be noted that the chronic RfD of 0.045 mg/kg/day is only a factor of about 2 lower than the acute RfD of 0.1 mg/kg [0.1 / 0.045 = 2.22]. Although this difference is relatively small, it is consistent with the pharmacokinetics of dicamba. As discussed in Section 3.1.3.1, the halftimes for dicamba and the 3,5-dichloro isomer of dicamba are about 0.83 hours and 13.3 hours, respectively. Using the longest of the two halftimes as a conservative estimate, the resulting elimination coefficient (k) would be about 1.25 $days^{-1}$ [ln(2) / (13.3 hour / 24 hours per day)]. Based on this elimination coefficient and the plateau principle (e.g., Goldstein et al. 1974, pp. 321-322), the ratio of the body burden after chronic daily dosing at a fixed amount to the body burden after a single dose of the same amount would be about 1.4:

$$\text{Ratio} = 1/(1-e^{-k}) = 1/(1 - 0.287) = 1.4025.$$

Thus, the relationship of the acute RfD to the chronic RfD is similar to the expected difference in body burdens between acute and chronic exposures.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

The use of dicamba in Forest Service programs may involve levels of exposure to workers and members of the general public that are of concern. At the typical application rate considered in this risk assessment, workers would not be exposed to levels of dicamba that are regarded as unacceptable. At the maximum application, however, worker exposure to dicamba would exceed the level of concern at the upper range of plausible exposures. Members of the general public could be at some risk at the typical application rate only in the event of worst-case exposure assumptions for two accidental exposures involving children. Based on multiple sources of exposure, however, the levels of exposure would modestly exceed the level of concern for adults at the typical application rate. At the highest application rate that might be used in Forest Service programs, many of the acute exposure scenarios exceed the level of concern at the upper range of exposure. For longer term exposures, no risks are apparent at the typical application rate. The highest application rate, however, the consumption of contaminated vegetation exceeds the level of concern at the upper range of non-accidental and plausible exposures.

3.4.2. Workers. A quantitative summary of the risk characterization for workers associated with exposure to dicamba is presented in Worksheet E02 (Supplement 1). The quantitative risk characterization is expressed as the hazard quotient, the ratio of the estimated doses from Worksheet E01 to the RfD. For acute exposures (i.e., accidental or incidental exposures), the acute RfD of 0.1 mg/kg/day is used to characterize risk (Section 3.3.3). For general exposures (i.e., daily exposures that might occur over the course of an application season), the chronic RfD of 0.045 mg/kg/day is used to characterize risk (Section 3.3.2).

As indicated in Section 2, the exposures in Worksheet E01 and the subsequent hazard quotients in Worksheet E02 are based on the typical application rate of 0.3 lb/acre and the "level of concern" is one – i.e., if the hazard quotient is below 1.0, the exposure is less than the RfD. For all exposure scenarios, the estimated dose scales linearly with application rate. Thus, at an application rate of 2lb/acre, the highest labeled application rate, the level of concern would be 0.15 – i.e., 0.3 lb/acre ÷ 2 lb/acre = 0.15.

The highest hazard quotient in Worksheet E02 for workers based on general exposures is 1 – the upper range for workers involved in broadcast ground sprays. Thus, at the typical application rate, the upper range of hazard quotients reaches but does not exceed the level of concern. At the highest application rate that might be used in Forest Service programs, the level of concern is not exceeded for any worker groups based on the central estimates of exposure. At the upper range of exposure, however, the level of concern (0.15) is exceeded for all groups of workers. For ground broadcast applications, the upper range of the level of concern would be exceeded for all applications above 0.3 lb/acre. For directed ground spray and aerial workers, the upper range of the level of concern would be exceeded for applications in excess of 0.6 lb/acre.

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. The highest hazard quotient for accidental worker exposures given in Worksheet E02 is 0.1 – i.e., the upper range for a worker wearing contaminated gloves for 1 hour and the upper range for a worker with a spill on the lower legs that is not removed for 1 hour. Because the estimate of the absorbed dose is linearly related to the hazard quotient, 10 hours would be required to reach a level of concern (a hazard quotient of one) at the typical application rate. At the maximum application rate, an exposure period of 1.5 hours would be required to reach a level of concern.

The simple verbal interpretation of this quantitative characterization of risk is that under a protective set of exposure assumptions, workers would not be exposed to levels of dicamba that are regarded as unacceptable at the typical application rate. At the maximum application, workers exposed at the upper range of plausible exposures would be exposed to levels of dicamba that would not be regarded as acceptable. It is unclear if overt effects would be likely. The hazard quotient in Worksheet E01 for workers involved in ground broadcast applications is 1.0. At the maximum application rate, this would exceed the level of concern (0.15) by a factor of about 7 and the resulting dose would be about 0.3 mg/kg/day (0.045 mg/kg/day × 1 ÷ 0.15). As discussed in Section 3.3.2, this dose is below the 45 mg/kg/day rat NOAEL used to derive the OPP RfD by a factor of about 150.

As discussed in Section 3.1.11, dicamba may be irritating to the eyes and cause mild and transient skin irritation. Quantitative risk assessments for skin and eye irritation are not derived; however, from a practical perspective, effects on the eyes and skin are likely to be the most common effects as a consequence of mishandling dicamba. These effects can be minimized or avoided by prudent industrial hygiene practices during the handling of dicamba.

3.4.3. General Public. The quantitative hazard characterization for the general public associated with exposure to dicamba is summarized in Worksheet E04. Like the quantitative risk characterization for workers, the quantitative risk characterization for the general public is expressed as the hazard quotient using the acute RfD of 0.1 mg/kg/day and the chronic RfD of 0.045 mg/kg/day.

For the acute/accidental scenarios, none of the central estimates of the hazard quotients in Worksheet E04 exceed 1.0, the level of concern for the typical application rate. At the upper range of exposure based on the typical application rate, two accidental scenarios for children – direct spray and consumption of contaminated water after a spill – exceed the level of concern (1.0). At the highest application rate, these accidental scenarios as well as the accidental direct spray scenario for a woman, the consumption of contaminated fruit, and the consumption of fish by subsistence populations exceed the level of concern (0.15). While the direct spray scenarios and spill into water are accidental, the scenarios involving the consumption of contaminated fruit and contaminated fish are scenarios that are plausible.

For longer term exposures, none of the exposure scenarios reach a level of concern at the typical application rate. At the highest application considered in this risk assessment, 2 lbs/acre, the

level of concern (0.15) is exceeded only for the consumption of contaminated vegetation (HQ=0.2). Since the hazard quotient is linearly related to the application rate, the level of concern would be reached at an application rate of 1.5 lbs/acre.

Each of the hazard quotients summarized in Worksheet E04 involves a single exposure scenario. In some cases, individuals could be exposed by more than one route and in such cases risks can be approximated by simply adding the hazard quotients for different exposure scenarios summarized in Worksheet E03. For dicamba, the consideration of multiple exposure scenarios does impact the risk assessment for acute exposures. For example, based on the upper ranges for typical levels of acute exposure for being directly sprayed on the lower legs, staying in contact with contaminated vegetation, eating contaminated fruit, drinking contaminated water from a stream, and consuming contaminated fish at rates characteristic of subsistence populations leads to a combined hazard quotient of 1.533 (0.2 + 0.03 + 0.6 + 0.003 + 0.7). It should be noted that most of the risk, about 85%, is associated with non-accidental scenarios, the consumption of contaminated vegetation and the consumption of contaminated fruit [(0.6 + 0.7)÷1.533=0.848]. For all of the chronic exposure scenarios, this is not the case. The only scenario that leads to any concern is the consumption of contaminated vegetation. All other scenarios are below the level of concern by factors of over 100,000.

Based on these numeric expressions of risk, the verbal interpretation of the risk characterization for dicamba is not simple. At the typical application rate, risks are confined to worst-case exposure assumptions for two accidental exposures involving children – direct spray and a large spill into a small pond – based on considerations of singe sources of exposure. Based on multiple sources of exposure, specifically the consumption of contaminated water and fish, the levels of exposure would modestly exceed the level of concern. At the highest application rate that might be used in Forest Service programs, many of the acute exposure scenarios exceed the level of concern at the upper range of exposure. For longer term exposures, no risks are apparent at the typical application rate. At the highest application rate, however, the consumption of contaminated vegetation exceeds the level of concern at the upper range of non-accidental and plausible exposures.

3.4.4. Sensitive Subgroups. The only identified sensitive subgroup for dicamba appears to be children. Since the RfD for dicamba explicitly considers the increased sensitivity of children with an additional safety factor and since exposure assessments for children are conducted in the risk assessment, this sensitive subgroup is addressed in the current risk assessment.

3.4.5. Connected Actions. There is no substantial evidence that dicamba will interact with other compounds. A study by Moody et al. (1991) indicates that dicamba does not induce cytochrome P-450 activity and does not substantially affect a variety of other xenobiotic metabolizing enzymes. After three intraperitoneal doses of 250 mg/kg given over three successive days, cytochrome P_{450} levels were significantly depressed, probably from direct liver damage. Although this finding does not rule out the possibility that dicamba may be involved in

toxicologically significant interactions, the induction of cytochrome P-450 is a major mechanism by which such interactions are known to occur.

3.4.6. Cumulative Effects. This risk assessment specifically considers the effect of repeated exposure based on a number of different exposure scenarios. Consequently, the risk characterizations presented in this risk assessment encompass the potential impact of long-term exposure and cumulative effects.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

Dicamba is relatively nontoxic by oral administration, with LD_{50} values ranging from approximately 500 mg/kg to >4600 mg/kg. There is no indication that either the dimethylamine salt or Banvel differs significantly from the toxicity of dicamba. The acute toxicity of dicamba to birds appears generally to be low and consistent with the gavage studies in rats. Very little information is available on the toxicity of dicamba to terrestrial invertebrates. In the honey bee, the acute LD_{50} is greater than 1000 mg/kg bw. Dicamba is an effective auxin herbicide and acts by mimicking the plant hormone indole-3-acetic acid. A large number of phytotoxicity studies are available on dicamba. In pre-emergence assays with standard non-target species, the most sensitive species appears to be soybean, with an LOEC of 0.0022 lb/acre and the least sensitive species appears to cabbage with an NOEC 0.53 lb/acre. In post-emergence applications, the most sensitive species appears to be soybean, with an LOEC of 0.004 lb/acre and the most tolerant species appears to be corn, with an NOEC of 3.9 lb/acre. There is very little indication that dicamba will adversely affect soil microorganisms.

Acute toxicity studies in fish indicate that dicamba is relatively non-toxic, with 24 to 96-hour LC_{50} values in the range of 28–516 mg/L, although salmonids appear to be more sensitive than other freshwater fish to the acute toxicity of dicamba. Amphibians seem to have a sensitivity to dicamba that is similar to that of fish with 24- to 96-hour LC_{50} values in the range of 166 to 220 mg/L. Some aquatic invertebrates appear to be somewhat more sensitive than fish and amphibians to the acute toxicity of dicamba, with lower ranges of EC_{50} values of about 4 to 10 mg/L. Some but not all aquatic plants are much more sensitive to dicamba than aquatic animals, with LC_{50} values of about 0.06 mg/L . Other aquatic plants are much more tolerant, with reported NOEC values of up to 100 mg/L.

4.1.2. Toxicity to Terrestrial Organisms.

4.1.2.1. Mammals – As summarized in Appendix 1 and discussed in the human health risk assessment (Section 3.1), there is a large number of toxicity studies on dicamba in experimental mammals that are relevant to the risk assessment for terrestrial mammals. These data indicate that dicamba is relatively nontoxic by oral administration, with LD_{50} values ranging from approximately 500 mg/kg to >4600 mg/kg. There is no indication that either the dimethylamine salt or Banvel differs significantly from the toxicity of dicamba. In terms of differences in species sensitivity, the best comparative study is that conducted by Edson and Sanderson (1965) because of the number of different species tested and because these authors used the same source of dicamba and dicamba derivatives in their study. With technical dicamba in this study, there is a slight but statistically insignificant indication that female rats may be somewhat less sensitive, compared with male rats. A more curious finding is that "pure" dicamba was apparently less toxic than technical grade dicamba to female rats. This cannot be overly interpreted, however, because details about the chemical composition of these two materials are not provided in the report.

In terms of the ecological risk assessment, the most significant pattern among all of these studies is the apparent pattern of interspecies scaling, with smaller animals being less sensitive than larger animals (Table 4-1). This pattern is consistent, at least in the qualitative nature of the pattern, with standard allometric dose scaling (e.g., Boxenbaum and D'Souze 1990; Davidson et al. 1986). This is discussed in more detail in Section 4.3.2, dose-response assessment for terrestrial mammals.

4.1.2.2. Birds – A relatively large number of acute and subchronic toxicity studies is available standard test species – i.e., mallard ducks and bobwhite quail – as well as other less commonly tested species – i.e., domestic chickens, Japanese quail, and pheasants (Appendix 6). Most of these studies were submitted to the U.S. EPA for the registration dicamba (specified in Appendix 6 by MRID numbers) but some have been published in the open literature (e.g., Edson and Sanderson 1965; Hill and Camardese 1986; Hoffman and Albers 1984).

The acute toxicity of dicamba to birds appears generally to be low and consistent with the gavage studies in rats in which gavage oral LD_{50} values are about 750 to 3000 mg/kg (Section 3.1 and Appendix 1). This range encompasses most of the acute gavage LD_{50} values reported for birds from 800 mg/kg in pheasant (Edson and Sanderson 1965) to about 1300 mg/kg in mallard ducks (Campbell and Beavers (1993) and bobwhite quail (Beavers 1986). The only exception appears to be the LD_{50} value of 216 mg/kg in bobwhite quail reported by Campbell et al. (1993). As noted in Appendix 6, the test material is reported as a 86.93% a.i. technical reference standard. It is unclear, however, why this bioassay resulted in an atypically low reported LD_{50} and a corresponding low NOEC – i.e., 62.5 mg/kg.

Grimes (1986a) explicitly compared the toxicity of dicamba to quail via a single dose gavage administration and a 5-day dietary exposure. In the gavage study, the oral LD_{50} was 969 mg/kg (95% CI of 644 to 1615 mg/k). In the dietary exposure, the LD_{50} was >5620 ppm (mg dicamba per kg food). Based on the reported food consumption values of 9 g food/ 30 g bw, this dietary concentration corresponds to a dose of 1686 mg/kg bw. Thus, dicamba appears to be less toxic in dietary than in gavage administration. This pattern is consistent with the rapid excretion of dicamba (Section 3.1.3) and has a substantial impact on the dose-response assessment (Section 4.3.2.2).

In one-generation studies in quail and mallard ducks, no effects on reproduction have been reported at dietary concentrations of 1600 ppm, corresponding to a dose of about 500 mg/kg/day (Beavers et al., 1994b). One study that suggests that avian eggs are sensitive to external applications of several pesticides including dicamba (Hoffman and Albers 1984). In this study, mallard eggs were immersed in aqueous emulsions of dicamba for 30 seconds and observed to hatch and post-hatch. The precise concentrations of dicamba used are not specified in the study, and the LC50 is reported as ">200 times the field level of application" (also not specified). The effects observed in the surviving birds include reduced growth and stunted eye development; however, the study does not provide details about the incidence of these malformations or the magnitude of the growth reductions.

4.1.2.3. Terrestrial Invertebrates – Very little information is available on the toxicity of dicamba to terrestrial invertebrates. In a standard acute contact toxicity bioassay in honey bees, the LD_{50} value is greater than 100 µg/bee (Atkins et al. 1975; FAO/WHO 2001; C&P Press 2003; Tomlin 1994). Taking an average weight of 0.093 g/bee or 0.000093 kg/bee (USDA/APHIS 1993) and making the very conservative assumption of 100% absorption, this would correspond to an LD_{50} greater than 1000 mg/kg bw [0.1 mg/bee ÷ 0.000093 kg bw/bee = 1075 mg/kg]. This order of toxicity is comparable to the LD_{50} values reported in experimental mammals (Section 4.1.2.1) and birds (Section 4.1.2.2). This suggests that the toxicity of dicamba to terrestrial invertebrates may be similar to the toxicity of this compound to terrestrial vertebrates. In a screening assay to determine the effects of pesticides on an egg parasitoid, *Trichogramma cacoeciae*, (a beneficial insect), Banvel was classified as harmless based on lack of toxicity to adult insects (Hassan et al. 1998). In a field study, no toxic effects were observed in earthworms after an application of 0.56 kg/ha [about 0.1 lb/acre] dicamba to turf (Potter et al. 1990). There are no data reported in this study regarding the toxicity of dicamba to other species of terrestrial invertebrates.

This essentially negative hazard identification must be qualified because of the very large number of terrestrial invertebrates in any diverse environment. Thus, the ability to characterized potential effects in species on which no data are available is limited to inferences based on the few test species for which data are available.

4.1.2.4. Terrestrial Plants (Macrophytes) – Dicamba is a benzoate auxin herbicide that acts by mimicking the plant hormone indole-3-acetic acid (IAA). Although the precise mechanism of action of auxin herbicides is not fully understood, the mechanism appears to involve a stimulation of ethylene production leading to an accumulation of abscisic acid and/or cyanide resulting in abnormal growth (Moreland 1999). At sufficiently high levels of exposure, the abnormal growth is so severe that vital functions cannot be maintained and the plant dies (Bovey 1971, Caux et al. 1993). The differential toxicity of dicamba to various plant species is based on variations in the ability of different plants to absorb, translocate, and degrade the herbicide (Frear 1976). The mode of action—the induction of hormonal imbalance—is specific to plants and does not affect animals. As discussed in the dose-response assessment (section 4.3), dicamba is generally much more toxic to plants than to animals. This is particularly evident in comparisons of LC_{50} and EC_{50} values of aquatic plants and animals in which exposure conditions are comparable.

As reviewed by Caux et al. (1993), dicamba is readily absorbed by foliage and roots and rapidly translocated. As a physiochemical interpretation of the translocation of herbicides in plants, Bromilow et al. (1990) suggest that the mobility of dicamba is attributable to its high degree of acidity (low pKa) and hyrophilicity (low Kow) [see Bromilow et al. 1990, Figure 5, p. 313]. The foliar absorption of dicamba from soil (0.4%–4.7%) is much less efficient than the absorption from an aqueous solution applied directly to the plant (65%–95%) (Al-Khatib et al. 1992). After foliar application, dicamba may be translocated to the roots and leach into the soil (Brady 1975a; Brady 1975b).

Surfactants can be used to enhance the absorption of dicamba but inconsistent results have been reported. An increase in the absorption of dicamba has been noted in honeyvine milkweed (Soteres et al. 1983), alfalfa, and dandelion (Hartwig 1980). In pine and hardwood trees, several surfactants failed to enhance absorption and translocation (Hall 1973). Based on studies with velvetleaf, which has a relatively smooth wax-free surface, and lambsquarters, which has dense deposits of wax projections, King et al. (1993) suggest that surfactants may be more effective in plants with waxy leaf surfaces. The type of dicamba salt used may also influence the efficacy of surfactants. Petersen et al. (1985) noted that surfactants were more effective with the potassium salt than with the dimethylamine salt.

Other adjuvants may also affect the phytotoxicity of dicamba. Calcium chloride has been shown to antagonize the phytotoxicity of the sodium and dimethylamine salts of dicamba. This antagonism can be reversed by the addition of diammonium sulfate or ammonium nitrate (Nalewaja and Matysiak 1993). The amine salt of dicamba as well as the amine salt of 2,4-D have been shown to antagonize the phytotoxicity of paraquat. The mechanism of this interaction is unclear but may involve an inhibition of paraquat uptake (O'Donovan and O'Sullivan 1982). It is not clear whether other salts of dicamba would interact in a similar way.

The metabolic pathways for dicamba in soil and plants are qualitatively similar. Quantitatively, however, the primary route for soil degradation involves conversion to the salicylic acid derivative followed by hydroxylation and mineralization. In plants, the primary route is hydroxylation to 5-hydroxydicamba followed by demethylation and conjugation (Frear 1976). The metabolite, 3,6-DCSA, is washed off vegetation more rapidly than dicamba (Carroll et al. 1993).

The kinetics of dicamba in terrestrial plants has been examined in several species. Typical half-times range from about 3-15 days; 14 days in grasses (Morton et al. 1967), 3–7 days in soybeans (Auch and Arnold 1978; Sirons et al. 1982). Longer half-times have been noted in sensitive species such as mustard and tartary buckwheat, with >20% eliminated after 20 days (Chang and Vanden Born 1971).

During some applications, herbicides or other pesticides may be deposited in unintended areas due to wind drift, volatilization, redeposition, or other factors. Wall (1994) examined damage to potatoes from the "simulated" drift of dicamba. In this study, drift was simulated by applying dicamba directly to post-emergent potatoes at rates much lower than those recommended for weed control: 2.8, 5.6, 11.1, and 22.2 g a.i./ha. These rates correspond to 0.003, 0.017, 0.012, and 0.024 lbs/acre. Over a 3-year study period, dicamba treatments were associated with a decrease in total yield of marketable tubers. No tuber malformations and no effect on weight of marketable-size tubers was observed.

Data regarding the toxicity of dicamba to plants are summarized in Appendix 10. Standard plant bioassays for seed germination, seedling emergence, and vegetative vigor are required for the registration of herbicides and typically form the basis of the dose-response assessment in

nontarget plant species. This type of assay using technical grade dicamba has been submitted to the U.S. EPA (Hoberg 1993a). Hoberg (1993a) assayed cabbage, corn, cucumber, lettuce, oat, onion, ryegrass, soybean, tomato, turnip in both pre-emergence and post-emergence (vegetative vigor) assays. The most sensitive plant species in the pre-emergence assay was soybean, with an LOEC of 0.0022 lb/acre. In post-emergence assays, the most sensitive species was soybean, with an LOEC of 0.004 lb/acre. The most tolerant species were oats and ryegrass, with an NOEC of 1 lb/acre.

Dose-dependent decreases in cotton yields were reported by Bruns et al. (1972). Single applications of 0.285 or 0.57 kg a.i./ha dicamba in irrigation water decreased the yield of 90-day-old cotton plants by 19% and 35%, respectively. Similarly, Hamilton and Arle (1979) observed decreases of 13% in total yield when pre-bloom cotton plants were exposed to 0.032 kg a.i./ha dicamba and decreases of 12% in total yield when blooming cotton plants were treated with only 0.008 kg a.i./ha dicamba.

Consistent with the standard plant bioassay by Hoberg (1993a), soybeans appear to be very sensitive to the effects of dicamba during early bloom and early pod growth stages (Auch and Arnold 1978). As indicated in Appendix 10, an application of 0.01 lb/acre dicamba to early bloom plants decreased total yield by 47% but had no effect when applied to plants in the early pod stage. Nevertheless, a higher application of 0.025 lb/acre dicamba to plants in the early pod stage resulted in a 45% decrease in total yield.

Of all the crops represented in Appendix 10, the most tolerant species in post-emergence applications appears to be corn, with an NOEC of 3.9 lb/acre (Hoberg 1993a). This is consistent with the report by Minotti et al. (1980) in which increases in the total yield of corn crops were noted after applications of 0.89 lb/acre dicamba to spike (>40% increase) and 8-inch corn (18% increase). Nevertheless, the same application to 12-inch corn decreased total yield by 13%. In 30-day-old wheat, applications of 0.12 and 0.24 kg a.i./ha dicamba increased the incidence of deformed heads by 34% and 209%, respectively (Ivany and Nass 1984).

The data presented in Appendix 10 suggest that applications of dicamba at a rate of 0.12 lb/acre adversely affected the total yield of rapeseed (O'Sullivan and Kossatz 1984) and several species of clover (Griffin et al. 1984), and that shade trees (Neely and Crowley 1974) and ornamental trees (Johnson 1985) were generally less sensitive than crop species to the effects of dicamba.

Scifres et al. (1973) conducted a series of greenhouse studies to determine the effects of dicamba in irrigation water on various seedling crops (Appendix 10). Each crop was exposed to a single pre-emergent application of 0, 1, 10, 50, 100, or 500 ppb dimethylamine salt of dicamba (DMA). The investigators determined the fresh weights of the crops after 30 days and reported that crop tolerance could be ranked from most tolerant to least tolerant as follows: sorghum > cotton > cucumber. For cucumbers, the most susceptible crop of seedlings examined in this study, the results for only one cultivar (Straight 8) are reported. Those results indicate that the fresh weight of the cucumbers increased significantly after exposure to 1 µg/L/day DMA; whereas exposure to

100 µg/L/day caused a 40% decrease in fresh weight, and the plants exposed to the highest concentration, 500 µg/L/day, died. The results for the cotton and sorghum seedlings are not quite as straightforward because more than one cultivar of each crop was tested. Nevertheless, of the crops tested, sorghum was clearly the most tolerant of exposure to DMA, with fresh weight decreasing by only 28% in the Pioneer 820 cultivar and increasing by 70% in RS-626 cultivar at the 500 µg/L/day concentration. The effects of dicamba on cotton seedlings varied among the three cultivars tested. Generally, there was a dose-dependent decrease in fresh weights for two of the cultivars (Paymaster and Dunn). This was not true, however, for the Blightmaster cultivar, which showed a general trend toward increasing fresh weights (67% at 500 µg/L/day) with increasing dicamba concentrations.

There is abundant literature regarding the efficacy of dicamba in the control of various pest species (e.g., Bovey et al. 1990, Ferguson et al. 1992). Additional data regarding the efficacy of the product are summarized by Sandoz (1993a,b). Based on an analysis of plant toxicity data in the PHYTOTOX database, plant species differ in their sensitivity to dicamba by a factor of up to 32 (Fletcher et al. 1990).

4.1.2.5. Terrestrial Microorganisms – There is very little indication that dicamba will adversely affect soil microorganisms. At a level of 10 µg/g in sandy loam soil, dicamba—and several other herbicides—caused a transient decrease in nitrification after 2 but not 3 weeks of incubation (Tu 1994). As discussed by this investigator, the decrease in nitrification is relatively mild and does not suggest the potential for a substantial or prolonged impact on microbial activity. In the same study, dicamba had no effect on ammonia formation or sulfur oxidation. At a concentration of 1 mg/kg soil, dicamba had no effect on urea hydrolysis or nitrification in four diverse soil types (Martens and Bremner 1993). At 50 mg/kg soil, dicamba had a slight (6% decrease) on urea hydrolysis in one of the four soil types and an inhibitory effect on nitrification in two of the soils at 7 and 14 but not at 21 days after application.

4.1.3. Aquatic Organisms.

4.1.3.1. Fish – Information on the toxicity of dicamba to fish is summarized in Appendix 7. The acute toxicity of dicamba was tested in eight species of freshwater fish (Appendix 7). Static bioassays involving nominal concentrations of dicamba and exposures durations ranging from 24 to 144 hours indicate that the agent is relatively nontoxic to freshwater fish (LC_{50} = 28–516 mg/L).

It appears from the limited data that salmonids are more sensitive than other freshwater fish to the acute toxicity of dicamba. Of the salmonids tested, the rainbow trout (*Oncorhynchus mykiss*) was clearly the most sensitive species (96-hour LC_{50} = 28 mg/L) (Johnson and Finley 1980). The reported LC_{50} values for 48-hour and 72-hour bioassays were 350 mg/L (Bohmont 1967) and 320 mg/L (Bond et al. 1965), respectively. Other salmonids, like cutthroat trout (*O. clarki*) and coho salmon (*O. kisutch*) appear to be more resistant to dicamba toxicity. For instance, the 96-hour LC_{50} for cutthroat trout (*O. clarki*) exceeded 50 mg/L, the highest test concentration used

(Woodward 1982). The 24-, 48- and 144-hour LC_{50} values for coho salmon (*O. kisutch*) were 151, 120, and >109 mg/L, respectively (Bond et al. 1965, Lorz et al. 1979).

The results of several 96-hour bioassays indicate that the highest test concentrations of dicamba were not toxic to bluegill sunfish (*Lepomis macrochirus*) (96-hour LC_{50} >50 mg/L) (Cope 1965, Hughes and Davis 1962, Johnson and Finley 1980). Similarly, Johnson (1978) reported that dicamba was not especially toxic to mosquito fish (*Gambusia affinis*), with 24-, 48-, and 96-hour LC_{50} values of 516, 510, and 465, respectively . In contrast, the study by Hashimoto and Nishiuchi (1981) indicates mortality among three species of *Cyprinidae* [goldfish (*Carassius auratus*), common carp (*Cyprinus carpio*), and medaka (*Oryzias latipes*)] after 48-hours of exposure to 40 mg/L dicamba, the highest concentration tested.

In the microcosm study by Yu et al. (1975), residues in fish were only 0.02 µg/g [20 µg/kg], indicating that no bioconcentration occurred over this period [20 µg/kg ÷ 166 µg/L = 0.12 kg/L]. The lack of bioconcentration has been reported in two other microcosm studies (Francis et al. 1985, Sanborn 1974).

The effects of subchronic or chronic exposure of these species to dicamba were not located in the available literature or in a search of the studies submitted to U.S. EPA in support of the registration of dicamba. Also, no chronic values for fish are listed on the product labels for either Banvel or Vanquish (C&P Press 2003). This imposes serious limitations on the ability to characterize risks for fish. This is discussed in Section 4.3 (Dose-Response Assessment) and Section 4.4 (Risk Characterization).

4.1.3.2. Amphibians – The effects of acute exposure to dicamba were tested using tadpoles of two species of frogs, *Adelotus brevis* and *Limnodynastes peroni* (Appendix 7). The LC_{50} values for 24- to 96-hour exposures ranged from 166 to 220 mg/L, suggesting that these amphibians are as tolerant as the fish to the acute toxicity of dicamba.

4.1.3.3. Aquatic Invertebrates – As summarized in Appendix 8, some invertebrates appear to be somewhat more sensitive than fish and amphibians to the acute toxicity of dicamba. The lowest range of LC_{50} values (3.9–10 mg/L) were observed in amphipods (*Gammarus lacustris*) during 24- to 96-hour static bioassays (Sanders 1970). In the other species of amphipods tested, *Gammarus fasciatus*, the LC_{50} values for 48- and 96-hours exposure were greater than the highest concentration of dicamba tested (Johnson and Finley 1980, Sanders 1970). With the exception of one species of water flea, *Daphnia pulex*, which appears to be relatively sensitive to dicamba exposure (48-hour LC_{50} = 11 mg/L), the other invertebrates listed in Appendix 8 had LC_{50} values that are over 100 mg/L and/or exceed the highest test concentrations of dicamba. As with fish, no longer-term terms studies have been encountered on the toxicity of dicamba to aquatic invertebrates.

4.1.3.4. Aquatic Plants – Standard toxicity bioassays to assess the effects of dicamba on aquatic plants were submitted to the U.S. EPA in support of the registration of dicamba and are

summarized in Appendix 9 along with studies published in the open literature (Fairchild et al. 1997; Cullimore 1975). The most sensitive species on which data are available is *Anabaene flos-aquae*, a species of freshwater algae, with an LC_{10} of 4.9 µg/L and an LC_{50} of 61 µg/L (Hoberg 1993c). Many other species of unicellular algae appear to be much less sensitive with NOEC values in the range of 3 to 10 mg/L. The aquatic macrophyte, *Lemna gibba*, appears to be more sensitive than most unicellular algae, with a reported NOEC of 0.25 mg/L in a standard 14-day assay (Hoberg 1993b). The much higher NOEC of 100 mg/L in *Lemna minor* reported by Fairchild et al. (1997) may reflect a true difference from the sensitivity of *Lemna gibba* or may simply reflect the shorter period of exposure used in the Fairchild et al. (1997) study – i.e., 4 days rather than 14 days.

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 7 mg/kg at an application rate of 0.3 lb/acre. Exposures anticipated from the consumption of contaminated vegetation by terrestrial animals range from central estimates of about 0.4 mg/kg for a small mammal to 8 mg/kg for a large bird with upper ranges of about 0.8 mg/kg for a small mammal and 23 mg/kg for a large bird. The consumption of contaminated water leads to much lower levels of exposure. A similar pattern is seen for chronic exposures. Estimated daily doses for a small mammal from the consumption of contaminated vegetation at the application site are in the range of about 0.003 mg/kg to 0.02 mg/kg. Large birds feeding on contaminated vegetation at the application site could be exposed to much higher concentrations, ranging from about 0.1 mg/kg/day to 3.3 mg/kg/day. The upper ranges of exposure from contaminated vegetation far exceed doses that are anticipated from the consumption of contaminated water, which range from about 0.0000002 mg/kg/day to 0.000001 mg/kg/day for a small mammal.

For terrestrial plants, five exposure scenarios are considered quantitatively: direct spray, spray drift, runoff, wind erosion and the use of contaminated irrigation water. In addition, vapor exposures associated with the volatilization of dicamba are also estimated Unintended direct spray is expressed simply as the application rate considered in this risk assessment, 0.3 lb/acre and should be regarded as an extreme/accidental form of exposure. Estimates for the other routes of exposure are much less. All of these exposure scenarios are dominated by situational variability because the levels of exposure are highly dependent on site-specific conditions. Thus, the exposure estimates are intended to represent conservative but plausible ranges that could occur but these ranges may over-estimate or under-estimate actual exposures in some cases. Spray drift is based on estimates using AgDRIFT. The proportion of the applied amount transported off-site from runoff is based on GLEAMS modeling of clay, loam, and sand. The amount of dicamba that might be transported off-site from wind erosion is based on estimates of annual soil loss associated with wind erosion and the assumption that the herbicide is incorporated into the top 1 cm of soil. Exposure from the use of contaminated irrigation water is based on the same data used to estimate human exposure from the consumption of contaminated ambient water and involves both monitoring studies as well as GLEAMS modeling.

Exposures to aquatic plants and animals are based on essentially the same information used to assess the exposure to terrestrial species from contaminated water. The peak concentrations of dicamba in contaminated water is estimated at 0.003 (0.00006 to 0.01) mg/L per 1 lb/acre applied. For longer-term exposures, average concentrations of dicamba in ambient water associated with the normal application of dicamba is estimated at 0.00001 (0.000005 to 0.00003) mg/L at an application rate of 1 lb/acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application rates considered in this risk assessment.

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

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

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

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

While a very large number of other exposure scenarios could be generated, the specific exposure scenarios developed in this section are designed as conservative screening scenarios that may

serve as guides for more detailed site-specific assessments by identifying the groups and routes of exposure that are of greatest concern.

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

For this risk assessment, three groups of direct spray exposure assessments are conducted. The first, which is defined in Worksheet F01, involves a 20 g mammal that is sprayed directly over one half of the body surface as the chemical is being applied. The range of application rates as well as the typical application rate is used to define the amount deposited on the organism. The absorbed dose over the first day (i.e., a 24-hour period) is estimated using the assumption of first-order dermal absorption. As discussed in Section 3.1.3.3, the dermal absorption rates estimated for humans based on Ko/w and molecular weight (Worksheet B03), encompass the first-order dermal absorption rate in rats from the study by Makery et al. (1986b). Because the study by Makery et al. (1986b) does not allow for an assessment of variability in dermal absorption rates and because the rates estimated in Worksheet B03 do encompass the measured value in rats from Makery et al. (1986b), the estimated rates from Worksheet B03 are used to estimate the dermal absorption rate in mammals. 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 dicamba.

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

Because of the relationship of body size to surface area, very small organisms, like bees and other terrestrial insects, might be exposed to much greater amounts of dicamba 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 dicamba by bees or other invertebrates, this

exposure scenario, detailed in Worksheet F02b, also assumes complete absorption over the first day of exposure.

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

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

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

It is reasonable to assume that for prolonged exposures an equilibrium may be reached between levels on the skin, rates of absorption, and levels on contaminated vegetation, although there are no data regarding the kinetics of such a process. The bioconcentration data on dicamba indicates that dicamba will not accumulate in the tissue of the fish. 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.

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

For the consumption of contaminated vegetation, a small mammal is used because allometric relationships indicate that small mammals will ingest greater amounts of food per unit body weight, compared with large mammals. The amount of food consumed per day by a small mammal (i.e., an animal weighing approximately 20 g) is equal to about 15% of the mammal's total body weight (U.S. EPA/ORD 1989). When applied generally, this value may overestimate or underestimate exposure in some circumstances. For example, a 20 g herbivore has a caloric requirement of about 13.5 kcal/day. If the diet of the herbivore consists largely of seeds (4.92 kcal/g), the animal would have to consume a daily amount of food equivalent to approximately 14% of its body weight [(13.5 kcal/day ÷ 4.92 kcal/g)÷20g = 0.137]. Conversely, if the diet of

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

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

For the acute exposures, the assumption is made that the vegetation is sprayed directly – i.e., the animal grazes on site – and that100% of the animal's diet is contaminated. While appropriately conservative for acute exposures, neither of these assumptions are plausible for longer-term exposures. Thus, for the longer-term exposure scenarios for the large mammal, two sub-scenarios are given. The first is an on-site scenario that assumes that a 70 kg herbivore consumes short grass for a 90 day period after application of the chemical. In the worksheets, the contaminated vegetation is assumed to account for 30% of the diet with a range of 10% to 100% of the diet. These are essentially arbitrary assumptions reflecting grazing time at the application site by the animal. Because the animal is assumed to be feeding at the application site, drift is set to unity - i.e., direct spray. This scenario is detailed in Worksheet 11a. The second sub-scenario is similar except the assumption is made that the animal is grazing at distances of 25 to 100 feet from the application site (lowing risk) but that the animal consumes 100% of the diet from the contaminated area (increasing risk). For this scenario, detailed in Worksheet F12b, AgDRIFT is used to estimate deposition on the off-site vegetation. Drift estimates from AgDRIFT are summarized in Worksheet A06 and this model is discussed further in Section 4.2.3.2.

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

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

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

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

In addition to the consumption of contaminated vegetation and insects, dicamba may reach ambient water and fish. Thus, a separate exposure scenario is developed for the consumption of contaminated fish by a predatory bird in both acute (Worksheet F08) and chronic (Worksheet F09) exposures. Because predatory birds usually consume more food per unit body weight than do predatory mammals (U.S. EPA 1993, pp. 3-4 to 3-6), separate exposure scenarios for the consumption of contaminated fish by predatory mammals are not developed.

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

4.2.3. Terrestrial Plants. In general, the primary hazard to non-target terrestrial plants associated with the application of most herbicides is unintended direct deposition or spray drift. In addition, herbicides may be transported off-site by percolation or runoff or by wind erosion of soil.

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

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

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

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

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

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

or

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

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

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

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

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

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

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

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

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

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

Based on the results of the GLEAMS modeling (Section 3.2.3.4.2), the proportion of the applied dicamba lost by runoff was estimated for clay, loam, and sand at rainfall rates ranging from 5 inches to 250 inches per year. These results are summarized in Worksheet G04 and indicate that runoff will be negligible in relatively arid environments as well as sandy or loam soils. In clay

soils, which have the highest runoff potential, off-site loss may reach up to about 3.5% of the applied amount in regions with very high rainfall rates.

4.2.3.4. Contaminated Irrigation Water – Unintended direct exposures of nontarget plant species may occur through the use of contaminated ambient water for irrigation. Although there are no studies in the literature addressing the impact of dicamba 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. 1991). Furthermore, given the mobility of dicamba, the contamination of irrigation water is a plausible scenario.

The levels of exposure associated with this scenario will depend on the concentration of dicamba in the ambient water used for irrigation and the amount of irrigation water that is applied. As discussed in section 3.2.3.4, some contamination of ambient water may be anticipated and can be quantified [Worksheet B06].

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

Based on the estimated concentrations of dicamba in ambient water and an irrigation rate of 1 inch per day, the estimated functional application rate of dicamba to the irrigated area is about 2×10^{-5} (4×10^{-7} to 7×10^{-5}) lb/acre (see Worksheet F15 for details of these calculations). This level of exposure is inconsequential relative to off-site drift and runoff. Specifically, off-site movement from runoff can result in functional offsite application rates of about 6×10^{-2} lb/acre (Worksheet G04) and offsite movement from drift can result in functional offsite application rates of about 5×10^{-3} lb/acre at 25 feet from the application site after ground broadcast applications (Worksheet G05a) and rates of about 4×10^{-2} lb/acre at 25 feet from the application site after aerial applications.

4.2.3.5. Wind Erosion – Wind erosion is a major transport mechanism for soil (e.g., Winegardner 1996). Although no specific incidents of nontarget damage from wind erosion have been encountered in the literature for dicamba, this mechanism has been associated with the environmental transport of other herbicides (Buser 1990). Numerous models have been developed for wind erosion (e.g., Strek and Spaan 1997; Strek and Stein 1997) and the quantitative aspects of soil erosion by wind are extremely complex and site specific. Field studies conducted on agricultural sites found that wind erosion may account for annual soil losses ranging from 2 to 6.5 metric tons/ha (Allen and Fryrear 1977). The upper range reported by Allen and Fryrear (1977) is nearly the same as the rate of 2.2 tons/acre (5.4 tons/ha) reported by

the USDA (1998). The temporal sequence of soil loss (i.e., the amount lost after a specific storm event involving high winds) depends heavily on soil characteristics as well as meteorological and topographical conditions.

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

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

4.2.3.6. Volatilization – Dicamba is atypical of many carboxylic acid herbicides in that significant and phytotoxic levels of dicamba vapor may be generated after application (Breeze 1993). Assuming a direct relationship between vapor release and dicamba concentrations in ambient air, it seems reasonable to argue that levels of exposure to dicamba vapor after Vanquish applications will be much less than levels of exposure to dicamba vapor after the application of Banvel (the dimethylamine salt of dicamba), under comparable conditions of exposure.

This may be illustrated by considering a scenario in which Vanquish or Banvel is applied to a right-of-way that is 35 feet (about 10.7 meters) wide. Because the width of the right-of-way is relatively narrow compared to downwind distances which could be of concern (e.g., ten meters versus hundreds of meters), these scenarios may be treated as infinite line sources (Turner 1993). In other words, lateral dispersion can be ignored as a conservative approximation in estimating air concentrations of dicamba downwind from the right-of-way. The right-of-way is thus treated

as a line. Each meter along the length of the right-of-way emits a quantity of material per unit of time, as estimated in the following paragraph.

Volatilization rates for dicamba salts have been determined by Behrens and Lueschen (1979). This study measured the volatilization of ^{14}C-labeled dicamba salts from glass surfaces, and observed a biphasic pattern for both the dicamba acid and the dimethylamine salts. For the dimethylamine salt, the initial volatilization rate was approximately 0.05 $hour^{-1}$ (half-time ≃ 14 hours) and the terminal rate was about 0.007 $hour^{-1}$ (half-time ≃ 99 hours). For the diethanolamine salt, the volatilization rate appeared to follow simple first order kinetics (although the duration of observation, 96 hours, was not adequate to detect higher order kinetics) with a volatilization rate of about 0.004 $hour^{-1}$ (half-time ≃ 173 hours). Thus, using the terminal volatilization rates, the diethanolamine salt volatilized 42% more slowly than the dimethylamine salt [1-(0.004 ÷ 0.007)]. While Behrens and Lueschen (1979) did not measure the volatilization rate of Vanquish, this may be approximated assuming a linear relationship between Henry's law constant for the salts in Banvel and Vanquish and the volatilization rate of the formulations. In terms of volatility, diethanolamine and diglycolamine are comparable with Henry's law constants of $3.87 \cdot 10^{-11}$ and $5.72 \cdot 10^{-12}$ atm-m^3/mole at 25°C, respectively, differing only by a factor of about 7. The corresponding value for dimethylamine, $1.77 \cdot 10^{-5}$ atm-m^3/mole at 25°C, is higher by a factor about 500,000 compared with diethanolamine, and 3 million compared with diglycolamine. Consequently, estimates of the relative evaporation rate of the diethanolamine salt compared with the dimethylamine salt should underestimate differences between the diglycolamine and dimethylamine salts of dicamba.

An application rate of 2 lbs a.i./acre, the highest application rate considered in this risk assessment, is equal to approximately 0.224 g/m^2. Thus, each meter in length of the right-of-way is treated with 2.4 grams of dicamba [10.7 $m^2 \cdot 0.224$ g/m^2]. During the first hour after treatment, the volatilization rate of dicamba from the applied Banvel is about 0.017 grams·hr^{-1}·$meter^{-1}$ [2.4 g · 0.007 hr^{-1} ÷ 1 meter] which is equivalent to 4.7 µg·sec^{-1}·$meter^{-1}$

$$17{,}000\ \mu g \cdot m^{-1} \cdot h^{-1} \div 3600\ sec \cdot h^{-1}\ .$$

The corresponding rate for Vanquish is about 0.0014 grams·$meter^{-1}$·hr^{-1} [2.4 g · 0.0006 hr^{-1} ÷ 1 meter] or 0.39 µg·sec^{-1}·$meter^{-1}$

$$1{,}400\ \mu g \cdot m^{-1} \cdot h^{-1} \div 3600\ sec\ h^{-1}\ .$$

In such a scenario, the concentration (µg/m^3) in air at any given distance downwind (***C***)can be approximated as:

$$\boldsymbol{C} = 2 \times q \div (2\pi^{0.5} \times \sigma_z \times u)$$

where q is the emission rate (µg·m^{-1}·sec^{-1}), u is the wind speed (m·sec^{-1}), and σ_z is the Pasquill-Gifford vertical dispersion parameter. The vertical dispersion parameter is directly

related to distance downwind – i.e., the greater the downwind distance the greater the vertical dispersion. The precise nature of the relationship is dependent on atmospheric stability. Assuming slightly unstable atmospheric conditions, a moderate wind, corresponds to a Class C Pasquill stability category and the relationship of σ_z to distance (*d*, in kilometers) downwind is:

$$\sigma_z = 61.141\ d^{0.91465}$$

Using these relationships and the above emission rates for the Banvel and Vanquish applications, the relationship of distance downwind to dicamba concentrations is plotted in Figure 4-1 for wind speeds of 5 miles/hour (2.235 $m \cdot sec^{-1}$). Note that the air concentration is directly related to the emission rate. Thus, the concentrations for dicamba from a Banvel application are uniformly estimated to be a factor of about 12 [0.007÷0.0006] higher than the corresponding application of Vanquish.

No field studies have been found in the literature that report concentrations of dicamba in air after defined applications. The only general monitoring study is the report by Sandmann et al. (1991) on concentrations of dicamba in air in an agricultural region in South Africa. In this report, dicamba was monitored in air at a concentration of 0.451 $\mu g/m^3$.

Because the concentration is directly proportional to application rate and inversely proportional to wind speed, estimates of other air concentrations for other distances and wind speeds can be made from Figure 4-1. For example, if Vanquish is applied at 0.5 lbs a.i. per acre at a wind speed of 2 miles/hour, the concentration at a given distance downwind would be a factor of 0.65 [(0.5/2)·5/2] of that read from Figure 4-1. For substantially different atmospheric conditions, such as strong winds, different methods must be used to estimate the Pasquill-Gifford vertical dispersion parameter based on the appropriate Pasquill stability category (Turner 1993).

4.2.4. Soil Organisms. For both soil microorganisms and soil invertebrates, the toxicity data are typically expressed in units of soil concentration – i.e., mg agent/kg soil which is equivalent to parts per million (ppm) concentrations in soil. The GLEAMS modeling discussed in Section 3.2.3.4 provides estimates of concentration in soil as well as estimates of off-site movement (runoff, sediment, and percolation). Based on the GLEAMS modeling, concentrations in clay, loam, and sand over a wide range of rainfall rates are summarized in Table 4-2. As indicated in this table, peak soil concentrations in the range of about 3.5 (sand and loam) to 4 ppm (clay) are likely immediately after at an application rate of 1 lb a.e./acre regardless of rainfall rates. Longer term concentrations in soil vary substantially with rainfall rates and range from about 0.3 ppm in very arid soils to about 0.01 ppm in regions with high rainfall rates.

The plausibility of these estimates may be assessed from the monitoring study by Scifres and Allen (1973). In this study, dicamba was applied to two grassland sites, one with sandy loam and the other with predominantly clay soil, in south central Texas. While specific records of daily rainfall are not provided in the publication, Scifres and Allen (1973) indicate that the study was conducted in an arid region with annual rainfall rates of 40 cm (about 15 inches) to 90 cm (about

35 inches). The dicamba was applied to different areas in each of the two sites at rates of 0.28 kg/ha (0.25 lb/acre) and 0.56 kg/ha (0.5 lb/acre) using a truck sprayer (38 L/ha). Residues were monitored immediately after spraying and at weeks 1, 2, 4, and 12 after spraying. Initial residues in the top 15 cm of soil were about 0.6 ppm at the lower application rate and 1.1 ppm at the higher application rate. These correspond to rates of about 2.4 ppm per lb/acre. Very little dicamba penetrated below 120 cm and none was detected below 150 cm. Based on analysis of the data presented in this paper (Scifres and Allen 1973, Table 3, p. 395), dicamba levels in the top 15 cm of soil dissipated at a rate of about 0.22 day-1 (t½ 3.3 days) over the first two weeks. After 14 days, no dicamba was detected, with the limit of detection of 0.01 ppm, in the top 15 cm of soil and residues at all depths were less than 0.1 ppm. The rates of dissipation in clay and loam were essentially identical.

For comparison to the GLEAMS modeling, the rainfall simulated at 25 inches per year most closely corresponds to the rainfall rates reported by Scifres and Allen (1973) – i.e., 15 inches + 35 inches ÷ 2 = 25 inches. The initial soil concentration of 2.4 ppm per lb/acre reported by Scifres and Allen (1973) is reasonably close to the 3.5 to 4 ppm per lb/acre modeled using GLEAMS (Table 4-2). At a rainfall rate of 25 inches per year, GLEAMS estimates average soil concentrations of about 0.03 to 0.04 ppm in all soils (Table 4-2). While not detailed in Table 4-2, soil concentrations at 28 days after application were about 0.07 ppm in clay, 0.6 ppm in loam, and 0.04 ppm in sand. Thus, for the application rates used in the study by Scifres and Allen (1973) soil concentrations in the range of 0.01 to about 0.035 ppm would be expected. These are somewhat higher than concentrations reported in Scifres and Allen (1973) – i.e., less than 0.01 ppm. As in the study by Scifres and Allen (1973), no dicamba was modeled below 24 inches in the soil horizon.

4.2.5. Aquatic Organisms. The potential for effects on aquatic species is based on estimated concentrations of dicamba in water that are identical to those used in the human health risk assessment (Worksheet B06). As summarized in Worksheet B06, the peak estimated rate of contamination of ambient water associated with the normal application of dicamba is 0.003 (0.00006 to 0.01) mg/L at an application rate of 1 lb/acre. For longer-term exposures, average estimated rate of contamination of ambient water associated with the normal application of dicamba is 0.00001 (0.000005 to 0.00003) mg/L at an application rate of 1 lb/acre. For the assessment of potential hazards, these contamination rates are adjusted based on the application considered in this risk assessment – i.e., 0.3 lb/acre. The consequences of using higher application rates is discussed in the risk characterization (Section 4.4).

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

The acute lethal potency of dicamba, expressed as the LD_{50}, is relatively well characterized in several mammalian species and indicates that larger vertebrates are more sensitive to dicamba than smaller vertebrates. This allometric relationship is reasonably consistent over two orders of magnitude in body weight (mice to rabbits). Based on an approximation of the LD_{50} in sheep, the relationships appear to hold over 3 orders of magnitude. Although the allometric relationship can be used to estimate the acute LD_{50} values for nontarget terrestrial species, LD_{50} values are not used directly in this risk assessment to assess potential effects in non-target species. Instead, this risk assessment uses NOAEL values for non-target species. For mammals, a NOAEL of 45 mg/kg/day is used for both acute and chronic exposures. This is consistent with the dose-response assessment for humans and the available pharmacokinetic data in mammals. Although dogs and other canids are typically considered more sensitive than other mammals to weak acids such as dicamba, the available toxicity data on dicamba in dogs does not suggest that dogs are more sensitive to dicamba than other species of mammals. For birds, the chronic dietary NOAEL in birds of 92 mg/kg/day is used to characterize risks for both acute and chronic exposures. The only data available on terrestrial invertebrates is the standard bioassay in honey bees in which the LD_{50} was about 1000 mg/kg bw.

The toxicity data for terrestrial plants involve standard bioassays for pre-emergent and post-emergent applications. For exposures involving the off-site drift of dicamba, the range of NOAEL values for post-emergence applications is 0.0014 lb/acre for sensitive species and 3.9 lb/acre for the most tolerant species. For exposures involving off-site runoff, the range of NOAEL values for pre-emergence applications is estimated at 0.00016 lb/acre for sensitive species and 0.53 lb/acre for tolerant species. In addition to these two common routes of exposure to herbicides, field studies have demonstrated that dicamba may volatilize from treated vegetation sufficiently rapidly and in sufficiently high concentrations to damage neighboring untreated vegetation. No explicit dose-response relationship is conducted for this route of exposure but damage from dicamba vapor is considered in the risk characterization.

While a relatively large number of toxicity studies are available on dicamba in several aquatic species, the reported values are highly variable, with LC_{50} values in some studies being less than reported NOEC values in the same species from another study. Some of the lowest LC_{50} values are from the older literature and experimental details are sparse. For the current risk assessment, the NOEC values are not used directly and risks are characterized using LC_{50} values. Based solely on LC_{50} values, the most sensitive species appears to be rainbow trout with a 96-hour LC_{50} value of 28 mg/L and the most tolerant species appears to be mosquito fish with a 96-hour LC_{50} value of 465 mg/L. Some species of aquatic invertebrates appear to be more sensitive than fish and an LC_{50} value of 3.8 mg/L is used for sensitive species. The LC_{50} value for tolerant species of aquatic invertebrates is taken as 750 mg/L. No information is available on the chronic toxicity of dicamba to aquatic animals and the available acute toxicity data do not permit reasonable estimates of toxicity values for chronic toxicity. This limits the risk characterization for aquatic animals.

The available toxicity data on aquatic plants are relatively standard. The most sensitive species on which data are available is the freshwater algae, *Anabaene flos-aquae*, with an EC_{50} of 0.061 mg/L and an EC_{10} of 0.0049 mg/L. Other species of freshwater algae are much more tolerant with NOEC values of up to 10 mg/L. Aquatic macrophytes appear to have an intermediate sensitivity and an NOEC of 0.25 mg/L is used to characterize risks to aquatic macrophytes.

4.3.2. Toxicity to Terrestrial Organisms.

4.3.2.1. Mammals – Typically, Forest Service risk assessments base the dose-response assessment for mammals on the NOAEL values used in the derivation of the acute and chronic RfDs (Section 3.3) and these NOAELs are applied to all species of mammals. As indicated in Section 3.2, the chronic NOAEL used for the chronic RfD is 45 mg/kg/day from the two generation reproduction study in rats by Masters (1993) in which adverse effects (significantly decreased pup growth) were noted at daily doses of 105-135 mg/kg/day. The NOAEL of 45 mg/kg/day is supported by a NOAEL 30 mg/kg/day from a shorter-term teratology study in rabbits (Hoberman 1992) in which adverse effects (signs of maternal toxicity as well as an increase in the number of spontaneous abortions) were noted at a dose of 150 mg/kg/day.

As also noted in Section 3.3, there is relatively little difference between the chronic RfD (0.045 mg/kg/day) and the acute RfD (0.1 mg/kg) and this is consistent with the pharmacokinetic data on dicamba which indicate that differences in body burden between acute and chronic exposures are likely to be less than a factor of about 1.4. In other words, the body burden in a chronic exposure at a fixed daily dose is not likely to be greater 1.4 times the body burden that would be seen after a single daily dose. This relationship follows from the very rapid elimination of the dicamba by mammals (Section 3.1.3). This relationship is important in setting an acute NOAEL because the U.S. EPA used a functional acute NOAEL of 30 mg/kg for setting the acute RfD (Section 3.3.3). As noted above, this functional NOAEL is supported by the short-term NOAEL of 30 mg/kg/day from a teratology study (Hoberman 1992).

In the current risk assessment, it would not be sensible to use the acute NOAEL of 30 mg/kg because this value is less than the chronic NOAEL of 45 mg/kg. In other words, if a dose of 45 mg/kg/day causes no effect of long-term exposures, it should be regarded as a NOAEL for shorter term exposures. Thus, for this risk assessment, the NOAEL of 45 mg/kg is used to characterize risks associated with both acute and chronic exposures.

One concern with this approach, however, is that systematic differences appear to exist in the acute toxicity of dicamba to mammals, with larger mammals being more sensitive than smaller mammals. Specific information on the acute toxicity of dicamba is in Table 4-1. Oral LD_{50} values range from approximately 600 to over 1000 mg/kg for mice, rats, guinea pigs, and rabbits. As discussed in the next section, LD_{50} values for birds also fall within this range. The most significant pattern among all of these studies is that small animals are less sensitive [i.e., have higher LD_{50} values] than large animals. This pattern is common in toxicology and is often used to extrapolate across species [e.g., Davidson et al. 1986] based on the general allometric relationship:

$$LD_{50} = a\ W^{b}$$

where ***a*** and ***b*** of allometric coefficients and ***W*** is the body weight.

All but one of the LD_{50} values in Table 4-2 are taken from the study by Edson and Sanderson (1965). This study is selected because it provides the greatest number of LD_{50} values for different species using the same protocol and conducted by the same investigators. Thus, the potential variability in LD_{50} values due to different experimental conditions, animal handling practices, and statistical methods is minimized. Edson and Sanderson (1965) report results for three preparations of dicamba (pure, technical grade, and formulated), but only data on technical grade and formulated dicamba are summarized in Table 4-1. These investigators do not provide detailed descriptions of the different preparations other than to characterize the *formulated* preparation as an aqueous sodium salt. Based on reported confidence intervals for the LD_{50} values, differences in toxicity between the technical grade and formulated product are not statistically significant.

Table 4-1 includes only results for which an LD_{50} was determined. For example, the LD_{50} for *pure* dicamba in female rats is reported as >2560 mg/kg in Edson and Sanderson (1965). LD_{50} values expressed this way usually indicate that few or no animals died at the specified dose level and consequently, the LD_{50} could not be determined. The only exception is the value for sheep reported by Palmer and Radeleff (1969). In this study, ten doses at 250 mg/kg did not produce any effects noticed by the authors in one sheep, while 2 doses at 500 mg/kg killed one sheep that was dosed. The geometric mean of this range (353 mg/kg) is included in the analysis as the estimated LD_{50} for sheep. This approach is taken because these data on sheep are the only bases for estimating acutely lethal levels in a relatively large mammal. In conducting allometric analyses, it is desirable to use as wide a range of body weights as possible to determine whether it is reasonable to use the allometric relationships for extrapolation. Nonetheless, this approach for estimating the LD_{50} value for sheep is at best a crude approximation. As noted below, however, this single value for sheep has little impact on the analysis of the allometric relationship.

The statistical analyses of these data are illustrated in Figure 4-2. The labeled points correspond to the data in Table 4-2. The thick solid line is the maximum likelihood estimate for the allometric relationship. The inner dashed lines are the 95% confidence interval for the correlation and the outer dashed lines are the 95% prediction intervals. These data yield the following allometric relationship:

$$LD_{50} = 748\ W^{-0.17}$$

where W is the body weight in kg and the LD_{50} is in units of mg/kg body weight. The squared correlation coefficient is 0.75, and both of the model estimates, ***a*** and ***b***, are statistically significant at $p<0.005$. Omitting the data on sheep has little effect on the model estimates [***a*** of 749 vs 748; ***b*** of -0.16 vs -0.17] although the squared correlation coefficient is less (0.56) as is the significance of the estimate of ***b*** [p=0.0.31 vs p=0.002].

The data summarized in Table 4-1 and the allometric relationship given in the above equation and illustrated in Figure 4-2 can be used directly to assess the acute lethal potency in nontarget terrestrial species. The relationships based on LD_{50} values from a single study are reasonably consistent over two orders of magnitude (mice to rabbits), and, based on an approximation in sheep, the relationships appear to hold over 3 orders of magnitude. Moreover, the relationships are based on two important groups of nontarget species, mammals and birds, between which no substantial differences in sensitivity are apparent.

Based on the above allometric equation, the LD_{50} for a 0.25 kg rat is estimated at about 950 mg/kg [$748 \times 0.25^{-0.17} = 946.8$] and the LD_{50} for a 4 kg rabbit is estimated at about 500 mg/kg [$748\times 4^{-0.17}=590.95$], indicating that rabbits would be more sensitive than rats to the acute lethal effects of dicamba by a factor of about 1.2 [590 mg/kg ÷ 500 mg/kg = 1.18]. This is reasonably consistent with the longer-term NOAELs, 45 mg/kg/day in rats and 30 mg/kg/day is rabbits, a factor of 1.5. It should be noted, however, the longer-term NOAELs are artifacts of the experimental designs (i.e., the NOAELs reflect the doses used in the different studies) and the concordance between the acute and chronic toxicity ratios may be specious. For the 70 kg animals, such as a deer, the estimated LD_{50} value would be about 363 mg/kg [$748 \times 70^{-0.17} = 363.3$] or about a factor 2.6 less than that of the rat [946.8 / 363.3 = 2.6]. Thus, at least in terms of acute toxicity, larger mammals may be more sensitive than smaller mammals by about a factor of 3. Whether or not these differences would be seen in chronic toxicity studies cannot clearly determined from the available data.

Another concern with the use of a 45 mg/kg/day NOAEL is the potential sensitivity of dogs and perhaps other canid species (e.g., foxes, wolves, and coyotes). Dicamba is a weak acid and dogs appear generally to have a lesser capacity to excrete weak acids than rodents or primates (e.g., Timchalk and Nolan 1997). While no detailed pharmacokinetic studies have been found in dogs, the study by Atallah and Yu (1980) suggests that dogs, as well as rats, mice, rabbits, will rapidly excrete dicamba. In addition, the available toxicity studies in dogs do not suggest that dogs are substantially more sensitive to dicamba than rodents. As discussed in Section 3.1.5, the one-year dog feeding study by Drench (1986) indicated a NOAEL of 65 mg/kg/day. In an earlier two-year dog feeding study, Davis et al. (1962) reported no signs of toxicity based on hematology, urinalysis, organ weights, gross pathology or histopathology at a dose of 0.75 mg/kg/day. The only effect observed was a decrease in weight gain. The significance of this effect is unclear, both statistically and biologically. In the study by Drench (1986), only transient effects on body weight were noted. In addition, the study by Davis et al. (1962) used only 3 dogs per dose group and statistically analyses of the body weight changes were not reported. Lastly, the study by Drench (1986) is classified as core by the U.S. EPA (1992b) while the earlier study by Davis et a. (1962) was considered only as supplemental because pharmacologic effects were not detailed, no gross pathology was done, there was no clinical chemistry data and only scant histopathology. Based on these considerations, there does not appear to be a clear basis for assuming that canids (with a NOAEL of 65 mg/kg/day) are substantially more sensitive to dicamba than other mammals (NOAEL of 45 mg/kg/day). Thus, for this risk assessment, a NOAEL of 45 mg/kg/day will be used to assess risks to all mammals from both acute and chronic exposures.

4.3.2.2. Birds – As discussed in the previous section and illustrated in Figure 4-2, no remarkable differences are apparent in the toxicity of dicamba to mammals and birds based on the comparative LD_{50} study by Edson and Sanderson (1965). As detailed in Appendix 6, bobwhite quail is the only species on which comparable toxicity data is available for the salts used in both Banvel and Vanquish. Based on the study by Campbell et al. (1993), the LD_{50} for the DMA salt of dicamba (i.e., the salt used in Banvel) is 187 mg a.e./kg with a 95% confidence interval of 141 mg a.e./kg to 250 mg a.e./kg. Grimes et al. (1986b,c) tested what appears to be a sample of a Vanquish formulation – i.e., the test material is identified only as 4 lb/gal diglycolamine salt of dicamba which is the same as Vanquish. In this assay, the LD_{50} for the formulation, expressed in acid equivalents, is 327 mg a.e./kg with a 95% confidence interval of 247 a.e./kg to 621 mg a.e./kg. Thus, the Vanquish formulation appears to be somewhat less toxic than the DMA salt of dicamba but the difference is only marginally significant.

As with mammals, the risk characterization for dicamba is based on NOAEL values rather than LD_{50} values. As detailed in Appendix 6, a large number of studies are available on dicamba. The most important endpoint appears to be neurotoxicity, an endpoint this is also identified concern in the human health risk assessment (Section 3.1.6).

Based on acute (single dose gavage) exposures, the LOAEL is 27 mg a.e./kg with a NOAEL of 13.6 mg a.e./kg from the study by Campbell et al. (1993) in Bobwhite quail. Somewhat higher NOAEL and LOAEL values have been reported by Grimes (1986a) for Vanquish in Bobwhite quail [LOAEL of 112 mg a.e./kg], Beavers (1986) for the IPA salt of dicamba in Bobwhite quail [LOAEL of 94 mg a.e./kg], Roberts et al. (1983) for an unspecified form of dicamba in chickens [LOAEL of 79 mg a.e./kg].

Two reproduction studies are available in birds, one in Mallard ducks (Beavers et al. 1994a) and the other in Bobwhite quail (Beavers et al., 1994b). Mallards appeared to be somewhat more sensitive, with a dietary NOAEL of 800 ppm and a LOAEL of 1600 ppm (Beavers et al. 1994a). The LOAEL was based on reduced hatchability and survival of offspring. No signs of neurotoxicity were reported. In Bobwhite quail, no effects were seen on any reproductive parameters at 1600 ppm (Beavers et al., 1994b). Based on measured body weight and food consumption (Appendix 6), the dietary NOAEL of 800 ppm would correspond to a dose of about 92 mg/kg/day and the LOAEL of 1600 ppm corresponds to a dose of about 184 mg/kg/day.

The discrepancy between the relatively high longer-term dietary NOAEL and the much lower acute NOAEL for neurotoxicity probably relates to the dosing method. All of the acute studies in which in which neurotoxic effects have been noted involve gavage administration. Thus, the test material is inserted directly into the crop of the bird in a very short period of time. This leads high peak plasma concentrations than the more gradual administration that occurs during a study involving dietary exposure.

Similar to the approach taken with mammals, the chronic NOAEL of 92 mg/kg/day will be used to characterize both acute and chronic risks in birds. In other words, it is reasonable to assume

that if a dose does not cause adverse effects over a period of 21 weeks no effects will be caused at this dose after a 1-day exposure. The NOAEL of 92 mg/kg is higher than the gavage LOAEL of 27 mg/kg. As noted above, however, this is likely to be an artifact of the gavage dosing method and will not be representative of exposures in the field.

4.3.2.3. Terrestrial Invertebrates – As discussed in Section 4.1.2.3, a standard bioassay was conducted on the toxicity of dicamba to honey bees in which the reported LD_{50} is reported (Atkins et al. 1975; C&P Press 2003; FAO/WHO 2001; Tomlin 1994) as greater than 100 µg/bee and corresponds to a dose of about 1000 mg/kg bw. This value is entered into Worksheet G02 and used to characterize risks associated with the direct spray of a bee. No quantitative dose-response assessment is conducted using the information from field studies (Section 4.1.2.3), but these are considered further in the risk characterization (Section 4.4).

4.3.2.4. Terrestrial Plants (Macrophytes) – As discussed in the exposure assessment for terrestrial plants (see section 4.2.2), there are three types of exposures to be considered for terrestrial plants: direct foliar contact, soil contamination from runoff, and vaporization of dicamba from treated vegetation to off-site plants.

As discussed in Section 4.1.2.4 and detailed further in Appendix 10, a large amount of data is available on the effect of dicamba on various non-target species in which dicamba was sprayed either directly on the leaves (post-emergence assays) or on soil prior to emergence (pre-emergence assays). For pre-emergence assays, the most sensitive species appears to be soybean, with an LOEC of 0.0022 lb/acre (Hoberg 1993a). As detailed in Appendix 10, an NOEC was not determined for this species but an NOEC can be approximated as 0.00016 lb/acre based on the relative potency values determined from the reported EC_{25} values. The least sensitive species was cabbage with an NOEC 0.53 lb/acre. These NOAEL values are entered into Worksheet G04 and used to characterize risks associated with the runoff of dicamba from treated soil (Section 4.4). For post-emergence assays, the most sensitive species appears to be sunflower, with an NOEC of 0.0014 lb/acre (Derksen 1989). The least sensitive species appears to be corn, with an NOEC of 3.9 lb/acre (Hoberg 1993a). These NOAEL values are used to characterize risks associated with offsite drift from ground applications (Worksheet G05a) and aerial applications (Worksheet G05b).

As discussed in section 4.2.3.6, dicamba and its various salts may volatilize from applied aqueous formulations and be transported to neighboring vegetation. For Vanquish, the rate of volatilization is likely to be about 90% less than the rate of volatilization for the dimethylamine salt. Concentrations of dicamba in air after applications comparable to those anticipated for the proposed program are the most relevant exposure metameter. While these levels can be modeled (section 4.2.2.2) there are no toxicity studies on plants in which dicamba air levels serve as the exposure metameter.

The most directly relevant study for assessing dose-response relationships is by Behrens and Lueschen (1979), which also serves as the basis of the exposure assessment. In this study, five

field trials were conducted in which the dimethylamine salt of dicamba was applied to corn at a rate of 0.28 kg a.i./ha (0.25 lbs a.i./acre). Potted soybeans were placed within the treated corn and at locations predominantly downwind and upwind of the treated corn at distances of 3 and 30 m from the treated corn. After 24 hours, damage to the soybeans was assessed using a relative injury index rating, in which 100 indicates complete kill and 0 indicates no effect. The most serious injury (68) occurred in soybeans placed within the area of the treated corn. At 3 m downwind, the average index rating was only slightly less, 61. At 30 m downwind, the index rating was approximately 50% (32) of that noted on the soybeans placed within the corn. For soybean plants placed upwind, the index ratings were much lower (approximately 10 at 3 m and 4 at 30 m). In another series of studies, soybeans were placed 3 m downwind of treated corn on days 1, 2, and 3 after treatment. Injury decreased with time but was still notable (injury index = 22) on day 3. Although this study demonstrates that the vapor release of dicamba may cause damage in neighboring plants, its direct usefulness in risk characterization is limited. As reviewed by Breeze (1993), only limited attempts have been made to define the kinetics of vapor uptake in plants. There is one aspect of the kinetics of dicamba uptake that appears to be clear, however: there is a linear relationship between the rate of pesticide absorption by the plant and pesticide concentrations in air. As discussed in the risk characterization (section 4.4), this relationship is an important factor in assessing the potential damage from dicamba applications.

4.3.2.5. Soil Microorganisms – Substantial toxic effects have not been demonstrated in soil microorganisms (Section 4.1.2.5). The lowest reported effect level is 10 ppm and was associated with a transient decrease in nitrification after 2 but not 3 weeks (Tu 1994). At 1 ppm, dicamba had no effect on urea hydrolysis or nitrification in four diverse soil types (Martens and Bremner 1993). These NOEC and LOEC values may be used for characterizing potential effects in soil microorganisms. Because the LOEC value is much higher than concentrations that may be expected in soil over periods of weeks, there is no need to elaborate on the dose-response assessment for soil microorganisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish – Standard acute studies are available on the toxicity of dicamba to fish and amphibians (Appendix 7) as well as aquatic invertebrates (Appendix 8). Some of these studies where submitted to U.S. EPA in support of the registration of dicamba and these studies are indicated with MRID numbers in the appendices. For these studies, relatively detailed information is available on experimental designs and test conditions and data are provided on both measures of acute lethal potency (LC_{50} values) as well as NOEC values. Several of the other studies, however, are from the older published literature. Most of these studies provide only limited experimental detail and do not provide any toxicity information other than LC_{50} values.

The NOEC values are generally the most relevant data for Forest Service risk assessments. Acute NOEC values are available in bluegill sunfish (56 mg/L in Vilkas 1977a; 100 mg/L in McAllister et al. 1985a), rainbow trout (56 mg/L in McAllister et al. 1985b), and sheepshead minnow (>180 mg/L from Vilkas 1977c). These NOEC values, however, are based on relatively

gross endpoints – i.e., no mortality and no over behavioral changes. The only study providing histopathologic evaluation is that of Lorz (1979) using Coho salmon. In this study, non-lethal concentrations of dicamba at a concentration of ≤ 100 mg/L was associated with histopathological changes in the liver but not in the kidneys or gills. Another issue with the reported NOEC values is the fact that some reported NOEC values are above other LC_{50} values. For example, as noted above, McAllister et al. (1985b) report an NOEC of 56 mg/L in rainbow trout. While this is consistent with the LC_{50} value of 320 mg/L reported by Bond et al. (1965) in rainbow trout, Johnson and Finley (1980) report an LC_{50} of 28 mg/L in rainbow trout. These sort of discrepancies are not uncommon with compounds for which many studies are conducted at different times by several different laboratories. Thus, the NOEC values will not be used directly in this risk assessment because they may not fully encompass sublethal toxicity. In addition, some of the reported NOEC values are exceed other reports of concentrations that are associated with lethality.

Based solely on LC_{50} values, the most sensitive species appears to be rainbow trout with a 96-hour LC_{50} value of 28 mg/L (Johnson and Finley 1980). The most tolerant species appears to be mosquito fish with a 96-hour LC_{50} value of 465 mg/L. These values are entered into Worksheet G03 and used in Section 4.4 to characterize risk to tolerant and sensitive species of fish.

As noted in Section 4.1.3.1, no chronic toxicity studies in fish have been encountered in either the published literature or in the studies submitted to U.S. EPA for the registration of dicamba. The lack of at least one subchronic or chronic study in fish is very unusual. To verify that no such studies are available, the U.S. EPA's Office of Pesticides kindly conducted supplemental searches of their database, which is more current than commercially available databases, for dicamba, Banvel, and Vanquish. No subchronic or chronic studies in fish were identified. In addition, as discussed below, no chronic studies were identified in invertebrates. Thus, it is not possible to estimate as chronic fish NOEC for dicamba using a ratio of acute to chronic values from invertebrates.

As indicated in Appendices 7 and 8, some data are available on concentration-duration relationships for dicamba in fish and invertebrates over relatively short periods of time – i.e., from 24 hours to 96 hours. As an exploratory effort, these data were analyzed using the following equation:

$$\boldsymbol{Log_{10} EC_{50} = a + k\ Log_{10}\ T}$$

where $\boldsymbol{a}$ is the $\log_{10}$ of the LC_{50} a 1-hour ($\log(1)=0$), $\boldsymbol{k}$ is the slope, the $\boldsymbol{T}$ is exposure time in hours. A summary of the data used in these analyses is illustrated in Figure 4-3 and the statistical analyses are summarized in Table 4-3. Table 4-3 also gives the estimated acute and chronic LC_{50} values. Acute LC_{50} values calculated at 1-day for all species. Chronic LC_{50} values calculated at 365 days for fish and amphibians and 14-days for invertebrates. The last column in Table 4-3 gives the acute-to-chronic ratio.

As indicated in Table 4-3, the regressions were only statistically significant for one species, the tadpoles of *Adelotus brevis* (Johnson 1976) and the estimated acute to chronic ratio for this species is very low – i.e., 2.1. Other acute to chronic ratios range from 1.6 in mosquito fish to 26 in bluegills based on the study by Hughes and Davis (1962). While acute to chronic ratios on the order of 10 or less are not uncommon, other acute to chronic ratios can exceed 100. Given the lack of consistency in the ratios in Table 4-3 as well as the general lack of statistical significance, the available dose-duration relationships for dicamba in aquatic vertebrates and invertebrates cannot be use to estimate chronic toxicity values.

Thus, in Worksheet G03, the acute values are applied to chronic exposure scenarios. This is an extremely unusual practice and leads to a very limited characterization of risk. This is discussed further in Section 4.4.3.

4.3.3.2. Amphibians – Based on the available acute toxicity data, amphibians appear to be about as sensitive to dicamba as fish. Given the limited data on amphibians as well as the limited data on fish, discussed above, a separate dose-response assessment for amphibians is not conducted.

4.3.3.3. Invertebrates – Some aquatic invertebrate appear to somewhat more sensitive to dicamba than fish or amphibians. The lowest reported 96-hour LC_{50} is 3.8 mg/L for *Gammarus lacustris*. While *Daphnia magna*, a common test species, appears to be relatively tolerant to dicamba – i.e., reported EC_{50} values from 750 mg/L to >1000 mg/L – *Daphnia pulex* is much more sensitive with an LC_{50} value of 11 mg/L (Hurlbert 1975). As with fish, NOEC values are only sporadically reported and are above some LC_{50} values. Thus, as with fish, EC_{50} values rather than NOEC values are used to characterize risk. The LC_{50} value for sensitive species is taken as 3.8 mg/L, the lowest reported value. The LC_{50} value for tolerant species is taken as 750 mg/L from the study by Forbes et al. (1985). Also as with fish, these acute values are applied to chronic exposure scenarios in Worksheet G03 and the interpretation of the resulting hazard quotients is discussed in Section 4.4.3.

4.3.3.4. Aquatic Plants – Unlike the data on aquatic vertebrates, in which no useable NOEC values are available or can be estimated, the available toxicity data on aquatic plants are relatively standard. The most sensitive species on which data are available is the freshwater algae, *Anabaene flos-aquae*, with an EC_{50} of 0.061 mg/L and an EC_{10} of 0.0049 mg/L. Other species of freshwater algae are much more tolerant with NOEC values of up to 10 mg/L. This range is used in Worksheet G03 to encompass the range of sensitivities in unicellular algae.

Aquatic macrophytes appear to have an intermediate sensitivity. The reported NOEC in *Lemna gibba* is 0.25 mg/L in a standard 14-day exposure study (Hoberg 1993b). A 4-day study in *Lemna minor* reports a higher NOEC of 100 mg/L (Fairchild et al. 1997). Because of the short duration of this study, however, it cannot be used to identify *Lemna minor* as a more tolerant macrophyte. Thus, in Worksheet G03, only the NOEC of 0.25 mg/L is used to characterize risks to macrophytes.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

For terrestrial vertebrates, some acute exposure scenarios but no chronic exposure scenarios exceed the level of concern but only at the highest application rate. At the typical application rate of 0.3 lb/acre, no adverse effects on mammals or birds are plausible for either acute or chronic exposures. At the highest application rate of 2 lb/acre, adverse reproductive effects are plausible in acute exposure scenarios involving mammals and birds consuming contaminated vegetation or contaminated insects. In chronic exposure scenarios at an application rate 2 lb/acre, the hazard quotients associated with the consumption of contaminated vegetation are below the level of concern by factors of 5 to over 16,000.

There is little basis for asserting that adverse effects would be expected in terrestrial insects or soil microorganisms. The very limited data in insects suggest that no lethal effects are likely in a direct spray. There are no data on sublethal effects in insects. At the highest application rate, transient effects might be seen in some populations of soil microorganisms.

Dicamba is an effective herbicide and even some tolerant plants that are directly sprayed with dicamba at normal application rates are likely to be damaged. The greatest risks – i.e., the highest hazard quotients – are associated with runoff but are highly site specific. Some sensitive plant species could be affected by runoff in areas in which runoff is favored – clay soil and surface conditions that are conducive to runoff. Damage associated with off-site drift of dicamba would also depend on local site-specific conditions but would most likely occur within a relatively small distance from the application site – i.e., up to about 100 feet. Vapor exposures to offsite vegetation could also cause damage. While this cannot be well quantified, it is likely that this effect would be less pronounced with Vanquish than with Banvel.

The risk characterization for aquatic animals is extremely limited by the available toxicity data. For the characterization of risk, NOEC values are not used directly and risks are characterized using LC_{50} values. Another very substantial limitation in the risk characterization is that no information is available on the chronic toxicity of dicamba to aquatic animals and the available acute toxicity data do not permit reasonable estimates of toxicity values for chronic toxicity. Within these very serious limitations, there is little basis for asserting that adverse effects in aquatic animals are plausible. This conclusion is consistent with a recent assessment by the U.S. EPA on the impact of dicamba on Pacific anadromous salmonids.

Unlike the risk characterization for aquatic animals, the risk characterization for aquatic plants is based on relatively consistent and standard toxicity data. At the typical application rate, adverse effects in aquatic plants are not likely. At the maximum application rate, peak concentrations in water could be associated with transient effects in sensitive species of algae as well as macrophytes. These concentrations, however, would rapidly diminish to levels substantially below a level of concern.

4.4.2. Terrestrial Organisms

4.4.2.1. Terrestrial Vertebrates – The quantitative risk characterization for mammals and birds is summarized in Worksheet G02a for the typical application rate of 0.3 lb/acre and Worksheet G02b for the highest application considered in this risk assessment, 2 lb/acre.

The toxicity values used for each group of animals is summarized at the bottom of Worksheet G02a and refer to values derived in the dose-response assessment (Sections 4.3.2.1 and 4.3.2.2). In this worksheet, risk is characterized as the estimated dose, taken from Worksheet G01, divided by toxicity value. This ratio is referred to as the hazard quotient (HQ). All exposures summarized in Worksheet G01 are based on the typical application rate of 0.3 lb/acre. At this application rate, an HQ of one or less indicates that the estimated exposure is less than the toxicity value. When this is the case, there is no basis for asserting that adverse effects are plausible. As discussed in Section 2 (Program Description), the maximum application rate that might be used in Forest Service programs is 2 lb/acre. Because exposure is directly related to application rate, the level of concern for the hazard quotients given in Worksheet G02a for an application rate of 2 lb/acre is 0.15 [0.3 lb/acre ÷ 2 lb/acre]. Worksheet G02b simply adjusts the hazard quotients from Worksheet G02a upward by a factor 6.66 – i.e., 2 lb/acre ÷ 0.3 lb/acre. Thus, hazard quotients presented in Worksheet G02b may be interpreted in the same was as those presented in Worksheet G02a – i.e., the level of concern is 1.

At the typical application rate (Worksheet G02a), none of the risk quotients for mammals or birds exceed 1.0 even at the upper ranges of exposure. Thus, there is no basis for asserting that mammals or birds are at risk from the use of dicamba at the typical application rate of 0.3 lb/acre even under reasonably foreseeable worst-case conditions. The highest hazard quotient is 0.3 and is associated with the upper range of exposure for a large mammal consuming contaminated vegetation. This acute hazard quotient if below the level of concern by a factor of about 3.3. The hazard quotients for chronic exposure as much lower. The highest chronic hazard quotient is 0.05 and is associated with the upper range of exposure for a large mammal consuming contaminated vegetation exclusively at the application site. This scenario is below the level of concern by a factor of 20.

At the highest application considered in this risk assessment (Worksheet G02b), none of the longer-term scenarios result in hazard quotients that exceed the level of concern. Some acute exposure scenarios, however, do modestly exceed the level of concern. The highest hazard quotient for mammals is 2 and is associated with the upper range of the dose from the consumption of contaminated vegetation by a large mammal. The dose associated with this scenario is about 97.2 mg/kg. This is higher than the NOAEL of 45 mg/kg and only somewhat below the corresponding LOAEL, 105-135 mg/kg/day, which is associated with decreased pup growth from a teratology study in rats (Section 4.3.2.1). The highest hazard quotient for birds is 1.7. This hazard quotient is also associated with the acute consumption of contaminated vegetation and corresponds to a dose of about 152 mg/kg/day. This dose approaches the dietary reproductive LOAEL of 184 mg/kg/day that was associated with reduced hatchability and survival of offspring (Section 4.3.2.2). Thus, for both birds and mammals, adverse effects on

offspring appear to be plausible at the upper ranges of exposure that are associated with the maximum application rate.

4.4.2.2. Terrestrial Invertebrates – Compared to mammals and birds, there is very little information is available on the toxicity of dicamba to terrestrial invertebrates. For the honey bee, the hazard quotient is based on the reported LD_{50} of 1000 mg/kg (Section 4.3.2.3). Even at the exposure associated with a direct spray, the hazard quotient of 0.002 is below the level of concern by a factor of 500 [1 ÷ 0.04] at the typical application rate (Worksheet G02a) and a factor of 100 [1 ÷ 0.01] at the maximum application rate (Worksheet G02b). Thus, there is no basis for expecting mortality in bees directly sprayed with dicamba.

There are, of course, a large number of other species for which no or very little toxicity data are available. As summarized in 4.1.2.3, one field study in earthworms reported no apparent effects at an application rate of 0.1 lb/acre (Potter et al. 1990). This study is below the typical application considered in this risk assessment by a factor of 3 and below the maximum application rate by a factor of 20. Thus, it is of little use in characterizing risks associated with applications that might be conducted by the Forest Service. Similarly, the screen study of Hassan et al. (1998) does not provide sufficient data to assess the risks to other species of insects.

4.4.2.3. Soil Microorganisms – There is no basis for asserting that toxic effects in soil microorganisms are likely. As summarized in Section 4.2.4, peak soil concentrations in the range of about 3.5 to 4 ppm are likely immediately after at an application rate of 1 lb/acre regardless of rainfall rates. Longer term concentrations in soil vary substantially with rainfall rates and range from about 0.3 ppm in very arid soils to about 0.01 ppm in regions with high rainfall rates. Adjusted for the typical application rate of 0.3 lb/acre, the peak soil concentrations would be about 1.1 to 1.3 ppm. The NOAEL for soil microorganisms is 1 ppm and LOAEL is 10 ppm, an exposure associated with transient decreases in nitrification (4.3.2.5). Thus, at the typical application rate, peak concentrations would modestly exceed the NOAEL but still be substantially below the LOAEL. Based on longer term concentrations in soil, exposures would be far below the NOAEL. At the maximum application rate, the peak soil concentrations would be about 23 to 26 ppm. These exposures however would be transient and longer term exposures would be in the range of 0.07 to 2 ppm. Thus, at the highest application rate, transient effects on soil microorganisms are plausible. Based on the study by Tu (1994), a short-term decrease in nitrification could be observed.

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

Dicamba is an effective herbicide and even some tolerant plants that are directly sprayed with dicamba at normal application rates are likely to be damaged. The greatest risks – i.e., the

highest hazard quotients – are associated with runoff but are highly site specific. As summarized in Worksheet G04, runoff could pose a substantial risk to sensitive non-target plant species (i.e., hazard quotients of up to 125) under conditions in which runoff is favored – i.e., clay soil over a wide range of rainfall rates. In areas in which runoff is not likely, risks to offsite plants is minimal. Tolerant plants species would not likely be impacted at the typical application rate (an LOC of 1 in Worksheet G04) or at the maximum application rate (LOC=0.15), even under conditions which favor runoff.

As indicated in Worksheets G05a, off-site drift of dicamba associated with ground broadcast or aerial applications may cause damage to sensitive plant species at distances of 100 feet or less from the application site. For both ground and aerial drift, the closer that the non-target species is to the application site, the greater is the likelihood of damage. Actual damage due to drift of dicamba would depend on a several site-specific conditions, including wind speed and foliar interception by the target vegetation. In other words, in some right-of-way applications conducted at low wind speeds and under conditions in which vegetation at or immediately adjacent to the application site would limit off-site drift, damage due to drift would probably be inconsequential or limited to the area immediately adjacent to the application site. Tolerant plant species would probably not be impacted by the drift of dicamba and might show relatively little damage unless they were directly sprayed.

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

As summarized in Section 4.2.3.5, daily soil losses due to wind erosion, expressed as a proportion of an application rate, could be in the range of 0.00001 to 0.001. This is substantially less than off-site losses associated with runoff from clay at annual rainfall rates of 15 inches or more (Worksheet G04) and similar to off-site losses associated with drift at a distance of 500 feet or more from the application site (Worksheet G05a). As with the drift scenarios, wind erosion could lead to adverse effects in sensitive plant species. Wind erosion of soil contaminated with any herbicide is most plausible in relatively arid environments and if local soil surface and topographic conditions favor wind erosion.

Volatilization of dicamba with transport and subsequent damage to vegetation beyond the application site has been well documented using bioassays [e.g., Behrens and Lueschen 1979]; however, specific air concentration-duration relationships associated with this effect have not been determined. Consequently, typical air dispersion modeling [e.g., Turner 1994] is of little use in numerically characterizing risk. By analogy to other types of damage caused by exposures to gases or vapors, it is plausible that the effect of dicamba vapor on terrestrial plants will follow

Haber's law [i.e., damage will be proportional to the product of the concentration in air and the duration of exposure (Amdur 1980)].

Although numerical expressions of hazard cannot be made directly, there is enough information regarding the vaporization rates of various dicamba salts to suggest that the diglycolamine salt of dicamba used in Vanquish is likely to generate dicamba vapor at a much slower rate than the dimethylamine salt of dicamba used in Banvel. Based on a quantitative analysis of evaporation rates from aqueous solutions, the rate of generation of dicamba vapor from Vanquish should be about 10–15% of the corresponding rate for Banvel, under identical application conditions. This should result in a decreased level of damage; however, the extent of the decrease cannot be characterized further.

The simple verbal interpretation for this quantitative risk characterization is that some sensitive plant species could be affected by runoff. Damage associated with off-site drift of dicamba would depend on local site-specific conditions but could occur within a relatively small distance from the application site – i.e., up to about 100 feet. Vapor exposures to offsite vegetation could also cause damage. While this cannot be well quantified, it is likely that this effect would be less pronounced with Vanquish than with Banvel.

4.4.3. Aquatic Organisms.

4.4.3.1. Aquatic Animals – The risk characterization for aquatic animals is summarized in Worksheet G03. This risk characterization, however, is extremely limited by the available toxicity data. As discussed in Section 4.3.3, a large number of toxicity studies are available on dicamba in several aquatic species but the reported values are highly variable, with LC_{50} values in some studies being less than reported NOEC values in the same species from another study. Consequently, for the characterization of risk, NOEC values are not used directly and risks are characterized using LC_{50} values. Another very substantial limitation in the risk characterization is that no information is available on the chronic toxicity of dicamba to aquatic animals and the available acute toxicity data do not permit reasonable estimates of toxicity values for chronic toxicity. Consequently, the longer term hazard quotients for aquatic animals presented in Worksheet G03 are simply the estimated longer term exposure divided by the acute LC_{50} value. This is an atypical expression of risk and is presented solely as means of comparing exposures to the available toxicity data.

Within these very serious limitations, there is little basis for asserting that adverse effects in aquatic animals are plausible. For acute exposures, the hazard quotients are in the range of 0.000003 to 0.0001. In other words, the projected peak exposures are below the LC_{50} values by factors of 10,000 to over 300,000. For longer term exposures, the hazard quotients are in the range of 0.000000009 to 0.000002 – i.e., the average concentrations in water are below the LC_{50} values by factors of 500,000 to over 1,000,000,000 (one billion). While these values cannot be overly interpreted, both acute and longer term NOAEL values are generally below LC_{50} values by factors of far less than 10,000. The basic conclusion that adverse effects in aquatic animals are

implausible is consistent with the conclusions reached by the U.S. EPA/OPP in the no effect determination for dicamba for Pacific anadromous salmonids (Turner 2003).

As detailed in Section 3.2.3.4.1, an accidental spill scenario is used in the human health risk assessment as a very conservative screening scenario. While this scenario is not in Worksheet G03, the concentrations in water modeled for the accidental spill range from 0.6 mg/L to 1.5 mg/L with a central estimate of about 1 mg/L (Worksheet D05). The upper limit of this range is below the LC_{50} value of 3.8 mg/L for the most sensitive aquatic animals by a factor of about 2.5 [3.8 mg/L ÷ 1.5 mg/L]. While this is an extremely arbitrary scenario and while the actual concentrations in the water after a spill would depend on the amount of compound spilled and the size of the water body into which it is spilled, this extreme scenario suggests that substantial mortality in aquatic animals would not be observed even after a large spill into a relatively small body of water.

4.4.3.2. Aquatic Plants – Unlike the risk characterization for aquatic animals, the risk characterization for aquatic plants is based on relatively consistent and standard toxicity data. As indicated in Worksheet G03, hazard quotients for the most sensitive aquatic plants are below a level of concern based either on peak concentration of dicamba in water associated with runoff (a hazard quotient of 0.6 at the upper range of exposure) as well as longer term concentrations that might be expected (hazard quotient of 0.002 at the upper range of exposure). Thus, at the typical application rate (LOC=1), there is no basis for asserting that effects in aquatic plants are plausible. At the maximum application rate (LOC=0.15), the upper ranges of the hazard quotients for the most sensitive aquatic plant exceeds the level of concern by about a factor of 4 [0.6 ÷ 0.15] for peak exposures. Thus, transient effects could be anticipated in sensitive species of algae as well as macrophytes. These concentrations, however, would rapidly diminish to levels substantially below a level of concern.

As noted above, accidental spills of large quantities of dicamba into relatively small bodies of water could lead to much higher concentrations – i.e., from 0.6 mg/L to 1.5 mg/L with a central estimate of about 1 mg/L (Worksheet D05). After spills of this magnitude, adverse effects on aquatic macrophytes as well as sensitive species of algae could be anticipated from dicamba as well as most other herbicides.

5. REFERENCES

Agnihotri PK; Murthy PS; Mukherjee SK. 1989. Effect of herbicide Banvel on rabbit vaginal mucus membrane. Indian J Exp Biol. 27 (12):1090-1091.

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.

Al-Khatib K; Parker R; Fuerst EP. 1992. Foliar absorption and translocation of dicamba from aqueous solution and dicamba-treated soil deposits. Weed Technol. 6 (1):57-61.

Amdur, M. 1980. Air pollutants. In: Doull, J.; Klaassen, C.D.; Amdur, M.O., eds. Toxicology: The Basic Science of Poisons. New York: Macmillan Publishing Co. p. 608-630.

Arnold EK; Beasely VR. 1989. The pharmacokinetics of chlorinated phenoxy acid herbicides: A literature review. Vet Hum Toxicol. 31 (2):121-125.

Atalay A; Hwang K-J. 1999. Extractability of 2,4-D, dicamba and MCPP from soil. Water Air Soil Pollut. 114 (1-2):155-170.

Atkins EL; Graywood EA; Macdonald RL. 1975. Toxicity of Pesticides and Other Argicultural Chemicals to Honey Bees – Laboratory Studies. Division of Agricultural Sciences, University of California Leafet 2287. MRID 00036935.

Auch DE; Arnold WE. 1978. Dicamba use and injury on soybeans (*Glycine max*) in South Dakota. Weed Sci. 26 :471-475.

Backus B. 1989. Toxicology Review for Dicamba. California Department of Food and Agriculture - EPA. U.S. EPA Toxicology Branch. February 27, 1989. Memorandum. 17 Pages. Toxicology review 007745.

Banks PA; Kirby MA; Santelemann PW. 1977. Influence of postemergence and subsurface layered herbicides on horsenettle and peanuts. Weed Sci. 25 (1):5-8.

Barr DB; Barr JR; Driskell WJ; Hill RH Jr; Ashley DL; Needham LL; Head SL; Sampson EJ. 1999. Strategies for biological monitoring of exposure for contemporary-use pesticides. Toxicol Ind Health. 15 (1-2):168-179.

Beasley VR; Arnold EK; Lovell RA. 1991. 2,4-D toxicosis: A pilot study of 2,4-D induced and dicamba-induced myotonia in experimental dogs. Vet Hum Toxicol. 33 (5):435-440.

Beavers J. 1985. Amendment to Report Acute Oral LD50 - Mallard Duck [Using] Banvel Technical: Final Report: Wildlife International Ltd. Project No. 107-151. Unpublished study prepared by Wildlife International Ltd. 2 p. MRID 00159794.

Beavers J. 1986. (Dicamba) - 3 Lb./Gal. Isopropylamine Salt of Dicamba: An Acute Oral Toxicity Study with Bob White: Project No. 107-217. Unpublished study prepared by Wildlife International Ltd. 24 p. MRID 00164105.

Beavers J; Haberlein D; Mitchell L; et al. 1994a. Technical Dicamba: A Reproduction Study with the Mallard: Lab Project Number: 131-183. Unpublished study prepared by Wildlife International Ltd. 178 p. MRID 43814003.

Beavers J; Haberlein D; Mitchell L; et al. 1994b. Technical Dicamba: A Reproduction Study with the Northern Bobwhite: Lab Project Number: 131-182. Unpublished study prepared by Wildlife International Ltd. 178 p. MRID 43814004.

Behrens, R; Lueschen, WE. 1979. Dicamba volatility. Weed Sci. 27(5): 5-8.

Bennick J. 1997. Dicamba DMA Salt: Final Report: Acute Inhalation Toxicity Study in Rats: Lab Project Number: 3863-97. Unpublished study prepared by Stillmeadow, Inc. 20 p. MRID 44502705.

Bennick J. 1998. Acute Inhalation Toxicity Study in Rats: Dicamba Sodium Salt: Final Report: Lab Project Number: 3871-97. Unpublished study prepared by Stillmeadow, Inc. 20 p. MRID 44524405.

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

Blaszcak D. 1994. A Repeated-Dose (21-Day) Dermal Toxicity Study of DGA Salt of Dicamba in the Rabbit: Final Report: Lab Project Number: 94/2326. Unpublished study prepared by Pharmaco LSR, Inc. 206 p. MRID 43554206.

Bohmont BL. 1967. Toxicity of herbicides to livestock, fish, honeybees, and wildlife. Proc. 20th West Weed Control Confer. 21 :25-27.

Bond CE; Fortune JD; Young F. 1965. Results of preliminary bioassays with kurosal-SL and dicamba. Prog Fish Cult. 27 :49-51.

Bovey RW; Meyer RE; Whisenant SG. 1990. Effect of simulated rainfall on herbicide performance in huisache (*Acacia farnesiana*) and honey mesquite (*Prosopis glandulosa*). Weed Technol. 4 (1):26-30.

Boxenbaum H; D'Souza RW. 1990. Interspecies Pharmacokinetic Scaling, Biological Design and Neoteny. Advances in Drug Research. 19 :139-196.

Boyd RS; Miller JH. 1997. Forest herbicide site preparation treatments have little impact on plant diversity 11 years posttreatment. Annual Meeting of the Ecological Society of America held jointly with the Nature Conservancy on changing ecosystems: Natural and human influences. Albuquerque, New Mexico, USA, August 10-14, 1997. Bull Ecol Soc Am. 78 (4 Suppl):58.

Bradlow HL; Davis D; Sepkovic DW; Tiwari R; Osborne MP. 1997. Role of the estrogen receptor in the action of organochlorine pesticides on estrogen metabolism in human breast cancer cell lines. Sci Total Environ. 208 (1-2):9-14.

Brady HA. 1975a. Aspects of dicamba behavior in woody plants. South. Weed Sci Soc Proc. 28 :236-243.

Brady HA. 1975b. Picloram and Dicamba Persistence in Forest Environment. In Southern Weed Science Society, 28th Annual Meeting, Proceedings, Memphis, TN 21-23 January 1975, p. 230-235.

Bromilow RH; Chamberlain K; Evans AA. 1990. Physicochemical aspects of phloem translocation of herbicides. Weed Sci. 38 (3):305-314.

Brown CD; Hollis JM. 1996. SWAT: A semi-empirical model to predict concentrations of pesticides entering surface waters from agricultural land. Pestic Sci. 47 (1):41-50.

Brown LM; Burmeister F; Everett GD; Balir A. 1993. Pesticide exposures and multiple myeloma in Iowa men. Cancer Causes Control. 4 (2):153-156.

Bruns VF; Hodgson JM; Arle HF. 1972. Response of Several Crops to Six Herbicides in Irrigation Water. Tech. Bull. No. 1461, USDA, Washington, DC. (Cited in Caux et al. 1993)

Bryant J. 1993. Letter Sent to R. Taylor dated May 28, 1993 concerning acute avian testing on quail and mallard ducks. Prepared by Sandoz Agro, Inc. 2 p. MRID 42794001.

Bryant J. 1995a. SAN821 H 480 SL 402 DP Product Identity and Composition: Amended: Lab Project Number: 083194-11. Unpublished study prepared by Sandoz Agro, Inc. 49 p. MRID 43643825

Bryant, J. (1995b) SAN 821 H 480 SL 402 DP Analysis and Certification of Product Ingredients: Amended: Lab Project Number: 083194-2. Unpublished study prepared by Sandoz Agro, Inc. 97 p. MRID 43643826

Bryant J; Graben M. 1997. Informative Summary, Aggregate Risk Assessment and Determination of Safety for Dicamba: Lab Project Number: 97/5357. Unpublished study prepared by BASF Corp. 12 p. MRID 44394101.

Budai P; Varnagy LE; Somlyay IM; Varga T. 1997. Ocular irritation study of some pesticides in HET-CAM test. Mededelingen faculteit landbouwkundige en toegepaste biologische wetenschappen universiteit gent. 62 (2A):265-268.

Budavari, S. (Ed). 1989. The Merck Index. 11th ed., Merck & Co., Inc., Rahway, New Jersey.

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

Buser H-R; Muller MD. 1998. Occurrence and transformation reactions of chiral and achiral phenoxyalkanoic acid herbicides in lakes and rivers in Switzerland. Environ Sci Technol. 32 (5):626-633.

C&P Press (Chemical and Pharmaceutical Press). 2003. Greenbook.net. http://www.greenbook.net/. Product Labels and MSDS's for Vanquish and Banvel. Last downloaded October 1, 2003.

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

California Department of Pesticide Regulation. 2002. Summary of Pesticide Use Report Data 2001, Indexed by Chemical. Available at: http://www.cdpr.ca.gov/docs/pur/pur01rep /chmrpt01.pdf.

Campbell S; Beavers J. 1993. Technical Dicamba: An Acute Oral Toxicity Study with the Mallard: Lab Project Number: 131-184A. Unpublished study prepared by Wildlife Intl. Ltd. 22 p. MRID 42774106.

Campbell S; Grimes J; Jaber M. 1993a. Technical Dicamba: An Acute Oral Toxicity Study with the Northern Bobwhite: Lab Project Number: 131-179A: DP 301262. Unpublished study prepared by Wildlife Intl. Ltd. 22 p. MRID 42774105.

Campbell S; Grimes J; Jaber M; et al. 1993b. Technical Dicamba: An Acute Oral Toxicity Study with the Northern Bobwhite: Report Amendment: Lab Project Number: 131-179A. Unpublished study prepared by Wildlife International Ltd. 23 p. MRID 42918001.

Carroll MJ; Hill RL; Pfeil E; Herner AE. 1993. Washoff of dicamba and 3,6-dichlorosalicylic acid from turfgrass foliage. Weed Technol. 7 (2):437-442.

Carroll MJ; Hill RL; Raturi S. 1998. Pesticide transport in turfgrass thatch and foliage. 216th National Meeting of the American Chemical Society, Boston, Massachusetts, USA, August 23-27, 1998. Abstracts of papers American Chemical Society. Agro. 216 (1-3):136.

Casey P; Vale JA. 1994. Deaths from pesticide poisoning in England and Wales: 1945-1989. Human Exper Toxicol. 13 (2):95-101.

Caux PY; Kent RA; Tache M; Grande C; Fan GT; MacDonald DD. 1993. Environmental fate and effects of dicamba: A Canadian perspective. Rev Environ Contam Toxicol. 133 :1-58.

Cessna AJ; Elliott JA; Kerr LA; Best KB; Nicholaichuk W; Grover R. 1994. Transport of nutrients and postemergence-applied herbicides during corrugation irrigation of wheat. J Environ Qual. 23 (5):1038-1045.

Chang FY; Vanden Born WH. 1971. Translocation of dicamba in Canada thistle. Weed Sci. 16 :176-181.

Collins C; Procter B. 1984. The Acute Toxicity of Inhaled Banvel 480 (Banvel Herbicide) In the Albino Rat. (Single Level Screen): Project No. 81974. Unpublished study prepared by Bio Research Laboratories, Ltd. 39 p. MRID 00143011.

Comfort, SD; Inskeep, WP; Macur, RE. 1992. Degradation and transport of dicamba in a clay soil. J. Environ. Qual. 21(4): 653-658.

Cope OB. 1965. Sport Fishery Investigations. In: The Effects of Pesticides on Fish and Wildlife. Circular No. 226, U.S. Fish and Wildlife Service, Columbia, MO. (Cited in Caux et al. 1993)

Cox C. 1994. Dicamba Factsheet. J Pest. Reform. 14(1):30-35.

Craven HT. 1995a. 122-2. Growth and Reproduction of Aquatic Plants - Tier 1. Species Tested: Selenastrum capricornutum. Pages 5-6 removed-registration data. U.S. EPA Ecological Effects Branch. February 22, 1995. DER. 7 Pages. MRID No. 427741-07.

Craven HT. 1995b. 123-2. Growth and Reproduction of Aquatic Plants - Tier 2. Species Tested: Anabaena flos-aquae. U.S. EPA Ecological Effects Branch. February 22, 1995. DER. 9 Pages. Pages 6-7 removed-registration data. MRID No. 427741-09.

Craven HT. 1995c. 123-2. Growth and Reproduction of Aquatic Plants - Tier 2. Species Tested: Duckweed (Lemna gibba). U.S. EPA Ecological Effects Branch. February 22, 1995. DER. 9 Pages. Pages 6-8 removed-registration data. MRID No. 427741-11.

Craven HT. 1995d. 123-2. Growth and Reproduction of Aquatic Plants - Tier 2. Species Tested: Navicula pelliculosa. U.S. EPAEcological Effects Branch. February 22, 1995. DER. 9 Pages. Pages 6-7 removed-registration data. MRID No. 427741-08.

Craven HT. 1995e. 123-2. Growth and Reproduction of Aquatic Plants - Tier 2. Species Tested: Skeletonema costatum. U.S. EPA Ecological Effects Branch. February 22, 1995. DER. 9 Pages. Pages 6-7 removed-registration data. MRID No. 427741-10.

Crome S; Stuart V; Anderson A; et al. 1987. Dicamba: Potential Tumorigenic Effects in Prolonged Dietary Administration to Mice: Report No. VCL 72/871205. Unpublished study prepared by Huntingdon Research Centre Ltd. 966 p. MRID 40872401.

Crosswhite F; Feldman W; Minch E. 1993. Impact of Pesticides on Cacti: Lab Project Number: E-009572-01-0. Unpublished study prepared by University of Arizona and Arizona Dept. of Agriculture. 33 p. MRID 43329501.

Cullimore DR. 1975. The *in vitro* sensitivity of some species of Chlorophyceae to a selected range of herbicides. Weed Res. 15 :401-406.

Current F; Thoma B; Fletcher D; et al. 1980. Final Report to Velsicol Chemical Corporation: Chronic Oral/Carcinogenic Toxicity Study with Dicamba (Technical Banvel) in Swiss White Mice: IBT No. 8580-10130. (Unpublished study received Aug 3, 1983 under unknown admin. no.; prepared by Industrial Bio-Test Laboratories, Inc., submitted by Velsicol Chemical Corp., Chicago, IL; CDL:2150920-A; 250928). MRID 00129986.

Davidson, LW; Parker, JC; Beliles, RP. 1986. Biological basis for extrapolation across mammalian species. Reg. Toxicol. Pharmacol. 6: 211-237.

Davis RK; Jolley WP; Stemmer KL; et al. 1962. The Feeding for Two Years of the Herbicide 2-Methoxy-3,6-dichlorobenzoic Acid to Rats and Dogs. Unpublished study. MRID 00028248.

De Sapio R. 1976. Calculus for the Life Sciences. W.H. Freeman and Company, San Francisco, California. 740 pp.

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

Derksen DA. 1989. Dicamba, chlorsulfuron, and clopyalid as sprayer contaminants on sunflower (*Helianthus annus*), mustard (*Brassica juncea*), and lentil (*Lens culinaris*), respectively. Weed Sci. 37 :616-621.

Doubovetzky M. 1997. Dicamba TC: 13-Week Feeding Study in Rats. (including 4-week recovery): Lab Project Number: 602R: 97/059: BS 12389. Unpublished study prepared by Novartis Crop Protection AG. 591 p. MRID 44623101.

Dowdy DL; Mckone TE; Hsieh DPH. 1996. Prediction of chemical biotransfer of organic chemicals from cattle diet into beef and milk using the molecular connectivity index. Environ Sci Technol. 30 (3):984-989.

Draper WH; Street JC. 1982. Applicator exposure to 2,4-D, dicamba and a dicamba isomer. J Environ Sci Health. B17 (4):321-339.

Drench G. 1986. (Dicamba) One Year Dietary Toxicity Study in Dogs: Laboratory Project I.D. 163-696. Unpublished study pre pared by International Research and Development Corp. 268 p. MRID 40321102.

Durkin PR; Diamond G. 2002. Neurotoxicity, Immunotoxicity, and Endocrine Disruption with Specific Commentary on Glyphosate, Triclopyr, and Hexazinone: Final Report. SERA TR 01-43-08-04a dated January 30, 2002. Available at www.fs.fed.us/foresthealth/pesticide/risk.htm.

Durkin P; Rubin L; Meylan W; Withey JR. 1995. Methods of Assessing Dermal Absorption with Emphasis of Uptake from Contaminated Surfaces. Toxicol Indust Health. 11 (1):63-79.

Ecobichon DJ. 1998. Occupational Hazards of Pesticide Exposure – Sampling, Monitoring, Measuring. Taylor & Francis, Philadelphia, PA. 251 pp.

Edson EF; Sanderson DM. 1965. Toxicity of the herbicides 2-methoxy-3,6-dichlorobenzoic acid (dicamba) and 2-methoxy-3,5,6-trichlorobenzoic acid (tricamba). Food Cosmet Toxicol. 3 :299-304.

Edwards GR; Crawley MJ; Heard MS. 1999. Factors influencing molehill distribution in grassland: Implications for controlling the damage caused by molehills. J Appl Ecol. 36 (3):434-442.

Eisenbeis SJ; Lynch DL; Hampel AE. 1981. The Ames mutagen assay tested against herbicides and herbicide combinations. Soil Sci. 131 (1):44-47.

Ekdawi M; Yu C; Sherman S. 1994. Dicamba: Physiological Dissociation of Amine Salts in Rats: Lab Project Number: 480065: 27: DP-301542. Unpublished study prepared by Sandoz Agro, Inc. 105 p. MRID 43288002.

Espandiari P; Thomas VA; Glauert HP; O'Brien M; Noonan D; Robertson LW. 1995. The herbicide dicamba (2-methoxy-3,6-dichlorobenzoic acid) is a peroxisome proliferator in rats. Cooperative Agreement No. U07-CCU-408035. Fundam Appl Toxicol. 26 (1):85-90.

Espandiari P; Glauert HP; Lee EY; Robertson LW. 1999. Promoting activity of the herbicide dicamba (2-methoxy-3,6-dichlorobenzoic acid) in two stage hepatocarcinogenesis. Int J Oncol. 14 (1):79-84.

Fairchild JF; Ruessler DS; Haverland PS; Carlson AR. 1997. Comparative sensitivity of Selenastrum capricornutum and Lemna minor to sixteen herbicides. Arch Environ Contam Toxicol. 32 (4):353-357.

FAO/WHO (Food and Agricultural Organization of the United Nations). 2001. FAO Specifications and Evaluations for Plant Protection Product: Dicamba (3,6-dichloro-2-methoxy-benzoic acid). Available at: http://www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/Specs/pdf/dicamba.pdf.

Ferguson GP; Coats GE; Wilson GB; Shaw DR. 1992. Postemergence control of wild garlic (*Allium vineale*) in turfgrass. Weed Technol. 6 (1):144-148.

Filkins K. 1998. Pesticides. Reprod Hazards Workplace. 92-256.

Fink R. 1977a. Acute Oral LD50. Mallard Duck. Banvel Technical. Final Report. Wildlife International Inc. November 3, 1977. Review. 2 Pages. Accession No. 232965.

Fink R. 1977b. Eight-day Dietary LC50. Bobwhite Quail. Banvel Technical, Final Report. Wildlife International Ltd. November 10, 1977. Review. 2 Pages. Accession No. 232965.

Fink R. 1977c. Eight-day Dietary LC50. Mallard Duck Banvel Technical, Final Report. Wildlife International Ltd. November 3, 1977. Review. 2 Pages. Accession No. 232965.

Flanagan RJ; Meredith TJ; Ruprah M; Onyon LJ; Liddle A. 1990. Alkaline diuresis for acute poisoning with chlorophenoxy herbicides and ioxynil. Lancet. 335 (8687):454-458.

Fletcher JS; Johnson FL; McFarlane JC. 1990. Influence of greenhouse versus field testing and taxonomic differences on plant sensitivity to chemical treatment. Environ Toxicol Chem. 9 :769-776.

Fletcher JS; Nellessen JE; Pfleeger TG. 1994. Literature review and evaluation of the EPA food-chain (Kenega) nomogram, an instrument for estimating pesticide residues on plants. Environ. Toxicol. Chem. 13(9):1383-1391.

Forbis A; Burgess D; Georgie L. 1985. Acute Toxicity of CN 10-6471 [(Banvel Herbicide)] to Daphnia magna: Report No. 33173. Unpublished study prepared by Analytical Bio-chemistry Laboratories, Inc. 37 p. [(Banvel Herbicide)] to Daphnia magna: Report No. 33173. Unpublished study prepared by Analytical Bio-chemistry Laboratories, Inc. 37 p. MRID 00153152.

Forbis A; Frazier S. 1986. Acute Toxicity of CN-11-4962 to Daphnia magna: Static Acute Toxicity Report #34107. Unpublished study prepared by Analytical Bio-Chemistry Laboratories, Inc. 41 p. MRID 00162069.

Formanski L. 1995. Confirmation of Dicamba and 3,6-dichlorosalicylic Acid Residues Detected in Goat Liver and Kidney from a Dicamba Metabolism Study Conducted at SAI: Final Report: Lab Project Number: 480068: 134: DP/301753. Unpublished study prepared by Sandoz Agro Analyt. MRID 43554205.

Fortune CR. 1998. Evaluation of Methods for Collecting Dislodgeagle Pesticide Residues from Turf. Govt Reports Announcements & Index (GRA&I), Issue 11.

Francis BM; Lampman RL; Metcalf RL. 1985. Model ecosystem studies of the environmental fate of five herbicides used in conservation tillage. Arch Environ Contam Toxicol. 14 :693-704.

Fostiak W; Yu CC. 1989. Determination of n-octanol/water partition coefficient for 2,6-dichlorosalicylic acid. MRID 419666-01.

Frank, R; Logan, L. 1988. Pesticide and industrial chemical residues at the mouth of the Grand, Saugeen, and Thames Rivers Ontario Canada 1981-1985. Arch. Environ. Contam. Toxicol. 17(6): 741-754.

Frank, R; Stripnieks, AJ; Clegg, BS. 1987. A system for rinsing herbicide residues form drums during highway right-of-way spray operations. Bull Environ. Contam. Toxicol. 39(4): 680-687.

Frank, R; Braun, HE; Ripley, BD; Clegg, BS. 1990a. Contamination of rural ponds with pesticide 1971-85. Ontario Canada. Bull. Environ. Contam. Toxicol. 44(3): 401-409.

Frank, R; Braun, HE; Clegg, BS; Ripley, BD; Johnson, R. 1990b. Survey of farms wells for pesticides Ontario Canada 1986 and 1987. Bull. Environ. Contam. Toxicol. 44(3): 410-419.

Frank, R; Logan, L; Clegg, BS. 1991. Pesticide and polychlorinated biphenyl residues in waters at the mouth of the Grand, Saugeen, and Thames Rivers, Ontario, Canada, 1986-1990. Arch Environ. Contam. Toxicol. 21(4): 585-595.

Fraser, AD; Isner, AF; Perry, RA. 1984. Toxicologic Studies in a Fatal Overdose of 2,4-D, Mecoprop, and Dicamba. J Forensic Sci. 29(4):1237-1241.

Frear DS. 1976. The Benzoic Acid Herbicides. In: Kearney, PC; Kaufman, DD. (eds). Herbicides: Chemistry, Degradation, and Mode of Action. 2nd ed, Marcel Dekker, New York. pp. 541-607.

Fricke R. 1995. Dicamba - Review of Subchronic Neurotoxicity Study (82-7). U.S. EPA Toxicology Branch. April 12, 1995. Memorandum. 15 Pages. Pages 10-14 removed, registrant data. Tox review 011493. MRID 432452-10.

Funari E. 1995. Human health implications associated with the presence of pesticides in drinking water. Pesticide risk in groundwater. Vighi, M and E. Funari (Ed.). CRC Press, Inc.: Boca Raton, Florida ISBN 0-87371-439-3.; 0 (0):121-130.

Gaines TB; Linder RE. 1986. Acute toxicity of pesticides in adult and weanling rats. Fund Appl Toxicol. 7 (2):299-308.

Garry VF; Schreinemachers D; Harkins ME; Griffith J. 1996. Pesticide appliers, biocides, and birth defects in rural Minnesota. Environ Health Perspect. 104 (4):394-399.

Geno PW; Camann DE; Harding HJ; Villalobos K; Lewis RG. 1996. Handwipe sampling and analysis procedure for the measurement of dermal contact with pesticides. Arch Environ Contam Toxicol. 30 (1):132-138.

Ghassemi M; Fargo L; Painter P; Quinlivan S; Scofield R; Takata A. 1981. Environmental Fates and Impacts on Major Forest Use Pesticides. U.S. EPA Contract No. 68-02-3174. Prepared by TRW Environ. Div., Redondo, CA. NTIS# PB83-124552.

Gladen BC; Sandler DP; Zahm SH; Kamel F; Rowland AS; Alavanja MCR. 1998. Exposure opportunities of families of farmer pesticide applicators. Am J Ind Med. 34 (6):581-587.

Gold, AJ; Morton, TG; Sullivan, WM; McClory, J. 1988. Leaching of 2,4-D and dicamba form home lawns. Water Air Soil Pollut. 37(1-2): 121-130.

Goldenthal EI; Wazeter FX; Dean WP. 1972. Acute Toxicity Studies in Rats and Rabbits: IRDC No. 163-114. (Unpublished study received Sep 25, 1972 under 2G1259; prepared by International Research and Development Corp., submitted by Velsicol Chemical Corp., Chicago, IL.; CDL:091790-C). MRID 00057555.

Goldenthal EI; Jessup DC; Rodwell DE. 1978. Teratology Study in Rabbits: IRDC No. 163-436. (Unpublished study received March 6, 1979 under 876-36; prepared by International Research and Development Corp., submitted by Velsicol Chemical Corp., Chicago, IL.; CDL:237995-E). MRID 00028236.

Goldenthal EI; Estes FL; Geil RG. 1979. 3-week Dermal Toxicity Study in Rabbits: IRDC No. 163-618. (Unpublished study received Apr 20, 1981 under 876-25; prepared by International Research and Development Corp., submitted by Velsicol Chemical Corp., Chicago, IL.; CDL:070030-K). MRID 00128091.

Goldenthal E; Jefferson N. 1982. Dicamba: Lifetime Dietary Toxicity and Oncogenicity Study in Rats: 163-694. (Unpublished study received Feb 1, 1983 under 876-36; prepared by International Research and Development Corp., submitted by Velsicol Chemical Corp., Chicago, IL; CDL:249425-A). MRID 00125333.

Goldenthal E. 1985. Lifetime Dietary Toxicity and Oncogenicity Study in Rats: Technical Dicamba: 163-694. Unpublished study prepared by International Research and Development Corp. 2101 p. MRID 00146150.

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.

Green LM. 1991. A cohort mortality study of forestry workers exposed to phenoxy acid herbicides. Br J Ind Med. 48 (4):234-238.

Griffin JL; Watson VH; Knight WE; Cole AW. 1984. Forage legume response to dicamba and 2,4-D applications. Argon J. 76 :487-490.

Grimes J. 1986a. CN-11-4962 4 LB/Gal Diglycolamine Salt of Dicamba: An Acute Oral Toxicity Study with the Bobwhite: Final Re port: Project No. 107-227. Unpublished study prepared by Wildlife International Ltd. 23 p. MRID 00162070.

Grimes J. 1986b. CN-11-4962 4 LB/Gal Diglycolamine Salt of Dicamba: A Dietary LC50 Study with the Bobwhite: Final Report: Project No. 107-225. Unpublished study prepared by Wildlife International Ltd. 20 p. MRID 00162071.

Grimes J. 1986c. CN-11-4962 4 LB/Gal Diglycolamine Salt of Dicamba: A Dietary LC50 Study with the Mallard: Final Report: Project No. 107-226. Unpublished study prepared by Wildlife International Ltd. 16 p. MRID 00162072.

Guirguis A; Yu C. 1994. Metabolism of Dicamba in Lactating Goats: Laboratory Final Report: Lab Project Number: 480065: 28: 114-002-12. Unpublished study prepared by Sandoz Agro, Inc. 156 p. MRID 43245201.

Hamilton KC; Arle HF. 1979. Response of cotton (*Gossypium hirsutum*) to dicamba. Weed Sci. 27 (6):604-607.

Hang SB; Ferreiro EA; de Bussetti SG. 1996. Picloram, dicamba and imazaquin mobility. Investigacion Agraria Produccion y Proteccion Vegetales. 11 (2):345-361.

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.

Hartwig NL. 1980. Alfalfa and Dandelion Control for No-Tillage Corn in an Old Alfalfa Sod. Porc Northeast Weed Soc. 34 :75.

Hashimoto Y; Nishiuchi Y. 1981. Establishment of bioassay methods for the evaluation of acute toxicity of pesticides to aquatic organisms. J Pestic Sci. 6 (2):257-264.

Hassan SA; Hafes B; DeGrande PE; Herai K. YEAR? The side-effects of pesticides on the egg parasitoid Trichogramma cacoeciae Marchal (Hym., Trichogrammatidae), acute dose-response and persistence tests. J Appl Entomol. 122 (9-10):569-573.

Hastings C. 1998. Dicamba: Toxicology Summary and Risk Assessment with Expanded Discussion of Mutagenicity and Carcinogenicity: Lab Project Number: 98/5142: 02B0266/976009. Unpublished study prepared by BASF Corp. 56 p. MRID 44609802.

Hayes WJ. 1982. Pesticides Studied in Man. Williams and Wilkins, Baltimore, MD. (Cited in Caux et al. 1993)

Hill EF; Camardese MB. 1986. Lethal Dietary Toxicities of Environmental Contaminants and Pesticides to *Coturnix*. Fish and Wildlife Technical Report No 2. U.S. Fish and Wildlife Service, Washington, DC.

Hoberg J. 1993a. Dicamba Technical: Determination of Effects on Seed Germination, Seedling Emergence and Vegetative Vigor of Ten Plant Species: Final Report: Lab Project Number: 93-3-4664: 10828.0892.6141.610: 301321. Unpublished study prepared by Springborn Labs, Inc. 2. MRID 42846301.

Hoberg J. 1993b. Dicamba Technical: Toxicity to the Duckweed, Lemna Gibba: Final Report: Lab Project Number: 93-3-4665: 10828.0892.6140.410: 100/92/06. Unpublished study prepared by Springborn Labs, Inc. 61 p. MRID 42774111.

Hoberg J. 1993c. Dicamba Technical: Toxicity to the Freshwater Alga, Anabaena flos-aquae: Final Report: Lab Project Number: 93-3-4702: 10828.0892.6139.420: 100/92/02. Unpublished study prepared by Springborn Labs, Inc. 605 p. MRID 42774109.

Hoberg J. 1993d. Dicamba Technical: Toxicity to the Freshwater Diatom, Navicula pelliculosa: Final Report: Lab Project Number: 92-11-4512: 10828.0892.6137.440: 100/92/03. Unpublished study prepared by Springborn Labs, Inc. 60 p. MRID 42774108.

Hoberg J. 1993e. Dicamba Technical: Toxicity to the Freshwater Green Alga, Selenastrum capricornutum: Final Report: Lab Project Number: 92-11-4498: 10828.0892.6136.430: 100/92/04. Unpublished study prepared by Springborn Labs, Inc. 59 p. MRID 42774107.

Hoberg J. 1993f. Dicamba Technical: Toxicity to the Marine Diatom, Skeletenoma costatum: Final Report: Lab Project Number: 93-3-4699: 10828.0892.6138.450: 100/92/05. Unpublished study prepared by Springborn Labs, Inc. 59 p. MRID 42774110.

Hoberman A. 1992. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of Technical Dicamba Administered Orally via Capsule to New Zealand White Rabbits: Final Report: Lab Project Number: 1819-004. Unpublished study prepared by Argus Research Lab. 420 p. MRID 42429401.

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.

Hoffman DJ; Albers PH. 1984. Evaluation of potential embryotoxicity and teratogenicity of 42 herbicides, insecticides, and petroleum contaminants to mallard (*Anas platyrhynchos*) eggs. Arch Environ Contam Toxicol. 13 (1):15-28.

Hogstedt C; Westerlund B. 1980. Cohort study of the fatality causes in forest workers exposed and unexposed to phenoxy acid preparations. Lakartidningen. 77 :1828-1831.

Hrelia P; Vigagni F; Maffei F; Morotti M; Colacci A; Perocco P; Grilli S; Contelli-Forti G. 1994. Genetic safety evaluation of pesticides in different short-term tests. Mutat Res. 32 (4):219-228.

Hughes JS; Davis JT. 1962. Comparative toxicity to bluegill sunfish of granular and liquid herbicides. Proc Conf Southeast Assoc Game Fish. 16 :319-323.

Hurlbert SH. 1975. Secondary effects of pesticides on aquatic ecosystems. Residue Rev. 57 :81-148.

Hutchinson C. 1984. Transfer Of Dicamba Residues To Tissues And Eggs Of Laying Hens: Final Report: Project No. 107-203. Unpublished study prepared by Wildlife International Ltd. 119 p. MRID 00146369.

Incledon BJ; Hall JC. 1997. Acetyl-coenzyme A carboxylase: Quaternary structure and inhibition by graminicidal herbicides. Pestic Biochem Physiol. 57 (3):255-271.

Inskeep WP; Wraith JM; Wilson JP; Snyder RD; Macur RE; Gaber HM. 1996. Input parameter and model resolution effects on predictions of solute transport. J Environ Qual. 25 (3):453-462.

Ivany JA; Nass HG. 1984. Effect of herbicides on seedling growth, head deformation and grain yield of spring wheat cultivars. Can J Plant Sci. 64 :25-30.

Johnson BJ. 1985. Toxicity of Turfgrass Herbicides to Woody Ornamentals. Research Report 489. Georgia Agriculture Experiment Stations, College of Agriculture, University of Georgia, Athens.

Johnson CR. 1976. Herbicide toxicities in some Australian anurans and the affect of subacute dosages on temperature tolerance. Zool J Linn Soc. 59 (1):79-83.

Johnson CR. 1978. Herbicide toxicities in the mosquito fish, *Gambusia affinis*. Proc Res Soc Queensl. 89 :25-27.

Johnson WW; Finley MT. 1980. Handbook of Acute Toxicity of Chemicals to Fish and Aquatic Invertebrates. Resource publication 137. U.S. Fish and Wildlife Service, Washington, DC.

King DL; Mostats M; Winslow N. 1993. Adjuvant effects on the delivery of dicamba and its salts. Pestic Sci. 38 (2-3):263-266.

Kocialski A. 1980. Subacute Inhalation Study in Rats. Inert Ingredient and Ingredient Source Material Deleted From Page 1. U.S. EPA Toxicology Branch. July 25, 1980. Memorandum. 8 Pages. EPA Reg. No. 876-25. Banvel 4S (Herbicide). Accession No. 242155. Caswell #295.

Kookana RS; Baskaran S; Naidu R. 1998. Pesticide fate and behaviour in Australian soils in relation to contamination and management of soil and water: A review. Aust J Soil Res. 36 (5):715-764.

Koskinen WC; Sorenson BA; Buhler DD; Wyse DL; Lueschen WE; Cheng HH. 1997. Use of field lysimeters to determine the persistence and movement of 14c-dicamba in soil. 213th National Meeting of the American Chemical Society, San Francisco, California, USA, April 13-17, 1997. Abstracts of papers American Chemical Society. Agro. 213 (1-3):58.

Knisel WG; Davis FM. 2000. GLEAMS (Groundwater Loading Effects of Agricultural Management Systems), Version 3.0, User Manual. U.S. Department of Agriculture, Agricultural Research Service, Southeast Watershed Research Laboratory, Tifton, GA. Pub. No.: SEWRL-WGK/FMD-050199. Report Dated May 1, 1999 and revised August 15, 2000. 194pp.

Kreuger J. 1998. Pesticides in stream water within an agricultural catchment in southern Sweden, 1990-1996. Sci Total Environ. 216 (3):227-251.

Krueger JP; Hsieh T; Butz RG; Atallah YH. 1988. Anaerobic Soil Metabolism of Dicamba. MRID 405479-06.

Kreuger J; Peterson M; Lundgren E. 1999. Agricultural inputs of pesticide residues to stream and pond sediments in a small catchment in southern Sweden. Bull Environ Contam Toxicol. 62 (1):55-62.

Krzyszowska AJ; Allen RD; Vance GF. 1994. Assessment of the fate of two herbicides in a Wyoming rangeland soil: Column studies. J Environ Qual. 23 (5):1051-1058.

Krzywszowska-Waitkus AJ; Allen RD; Vance GF; Zhang R; Legg DE. 1999. A field lysimeter study to evaluate herbicide transport in a Wyoming irrigated pasture. Commun Soil Sci Plant Anal. 30 (1-2):245-263.

Kuhn J. 1997. Dicamba DMA Salt: Primary Dermal Irritation Study in Rabbits: Final Report: Lab Project Number: 3865-97. Unpublished study prepared by Stillmeadow, Inc. 13 p. MRID 44502707.

Kuhn J. 1998a. Acute Dermal Toxicity Study in Rabbits: Dicamba Sodium Salt: Final Report: Lab Project Number: 3870-97. Unpublished study prepared by Stillmeadow, Inc. 12 p. MRID 44524404.

Kuhn J. 1998b. Acute Oral Toxicity Study in Rats: Dicamba Sodium Salt: Final Report: Lab Project Number: 3869-97. Unpublished study prepared by Stillmeadow, Inc. 11 p. MRID 44524403.

Kuhn J. 1998c. Dermal Sensitization Study in Guinea Pigs: Dicamba Sodium Salt: Final Report: Lab Project Number: 3874-97: 3537-97. Unpublished study prepared by Stillmeadow, Inc. 18 p. MRID 44524408.

Kuhn J. 1998d. Dicamba DMA Salt: Dermal Sensitization Study in Guinea Pigs: Final Report: Lab Project Number: 3866-97. Unpublished study prepared by Stillmeadow, Inc. 18 p. MRID 44502708.

Kuhn J. 1998e. Dicamba DMA Salt: Final Report: Acute Dermal Toxicity Study in Rabbits: Lab Project Number: 3862-97. Unpublished study prepared by Stillmeadow, Inc. 12 p. MRID 44502704.

Kuhn J. 1998f. Dicamba DMA Salt: Final Report: Acute Oral Toxicity Study in Rats: Lab Project Number: 3861-97. Unpublished study prepared by Stillmeadow, Inc. 18 p. MRID 44502703.

Kuhn J. 1998g. Dicamba DMA Salt: Final Report: Primary Eye Irritation Study in Rabbits: Lab Project Number: 3864-97. Unpublished study prepared by Stillmeadow, Inc. 17 p. MRID 44502706.

Kuhn J. 1998h. Primary Eye Irritation Study in Rabbits: Dicamba Sodium Salt: Final Report: Lab Project Number: 3872-97: S9-FF81-4-6. Unpublished study prepared by Stillmeadow, Inc. 17 p. MRID 44524406.

Kuhn J. 1998i. Primary Dermal Irritation Study in Rabbits: Dicamba Sodium Salt: Final Report: Lab Project Number: 3873-97: S9-FF81-5. Unpublished study prepared by Stillmeadow, Inc. 13 p. MRID 44524407.

Kurinnyi AI; Pilinskaya MA; German IV; L'Vova TS. 1982. Implementation of a program of cytogenic study of pesticides: Preliminary evaluation of cytogenic activity and potential mutagenic hazard of 24 pesticides. Tsitol Genet. 16 :45-49.

Lampman W. 1995. Susceptibility of groundwater to pesticide and nitrate contamination in predisposed areas of southwestern Ontario. Water Qual Res J Can. 30 (3):443-468.

Laveglia J; Rajasekaran D; Brewer L. 1981. Thirteen-week Dietary Toxicity Study in Rats with Dicamba. IRDC No. 163-671. Unpublished study. MRID 00128093.

Lehman AJ. 1959. Appraisal of the Safety of Chemicals in Food, Drugs, and Cosmetics. Association of Food and Drug Officials. (Cited in Caux et al. 1993)

Leibold E; Hoffmann H; Hildebrand B. 1998. Report: (carbon 14)-Dicamba--Study of the Plasma Kinetics in Rats: Lab Project Number: 02B0266/976009: BASF 98/10553. Unpublished study prepared by BASF Aktiengesellschaft. 56 p. MRID 44609801.

Leifer Z; Kada T; Mandel L; Zeiger E; Stafford R; Rosenkranz HS. 1981. An evaluation of tests using DNA repair-deficient bacteria for predicting genotoxicity and carcinogenicity. A report of the U.S. EPA's Gene Tox Program. Mutat Res. 87 :211-297.

Lorz HW; Glenn SW; Williams RH; Kunkel CM; Norris LA; Loper BR. 1979. Effects of Selected Herbicides on Smolting of Coho Salmon. Ecological Res. Series, EPA-600/3-79-071. Corvallis Environ. Lab. U.S. EPA, Corvallis, OR.

Lusby AF; Simmons Z; McClure PM. 1979. Variation in mutagenicity of *s*-triazine compounds tested on four Salmonella strains. Environ Mutagen. 1 :287-290.

Ma TH; Xu Z; Cabrera GL; Valtierra RM; Arreola GG. 1987. The efficacy of the root tip cell micronucleus assay for water pollutants. Environ Mutat. 9 (Suppl 8):65-66.

Maciorowski A. 1995. Review Guideline Series 123-1, 71-1, 123-2. Dicamba Herbicide: Data Review (D192304, D193254). U.S. EPA Ecological Effects Branch. March 24, 1995. Memorandum. 11 Pages. Page 11 removed, registrant data. MRID Nos. 429180-01, 427741-06 thru 11 & 428463-01.

Magnusson MU; Wyse DL. 1987. Tolerance of soybean (*Glycine max*) and sunflower (*Helianthus annuus*) to fall-applied dicamba. Weed Sci. 35 :846-852.

Makary MH; Street JC; Sharma RP. 1986a. Toxicokinetics of dicamba, 3,6-dichloro-2-methoxybenzoic-acid and its 3,5-dichloro isomer following intravenous administration to rats. Pestic Biochem Physiol. 25 (1):98-104.

Makary MH; Street JC; Sharma RP. 1986b. Pharmacokinetics of dicamba isomers applied dermally to rats. Pestic Biochem Physiol. 25 (2):258-263.

Malish SL. 1993. Dicamba: Developmental Toxicity Study in Rabbits. Memorandum to Robert Taylor and Vickie Walters dated October 5, 1993. Obtained under Freedom of Information Act Request to Janet Bressant, U.S. EPA/OPP.

Martens DA; Bremner JM. 1993. Influence of herbicides on transformations of urea nitrogen in soil. J Environ Sci Health Part B Pestic Food Contam Agric Wastes. 28 (4):377-395.

Masters R. 1993. Technical Dicamba: A Study of the Effect on Reproductive Function of Two Generations in the Rat: Lab Project Number: SNC 140/921437. Unpublished study prepared by Huntingdon Research Centre Ltd. 392 p. MRID 43137101.

McAllister W; Bowman J; Cohle P. 1985a. Acute Toxicity of CN 10-6471 [(Banvel Herbicide)] to Bluegill Sunfish. (Lepomis macrochirus): Report No. 33171. Unpublished study prepared by Analytical Bio-chemistry Laboratories, Inc. 53 p. MRID 00153150.

McAllister W; Bowman J; Cohle P. 1985b. Acute Toxicity of CN 10-6471 [(Banvel Herbicide)] to Rainbow Trout. (Salmo gairdneri): Report No. 33172. Unpublished study prepared by Analytical Biochemistry Laboratories, Inc. 58 p. MRID 00153151.

Mersch-Sundermann V; Schneider U; Klopman G; Rosenkranz HS. 1994. SOS induction in Escherichia coli and Salmonella mutagenicity: A comparison using 330 compounds. Mutagenesis. 9 (3):205-224.

Menetrez M. 1996. Dicamba Amine Salts 84-2; Micronucleus Assay in Mice (IPA Salt) Pages 8, 10, 18, 20, 30, 32 removed, registrant data. U.S. EPA Toxicology Branch. April 17, 1996. DER. 32 Page(s). Tox review 012293 (excerpt). MRID 43354334.

Meylan, WM; Howard, PH. 1991. Bond contribution method for estimating henry's law constant. Environ. Toxicol. Chem. 10: 1283-1293.

Meylan, WM; Howard, PH; Boethling, RS. 1992. Molecular topology/fragment contribution method for predicting soil sorption coefficients. Environ. Sci. Technol. 26: 1560-1567.

Meylan, WM; Howard, PH. 1993. Computer estimation of the atmospheric gas-phase reaction rate of organic compounds with hydroxyl radicals and ozone. Chemosphere 26: 2293-2299.

Meylan, WM; Howard, PH. 1995. Atom/Fragment contribution method for estimating octanol-water partition coefficients. J. Pharm. Sci. 84: 83-92.

Miller JH; Boyd RS; Edwards MB. 1999. Floristic diversity, stand structure, and composition 11 years after herbicide site preparation. Can J Forest Res. 29 (7):1073-1083.

Miller JJ; Foroud N; Hill BD; Lindwall CW. 1995a. Herbicides in surface runoff and groundwater under surface irrigation in southern Alberta. Can J Soil Sci. 75 (1):145-148.

Miller JJ; Hill BD; Lindwall CW. 1995b. Residue detections in soil and shallow groundwater after long-term herbicide applications in southern Alberta. Can J Soil Sci. 75 (3):349-356.

Minnema D. 1993. Acute Neurotoxicity Study of Technical Dicamba by Gavage in Rats: Final Report: Lab Project Number: HWA 686-177. Unpublished study prepared by Hazleton Washington, Inc. 475 p. MRID 42774104.

Minnema D. 1994. Subchronic Neurotoxicity Study of Dietary Technical Dicamba in Rats: Final Report: Lab Project Number: HWA 686-178: 535: 0686178. Unpublished study prepared by Hazleton Washington, Inc. 426 p. MRID 43245210.

Minotti PL; Hughes BJ; Sweet RD; Warholic DT. 1980. Sweet Corn and Weed Response to Differently Timed Post Emergence Application of Atrazine, 2,4-D, Dicamba, and Metolachlor. Vegetable Crops Dept, Cornell Univ, Ithaca, NY. (Cited in Caux et al. 1993)

Mohammad K; Ma T. 1983. Tradescantia-micronucleus (TRAD-MCN) tradescantia-stamen hair mutation (TRAD-SHM) tests on mutagenicity of common pesticides. Environ Mutagen. 5 :370-371.

Mohammed KB; Ma TH. 1999. Tradescantia-micronucleus and -stamen hair mutation assays on genotoxicity of the gaseous and liquid forms of pesticides. Mutat Res. 426 (2):193-199.

Moody DE; Narloch BA; Shull LR; Hammock BD. 1991. The effect of structurally divergent herbicides on mouse liver xenobiotic-metabolizing enzymes (P-450-dependent monooxygenases, epoxide hydrolases and glutathione S-transferases) and carnitine acetyltransferase. Toxicol Lett. 59 (1-3):175-186.

Moreland DE. 1999. Biochemical mechanisms of action of herbicides and the impact of biotechnology on the development of herbicides. J Pestic Sci. 24 (3):299-307.

Moriya M; Ohta T; Watanabe K; Miyazawa T; Kato K; Shirasu Y. 1983. Further mutagenicity studies on pesticides in bacterial reversion assay systems. Mutat Res. 116 (3-4):185-216.

Morrison JI; Wilkins K; Semenciw R; Mao Y; Wigle D. 1992. Herbicides and cancer. J Natl Cancer Inst. 84 (24):1866-1874.

Morton HL; Robinson ED; Meyer RE. 1967. Persistence of 2,4-D, 2,4,5-T, and dicamba in range forage grasses. Weeds. 15 :268-271.

Muir D CG; Grift NP. 1995. Fate of herbicides and organochlorine insecticides in lake waters. Ragsdale NN, Kearney PC, Plimmer JR (eds.). ACS Conference Proceedings Series: Eighth International Congress of Pesticide Chemistry Options 2000 Conference. Washington, DC, USA, July 4-9, 1994. Xiv+450p. American Chemical Society, Washington, DC, USA. ISBN 0-8412-2995-3. 0 (0):141-156.

Mukerjee S; Ellenson WD; Lewis RG; Stevens RK; Somerville MC; Shadwick DS; Willis RD. 1997. An environmental scoping study in the Lower Rio Grande Valley of Texas: III. Residential microenvironmental monitoring for air, house dust, and soil. Environ Int. 23 (5):657-673.

Nalewaja JD; Matysiak R. 1993. Spray carrier salts affect herbicide toxicity to kochia (*Kochia scoparia*). Weed Technol. 7 (1):154-158.

Nash, RG. 1989. Volatilization and dissipation of acidic herbicides from soil under controlled conditions. Chemosphere. 18(11-12): 2363-2374.

Neary, DG; Bush, PB; Michaels, JL. 1993. Fate, dissipation and environmental effects of pesticides in southern forests: A review of a decade of research progress. Environ. Toxicol. Chem. 12: 411-428.

Neely D; Crowley WR. 1974. Toxicity of soil-applied herbicides to shade trees. Hort Sci. 9 (2):147-149.

Nietschmann D; Yu C. 1994. Dicamba: Metabolism in Laying Hens: Laboratory Final Report: Lab Project Number: 480065: 25: DP301493. Unpublished study prepared by Sandoz Agro, Inc. 80 p. MRID 43245202.

Nishioka MG; Burkholder HM; Brinkman MC; Gordon SM; Lewis RG. 1996. Measuring transport of lawn-applied herbicide acids from turf to home: Correlation of dislodgeable 2,4-D turf residues with carpet dust and carpet surface residues. Environ Sci Technol. 30 (11):3313-3320.

Nishioka MG; Burkholder HM; Brinkman MC; Gordon SM. 1998a. Simulation of track-in of lawn-applied pesticides from turf to home: Comparison of dislodgeable turf residues with carpet dust and carpet surface residues. GRA&I. Issue 05.

Nishioka M; Hines C; Brinkman M; Burkholder H; Lewis RG. 1998b. Comparison of commercial vs homeowner application for transport of lawn-applied herbidide 2,4-D into homes. GRA&I. Issue 06.

Norris, LA; Montgomery, MM. 1975. Dicamba residues in streams after forest spraying. Bull. Environ. Contam. Toxicol. 13(1): 1-8.

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

Odin M; Basu D. 1992. Revised and Updated Drinking Water Quantification of Toxicologic Effects for Dicamba. Prepared by Syracuse Research Corporation under Contract No. 68-CO-0043. Prepared for Environmental Criteria and Assessment Office, U.S. EPA, Cincinnati, OH. SRC TR-92-090. 31 p.

O'Donovan JT; O'Sullivan PA. 1982. Amine salts of growth regulator herbicides antagonize paraquat. Weed Sci. 30 (6):605-608.

Oehler DD; Ivie GW. 1980. Metabolic fate of the herbicide dicamba in a lactating cow. J Agric Food Chem. 28 (4):685-689.

O'Sullivan PA; Kossatz VA. 1984. Canada thistle suppression and rapeseed tolerance with dicamba and picloram. Can J Plant Sci. 64 :917-977.

Palmer JS; Radeleff RD. 1964. The toxicological effects of certain fungicides and herbicides on sheep and cattle. Ann NY Acad Sci. 111 :729-735.

Palmer JS; Radeleff RD. 1969. The Toxicity of Some Organic Herbicides in Cattle, Sheep, and Chickens. Prod. Res. Report No. 106, U.S. Dept. Agric, U.S. Gov Printing Office, Washington, DC. (Cited in Caux et al. 1993)

Pearson RJ; Inskeep WP; Wraith JM; Gaber HM; Comfort SD. 1996. Observed and simulated solute transport under varying water regimes: II. 2,6-difluorobenzoic acid and dicamba. J Environ Qual. 25 (4):654-661.

Perocco P; Nacora G; Rani P; Valenti AM; Mazzullo M; Colacci A; Grilli S. 1990. Evaluation of genotoxic effects of the herbicide dicamba using *in vivo* and *in vitro* test systems. Environ Mol Mutagen. 15 (3):131-135.

Petersen PF; Haderlie LC; Hoefer RH; McAllister RS. 1985. Dicamba absorption and translocation as influenced by formulation and surfactant. Weed Sci. 33 (5):717-720.

Petit F; Le Goff P; Cravedi J-P; Valotaire Y; Pakdel F. 1997. Two complementary bioassays for screening the estrogenic potency of xenobiotics: Recombinant yeast for trout estrogen receptor and trout hepatocyte cultures. J Mol Endocrinol. 19 (3):321-335.

Plewa MJ; Wagner ED; Gentile GJ; Gentile JM. 1984. An evaluation of the genotoxic properties of herbicides following plant and animal activation. Mutat Res. 136 (3):233-246.

Poole DC; Simmon VF; Newell GW. 1977. In vitro mutagenic activity of fourteen pesticides. Toxicol Appl Pharmacol. 46 :196.

Potter WT; Garry VF; Kelly JT; Tarone R; Griffith J; Nelson RL. 1993. Radiometric assay of red cell and plasma cholinesterase in pesticide appliers form Minnesota. Toxicol Appl Pharmacol. 119 (1):150-155.

Putman D; Young R. 1994a. Micronucleus Cytogenetic Assay in Mice: DGA Salt of Dicamba: Final Report: Lab Project Number: TE237/122. Unpublished study prepared by Microbiological Associates, Inc. 35 p. MRID 43354333.

Putman D; Young R. 1994b. Micronucleus Cytogenetic Assay in Mice: DMA Salt of Dicamba: Final Report: Lab Project Number: TE236.122. Unpublished study prepared by Microbiological Associates, Inc. 35 p. MRID 43354332.

Quellet M; Bonin J; Rodrigue J; DeSgranges J-L; Lair S. 1997. Hindlimb deformities (Ectromelia, Ectrodactyly) in free-living anurans from agricultural habitats. J Wildl Dis. 33 (1):95-104.

Reddy KN; Locke MA. 1996. Molecular properties as descriptors of octanol-water partition coefficients of herbicides. Water Air Soil Pollut. 86 (1-4):389-405.

Rieder D. 1996a. Proposed Label Changes for Dicamba, dimethylamine salt (PC No. 029802;D220431 and D220470), Dicamba, sodium salt (PC No 29806; D220472), and Dicamba, diglycoamine salt (PC No. 128931; D220475); Submission of Avia Reproduction Studies. U.S. EPA Environmental Risk Characterization. June 17, 1996. Memorandum. 10 Pages. MRID Nos. 43814003 & 43814004.

Reider D. 1996b. Proposed Label Changes for Dicamba. Submission of Avian Reproduction Studies U.S. EPA Environmental Risk Characterization Branch. June 17, 1996. Memorandum. 24 Page(s). MRIDs 43814003 and 43814004.

Ritter WF; Chirnside AEM; Scarborough RW. 1996. Leaching of dicamba in coastal plain soil. J Environ Sci Health Part A Environ Sci Eng Toxic Hazard Subst Control. 31 (3):505-517.

Roberts N; Fairley C; Fish C; et al. 1983. The Acute Oral Toxicity (LD50) and Neurotoxic Effects of Dicamba in the Domestic Hen: HRC Report No. VCL 24/8355. (Unpublished study received September 22, 1983 under 876-36; prepared by Huntingdon Research Centre, Eng., submitted by Velsicol Chemical Corp., Chicago, IL; CDL:251443-A). MRID 00131290.

Rostad CE. 1997. Concentration and transport of chlordane and nonachlor associated with suspended sediment in the Mississippi River, May 1988 to June 1990. Arch Environ Contam Toxicol. 33 (4):369-377.

Rowland J. 1995a. Dicamba--Diglycoamine & Isopropanolamine Salts: Core Data for Toxicology Data Requirement 82-2. U.S. EPA Toxicology Branch. August 17, 1995. Memorandum. Page(s). Tox review 011636. MRID 435542-06, -07.

Rowland J. 1995b. Dicamba: Reproductive Toxicity Study. U.S. EPA Toxicology Branch. January 17, 1995. Memorandum. Submitted in Response to DCI [Action: 627 Core Data].

Rowland J. 1995c. Dicamba: Re-review of the Developmental Toxicity Studies in Rat and Rabbit as Requested by the HED RfD Committee. U.S. EPA Toxicology Branch. October 23, 1995. Memorandum. 18 Pages. Tox. Review 011702. Obtained under Freedom of Information Act Request to Janet Bressant, U.S. EPA/OPP.

Rowland J. 1996a. Dicamba: Request for New Chronic Toxicity/Carcinogenicity Study in Rats - A Follow-Up to the HED RfD Committee's Recommendations. U.S. EPA Toxicology Branch. September 9, 1996. Memorandum.

Rowland J. 1996b. Dicamba: Review of Mutagenicity Studies with the Dimethylamine (DMA), Diglycoamine (DGA) and Isopropylamine (IPA) Salts of Dicamba. U.S. EPA Toxicology Branch. July 26, 1996. Memorandum. 76 Page(s). Tox review 012000 excerpt. Attachment(s). MRIDs 43310301 thru 43310306.

Rowland J. 1996c. (continued) Pages 12-13, 22, 24, 26, 28, 36-37, 46, 48, 50, 52, 60-61, 70, 72, 74 and 76 removed, registrant data. U.S. EPA Toxicology Branch. July 26, 1996. Memorandum. Page(s).

Rowland J. 1997. Dicamba: Review of Mutagenicity Studies with the Dimethylamine (DMA), Diglycoamine (DGA) and Isopropylamine (IPA) Salts of Dicamba. MRIDs 43354332, 43354333, 43354334. Pages 12, 14, 23, 25, 33, 35 removed, registrant data. U.S. EPA Toxicology Branch. August 12, 1997. Memorandum. 35 Page(s). Tox review 012293 excerpt.

Rowland J. 1998. Dicamba - Report of the Hazard Identification Assessment Review Committee. U.S. EPA Health Effects Division. January 15, 1998. Memorandum. 13 Pages. Obtained under Freedom of Information Act Request to Janet Bressant, U.S. EPA/OPP.

Sadik OA; Witt DM. 1999. Monitoring endocrine-disrupting chemicals. Environ Sci Technol. 33 (17):368A-374A.

San R; Clarke J. 1994a. L5178Y/TK+/- Mouse Lymphoma Mutagenesis Assay with a Confirmatory Assay: DGA Salt of Dicamba: Final Report: Lab Project Number: TE237.701020: DP 301598: SPGT701020. Unpublished study prepared by Microbiological Associates, Inc. 40 p. MRID 43310305.

San R; Clarke J. 1994b. L5178Y/TK+/- Mouse Lymphoma Mutagenesis Assay with a Confirmatory Assay: DMA Salt of Dicamba: Final Report: Lab Project Number: TE236.701020: SPGT701020. Unpublished study prepared by Microbiological Associates, Inc. 40 p. MRID 43310304.

San R; Pugh D. 1994a. Salmonella Plate Incorporation Mutagenicity Assay. (Ames Test) with a Confirmatory Assay: DGA Salt of Dicamba: Final Report: Lab Project Number: TE237.501014: DP 301605: SPGT501014. Unpublished study prepared by Microbiological Associates, Inc. 58 p. MRID 43310302.

San R; Pugh D. 1994b. Salmonella Plate Incorporation Mutagenicity Assay. (Ames Test) with a Confirmatory Assay: DMA Salt of Dicamba: Final Report: Lab Project Number: TE236.501014: DP 301604: SPGT501014. Unpublished study prepared by Microbiological Associates, Inc. 58 p. MRID 43310301.

San R; Pugh D. 1994c. Salmonella Plate Incorporation Mutagenicity Assay. (Ames Test) with a Confirmatory Assay: IPA Salt of Dicamba: Final Report: Lab Project Number: TE238.501014: DP 301606: SPGT501014. Unpublished study prepared by Microbiological Associates, Inc. 58 p. MRID 43310303.

Sanborn J. 1974. The Fate of Select Pesticides in the Aquatic Environment. EPA-66013-74-025. (Cited in Day 1990)

Sanders HO. 1969. Toxicity of Pesticides to the Crustacean *Gammarus lacustris*. USDI Tech Paper 25, Bureau of Sport Fisheries and Wildlife, U.S. Fish and Wildlife Service, Columbia, MO. (Cited in Caux et al. 1993)

Sanders HO. 1970. Toxicities of some herbicides to six species of freshwater crustaceans. J Water Pollut Control Fed. 24 (8):1544-1550.

Sandmann, ER; De Beer, PR; Van Dyk, LP. 1991. Atmospheric pollution by auxin type herbicides in Tala Valley, Natal (South Africa). Chemosphere. 22(1-2): 137-146.

Sandoz (Sandoz Argo, Inc.). 1993a . Vanquish Specimen Label. Provided by Sandoz Agro, Inc. Dated December, 1993.

Sandoz (Sandoz Argo, Inc.). 1993b. Vanquish Herbicide: The New Generation Herbicide from Sandoz for Roadways, Utilities and Railways. Promotional pamphlet provided by Sandoz Agro, Inc.

Scifres, CJ; Allen, TJ. 1973. Dissipation of dicamba from grassland soils of Texas. Weed Sci. 21(5): 393-396.

Scifres CJ; Allen TJ; Leinweber CL; Pearson KH. 1973. Dissipation and phytotoxicity of dicamba residues in water. J Environ Qual. 2 :306-309.

SERA (Syracuse Environmental Research Associates, Inc.). 1995. VANQUISH Risk Assessment, FINAL DRAFT, SERA TR 95-22-02f, dated October 16, 1995. Prepared under USDA Contract No. 43-3187-5-0787. Syracuse Environmental Research Associates, Inc., Fayetteville, NY. Available at: http://www.fs.fed.us/foresthealth/pesticide/health.htm.

SERA (Syracuse Environmental Research Associates, Inc.). 2001. Preparation of Environmental Documentation and Risk Assessments, SERA MD 2001-01a, draft dated July 2001. Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

SERA (Syracuse Environmental Research Associates, Inc.). 2003. Documentation for Worksheets Version 2.04 - Human Health and Ecological Risk Assessments, SERA WSD 01-2.04, report dated February 25, 2004. Syracuse Environmental Research Associates, Inc., Fayetteville, NY.

SERA (Syracuse Environmental Research Associates, Inc.). 2004. Documentation for the Use of GLEAMS (Version 3) and Auxiliary Programs in Forest Service Risk Assessments (Version 2.04), SERA TD 2004-02.04a, dated February 8, 2004.

Shang C; Arshad MA. 1998. Sorption of clopyralid, dicamba and MCPA by two soils with conventional and no-till management. Can J Soil Sci. 78 (1):181-186.

Shealy DB; Bonin MA; Wooten JV; Ashley DL; Needham LL; Bond AE. 1996. Application of an improved method for the analysis of pesticides and their metabolites in the urine of farmer applicators and their families. Environ Int. 22 (6):661-675.

Shults S; Brock A; Laveglia J. 1995. Primary Eye Irritation Study in Albino Rabbits with Sodium Dicambate Technical: Lab Project Number: 6298-94-0232-TX-001: 94-0232. Unpublished study prepared by Ricerca, Inc. 33 p. MRID 43599101.

Sirons GJ; Anderson GW; Frank R; Ripley BD. 1982. Persistence of hormone-type herbicide residue in tissue f susceptible crop plants. Weed Sci. 30 (6):572-578.

Smetnik AA; Gorbatov VS; Spiridonov YY; Kolupaeva VN. 1995. Migration of picloram dicamba and chlorosulfuron in soddy-podzolic soil and modal chernozem. Agrokhimiya. 0 (11):93-102

Smith, AE. 1973. Degradation of dicamba in prairie soils. Weed Res. 13: 373-378.

Smith, AE. 1974. Breakdown of the herbicide dicamba and its degradation product 3,6-dichlorosalicyclic acid in prairie soils. J. Agric. Food Chem. 22: 601-605.

Smith AE; Bridges DC. 1996. Movement of certain herbicides following application to simulated golf course greens and fairways. Crop Sci. 36 (6):1439-1445.

Smith, AE; Hayden, BJ. 1976. Field persistence studies with eight herbicides commonly used in Saskatchewan. Can. J. Plant Sci. 56: 769-771.

Smith, SH; O'Loughlin, CK; Salamon, CM; et al. 1981. Teratology study in albino rats with technical dicamba. Toxigenetics Study No. 450-0460. Unpublished study. MRID 00084024.

Soteres JR; Murray DS; Basler E. 1983. Absorption of 2,4-D, Dicamba and Glyphosate by Excised (*Cyanchum laeve*) leaves. Weed Sci. 31 :271-274.

Spencer H. 1996. RfD/Peer Review Report of DICAMBA: 2-Methoxy-3,6-.U.S. EPA Science Analysis Branch/HED. July 29, 1996. Memorandum.

Sterling S. 1996. To: Dr. Jonathan Bryant, Sandoz Agro, Inc. Subject: September 9, 1996 Request for New Chronic Toxicity/Carcinogenicity Study in Rats- RfD Committee Recommendations. U.S. EPA SRRD. October 21, 1996. Letter. 10 Pages. Attachment(s).

St. John LE; Lisk DJ. 1969. Metabolism of Banvel-D herbicide in a dairy cow. J Dairy Sci. 52 (3):392-393.

Starrett SK; Starrett SK; Najjar Y; Adams G; Hill J. 1998. Modeling pesticide leaching from gold courses using artificial neural networks. Commun Soil Sci Plant Anal. 29 (19-20):3093-3106.

Stehouwer, RC; Dick, WA; Traina, SJ. 1994. Sorption and retention of herbicides in vertically oriented earthworm and artificial burrows. J. Environ. Qual. 23(2): 286-292.

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.

Strouse J; Nass D. 1986. 21-Day Dermal Toxicity Study in Rabbits with Banvel Herbicide: Laboratory Project ID WIL-15163. Unpublished study prepared by WIL Research Laboratories, Inc. 261 p. MRID 40547901.

Suresh T. 2000. Acute Toxicity Studies: Gharda Dicamba DMA Manufacturing Concentrate: Lab Project Number: 2733/99: 2736/99: 2731/99. Unpublished study prepared by Rallis Research Centre. 167 p. MRID 45646602.

Sutherland C; Kendall T; Krueger H; et al. 2000. Distinct Herbicide: A 48-Hour Flow-Through Acute Toxicity Test with the Cladoceran. (Daphnia magna): Lab Project Number: 147A-169: 63754: 2000/5011. Unpublished study prepared by Wildlife International, Ltd. 37 p. {OPPTS 850.1010}. MRID 45040201.

Syslo S. 1998a. DP Barcode: D167608 D167731 D192290 D198961 Chemical No: 029801, 029806, 129043. review of environmental fate studies in response to the Reregistration Standard. waiver request for laboratory accumulation in fish. U.S. EPA Environmental Risk Branch. November 24, 1998. Memorandum. 186 Pages. Attachment(s).

Syslo S. 1998b. (continued) Pages 23-43, 63-68, 74-88, 93-107, 112-138, 144-166, 172-179, 182-184 removed, registrant data. U.S. EPA Environmental Risk Branch. November 24, 1998. Memorandum. GDLN 161-1, -2, -3, 162-1, -2, 163-1, -2, 164-1, 165-4. MRIDs 40335501, 40547902 thru 4057908, 41966601, 41966602, 42774101 thru 42774103.

Teske ME; Curbishley TB. 1990. Forest Service Aerial Spray Computer Model, FSCBF 4.0, User Manual. Continuum Dynamics, Inc, Princeton, NJ. CDI Report No. 90-06.

Teske ME; Bird SL; Esterly DM; Ray SL; Perry SG. 2001. A User's Guide for AgDRIFT 2.0: A Tiered Approach for the Assessment of Spray Drift. Continuum Dynamics, Inc. Public Use Version. C.D.I. Report No. 01-01. Available, with executable model at: http://www.agdrift.com/

Timchalk C; Nolan RJ. 1997. Pharmacokinetics of triclopyr (3,5,6-trichloro-2-pyridinyloxyacetic acid) in the beagle dog and rhesus monkey: perspective on the reduced capacity of dogs to excrete this organic acid relative to the rat, monkey, and human. Toxicology and Applied Pharmacology. 144 (2): 268-278.

Tindall JA; Vencill WK. 1995. Transport of atrazine 2 4-D and dicamba through preferential flowpaths in an unsaturated claypan soil near centralia Missouri. J Hydrol (Amsterdam). 166 (1-2):37-59.

Tisdel M. 2000. Summary of Acute Toxicology Studies with CGA-77102/G-30027/II/SAN837 4SC-A. (Sequence II): Lab Project Number: 1048-00. Unpublished study prepared by Novartis Crop Protection, Inc. 9 p. MRID 45190304.

Tomlin C. 1994. The Pesticide Manual. 10th ed. Crop Protection Publications, British Crop Protection Council, 49 Downing St, Farnham, Survey GU9 7PH, United Kingdom. p. 298-299.

Tong TMR; Moore P; Atallah YH. 1993. Soil Adsorption and Desorption of Dicamba, Unaged, by the Batch Equilibrium Method. MRID 427741-01.

Touart LW. 1983a. Data Evaluation Record for Dicamba. The Acute Toxicity of Banvel Technical to the Fiddler Crab. U.S. EPA Ecological Effects Branch. March 2, 1983. Data Evaluation. Received. 3 Pages. UCES Project #11506-03-18. MRID 00034704.

Touart LW. 1983b. Data Evaluation Record for Dicamba. The Acute Toxicity of Banvel Technical to the Grass Shrimp. U.S. EPA Ecological Effects Branch. March 2, 1983. Data Evaluation. Received. 3 Pages. MRID 00034702.

Timchalk C; Nolan RJ. 1997. Pharmacokinetics of triclopyr (3,5,6-trichloro-2-pyridinyloxyacetic acid) in the beagle dog and rhesus monkey: perspective on the reduced capacity of dogs to excrete this organic acid relative to the rat, monkey, and human. Toxicology and Applied Pharmacology. 144 (2): 268-278.

Trichell, DW; Morton, HL; Merkle, MG. 1968. Loss of herbicides in runoff water. Weed Sci. 16: 447-449.

Tu CM. 1994. Effects of herbicides and fumigants on microbial activities in soil. Bull Environ Contam Toxicol. 53 (1):12-17.

Turner, DB. 1994. Atmospheric Dispersion Estimates. Lewis Publishers, Chelsea, MI. [pagination not continuous].

Tye R; Engel D. 1967. Distribution and excretion of dicamba by rats as determined by radiotracer technique. J Agric Food Chem. 15 :837-840.

USDA 1989a Final Environmental Impact Statement: Vegetation Management in the Coastal Plain/Piedmont, Management Bulletin R8-MB-23, dated January, 1989. 1213 pp.

USDA 1989b Draft Environmental Impact Statement: Vegetation Management in the Ozark/Ouachita Mountains, Management Bulletin R8-MB-23, dated June, 1989. 499 pp.

USDA 1989c Final Environmental Impact Statement: Vegetation Management in the Appalachian Mountains, Management Bulletin R8-MB-38, dated July, 1989. 1104 pp.

USDA/APHIS (U.S. Department of Agriculture Animal and Plant Health Inspection Service). 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 Database. Http://wizard.arsusda.gov/rsml/testfiles. XXX listing last updated May 1995.

USDA/FS (United States Department of Agriculture/Forest Service). 2001. Regional Reports of Pesticide Use on National Forest System Lands: Fiscal Year 2001. Available at: www.fs.fed.us/foresthealth/pesticide/pur/reports.html.

USDE (U.S. Department of Energy). 1983. Final Environmental Impact Statement Transmission Facilities Vegetation Management Program. DOE/EIS-0097. Bonneville Power Administration, Washington, DC.

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

USGS (U.S. Geological Survey). 2003. National Water Quality Assessment Program (NAWQA) Pesticide National Synthesis Project http://ca.water.usgs.gov/pnsp/.

U.S. EPA. (United States Environmental Protection Agency). 1977. The Acute Toxicity of Banvel Technical to the Sheepshead Minnow Cyprinodon variegatus. Ecological Effects Branch. Washington, DC. December 14, 1977. Review. 1 Page. Accession No. 232965.

U.S. EPA. (United States Environmental Protection Agency). 1978. Dicamba Data Submission for Review. Taylor. Efficacy & Ecological Effects Branch. Washington, DC. July 12, 1978. Review. 4 Pages. EPA Reg. No. 876-36. Attachment(s).

U.S. EPA. (United States Environmental Protection Agency). 1984. Guidance for the Reregistration of Pesticide Products Containing Dicamba as the Active Ingredient. PB84-243492.

U.S. EPA (United States Environmental Protection Agency). 1988. Health Advisories for 50 Pesticides. Office of Drinking Water, Washington, DC. NTIS/PB88-245931.

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

U.S. EPA (United States Environmental Protection Agency). 1992b. Integrated risk information system (IRIS). http://www.epa.gov/iriswebp/iris/index.html.

U.S. EPA/OPP (U.S. Environmental Protection Agency/Office of Pesticide Programs). 1999. Dicamba Pesticide Tolerance. Federal Register. 64(3): 759-769.

U.S. EPA/ORD (U.S. Environmental Protection Agency/Office of Research and Development). 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.

USGS (U.S. Geological Survey). 2003. National Water Quality Assessment Program (NAWQA) Pesticide National Synthesis Project http://ca.water.usgs.gov/pnsp/

van Dijk HFG; Guicherit R. 1999. Atmospheric dispersion of current-use pesticides: A review of the evidence from monitoring studies. Water Air Soil Pollut. 115 (1-4):21-70.

van Hemmen JJ. 1992. Agricultural pesticide exposure data bases for risk assessment. Rev. Environ. Contam. Toxicol. 126: 1-85.

Velsicol Chemical Corporation. 1979. Technical Information Dicamba (Banvel) Herbicide. Bulletin 521-2. (Cited in Ghassemi et al. 1981)

Velsicol Chemical Corporation. 1961. Velsicol Banvel D: 2-Methoxy- 3,6-dichlorobenzoic acid (Velsicol 58-CS-11, Compound B). Chicago, Ill.: VCC. Bulletin no. 521-2. MRID 00023088

Velsicol Chemical Corporation. 1984. Banvel Herbicide: Product Chemistry Data Submitted in Partial Fulfillment of Requirements for the Re-registration of Dicamba. Unpublished compilation. 15 p. MRID 00143504

Vighi M. and Funari E (eds.). 1987. Pesticide risk in groundwater. CRC Press, Inc., Boca Raton, Florida, USA; London, England, UK. ISBN 0-87371-439-3. 0 (0):121-130.

Vilkas A. 1977a. The Acute Toxicity of Banvel Technical to the Bluegill Sunfish. Union Carbide Environmental Services. November 21, 1977. Review. 2 Pages. Accession No. 232965.

Vilkas A. 1977b. The Acute Toxicity of Banvel Technical to the Fiddler Crab. Union Carbide Corporation Environ. Services. December 7, 1977. Review. 1 Page. Accession No. 232965.

Vilkas A. 1977c. The Acute Toxicity of Banvel Technical to the Sheepshead Minnow. Union Carbide Environmental Services. December 14, 1977. Review. 1 Page. Accession No. 232965.

Wagner SL. 1990. Pesticide illness surveillance review of the National Pesticide Hazard Assessment Program. Technical Workshop of the Conference on Agricultural, Occupational, and Environmental Health: Policy Strategies for the Future, Iowa City, Iowa. September 17-30. Am J Ind Med. 18 (3):307-312.

Waite, DT; Grover, R; Westcott, ND; Sommerstad, H; Kerr, L. 1992. Pesticides in groundwater, surface water, and spring runoff in a small Saskatchewan watershed. Environ. Toxicol. Chem. 11(6): 741-748.

Waite DT; Grover R; Westcott ND; Irvine DG; Kerr LA; Sommerstad H. 1995. Atmospheric deposition of pesticides in a small southern Saskatchewan watershed. Environ Toxicol Chem. 14 (7):1171-1175.

Waldrop W. 1995. Subject: January 17, 1995 Review of Reproductive Tox Study with Dicamba Acid. To: Dr. Jonathan E. Bryant, Sandoz Agro, Inc. U.S. EPA Registration Branch. January 23, 1994. Letter. 24 Pages. Attachment(s). MRID 43137101.

Wall DA. 1994. Potato (*Solanum tuberosum*) response to simulated drift of dicamba, clopyralid and tribenuron. Weed Sci. 42 (1):110-114.

Warren S; Muller P; Hopley J. 1991. A 13-Week Pilot Feeding Study in Mice: San 835 H: Lab Project Number: 445-M: 91/5258: I.7481/90. Unpublished study prepared by Sandoz Agro Ltd. 77 p. MRID 44663801.

Waters MD; Simmon VF; Mitchell AD; Jorgenson TA; Valencia R. 1980. An overview of short-term tests for the mutagenic and carcinogenic potential of pesticides. J Environ Sci Health [B]. 15 :867-906.

Wauchope RD et al. 1991. The SCS/ARS/CES Pesticide Properties Database for environmental decision-making. Rev. Environ. Contam. Toxicol. 123: 1-35.

Wazeter FX; Goldenthal EI; Jessup DC; et al. 1977. Pilot Teratology Study in Rabbits. IRDC No. 163-436. Unpublished study. MRID 00025373.

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

Witherup S; Cleveland FP. 1962. The toxicological investigation of 2-methoxy-3,6-dichlorobenzoic acid. Divn Agric Fd Chem Sect B, Pestic Subdivn Proc Am Chem Soc 142nd Meeting. September 1962 Atlantic City, NJ. p.17A.

Witherup S; Stemmer KL; Roell M; et al. 1966. The Effects Exerted upon the Fertility of Rats and upon the Viability of their Offspring by the Introduction of Banvel D into their Diets. Unpublished study. MRID 00028249.

Woodward DF. 1982. Acute toxicity of mixtures of range management herbicides to cutthroat trout. J Range Management. 35 (4):539-540.

WSSA (Weed Science Society of America). 1989. Herbicide Handbook of the Weed Science Society of America. 6th ed, Champaign, IL.

Xu HH; Schurr KM. 1990. Genotoxicity of 22 pesticides in Microtitration SOS Chromotest. Toxic Assess. 5 (1):1-14.

Yeary RA. 1984. Oral intubation of dogs with combinations of fertilizer, herbicide, and insecticide chemicals commonly used on lawns. Am J Vet Res. 45 (2):288-290.

Yu CC. 1988a. Hydrolysis of ^{14}C-Dicamba. MRID 405479-02.

Yu CC. 1988b. Photolysis of ^{14}C-Dicamba in Aqueous Solution. MRID 405479-03.

Yu CC. 1988c. Addendum to report No. 480060-6 on volatility of three dicamba formulations. MRID 419666-02.

Yu CC; Hansen DJ; Booth GM. 1975. Fate of Dicamba in a Model Ecosystem. Illinois Natural History Survey and Illinois Agricultural Experiment Station, Urbana, IL.

Zahm SH. 1997. Mortality study of pesticide applicators and other employees of a lawn care service company. J Occup Environ Med. 39 (11):1055-1073.

Zhao H; Jaynes WF; Vance GF. 1996. Sorption of the ionizable organic compound, dicamba (3,6-dichloro-2-methoxy benzoic acid), by organo-clays. Chemosphere. 33 (10):2089-2100.

Table 2-1: Physical and chemical properties of dicamba.

Property	Value	Reference
CAS Registry No.	1918-00-9 – dicamba acid	Budavari et al. 1989
	2300-66-5 – dimethyl amine salt	
	104040-79-1 – diglycolamine salt	
Molecular weight	221.04 – dicamba acid	Budavari et al. 1989
	266.13 – dimethyl amine salt (0.83 a.e.)	
	326.18 – diglycolamine salt (0.67 a.e.)	
Melting point (°C)	114-116	Budavari et al. 1989
Density (g/cm^3)	1.57	Tomlin 1994
Vapor pressure (mm Hg)	$3.41x10^{-5}$ (25°C)	WSSA 1989
Water solubility (mg/L)	6500	Tomlin 1994
pKa	1.87	Tomlin 1994
Log K_{ow}	2.21 (non-ionized form) 0.60 (pH 5) -0.80 (pH 7) -0.24 (pH 9) 2.49 (non-ionized form) -0.26 -0.23 (pH 5) -0.56 (pH 7) [$K_{o/w}$ = 0.271] -1.12 (pH 9)	Hansch et al. 1995 Tomlin 1994 Jafvert et al. 1990 USDA/ARS 1995 Fostiak and Yu 1989
K_{oc}	0.078–511 2.2 (mean) 2 2.41 (clay loam) 13.6 (silt loam) 32.5 (sandy loam) 15.83 (sediment)	Mullins et al. 1993 Rao and Davidosn 1982 Knisel and Davis 2000 Yong et al. 1993
Kd	0.16 loam 0.1 clay loam 0.53 silt loam 0.07 sandy loam 0.21 loam	USDA/ARS 1995
Photolysis	0.0035 day^{-1} in soil 0.018 day^{-1} in water	USDA/ARS 1995
Foliar half-time (days)[e]	9.3 9	Mullins et al. 1993 Knisel and Davis 2000
Foliar washoff fraction	0.65	Knisel and Davis 2000
Volatility	about 4 to 5×10^{-4} µg/cm^2 from moist soil. about 3.5 to 6×10^{-4} µg/cm^2 from corn seedling leaves	Yu 1988c

Property	Value	Reference

Table 2-1: Physical and chemical properties of dicamba (*continued*).

Property	Value	Reference
Soil dissipation half-time (days)	3.24–35.2 25 (average) 7–42 4.4-31 14	Mullins et al. 1993 Neary et al. 1993 U.S. EPA 1988b USDA/ARS 1995 Knisel and Davis 2000
Soil metabolism halftime (days)	58 (anaerobic, loam) 31 (aerobic, loam)	Krueger et al. 1988
Water half-time	<7 days (surface water dissipation) negligible hydrolysis about 1 to 22 hours depending on light intensity	Mullins et al. 1993 USDA/ARS 1995; Yu 1988a Yu 1988b

Table 2-2: Use of Dicamba by USDA/Forest Service in 2001 (USDA/FS 2002).

Regions	Pounds	Acres	Pounds per Acre	Prop. by Pounds	Prop. by Acres
Region 1	160.156	608.7	0.26	0.06	0.07
Region 2	466.8725	575.025	0.81	0.17	0.06
Region 3	232	479	0.48	0.08	0.05
Region 4	1650.75	7164.95	0.23	0.59	0.77
Region 6	302.795	435	0.70	0.11	0.05
Grand Total	2812.574	9262.675	**0.30**		

Table 3-1: Chemical and site parameters used in GLEAMS Modeling for dicamba.

Chemical Specific Parameters

Parameter	Clay	Loam	Sand	Comment/ Reference
Halftimes (days)				
Aquatic Sediment	58	58	58	Note 1
Foliar	9	9	9	Note 2
Soil	31	31	31	Note 3
Water	39	39	39	Note 4
Ko/c, mL/g	2.4	13.6	32.5	Note 5
K_d, mL/g	0.1	0.16	0.07	Note 6
Water Solubility, mg/L		6500		Tomlin 1994
Foliar wash-off fraction		0.65		Note 7

Note 1 No data found on halftimes in aquatic sediment. The anaerobic halftime from Krueger et al. (1988) is used as a surrogate.

Note 2 Value for GLEAMS recommended by Knisel and Davis (2000). Very close to 9.3 day halftime reported by Mullins et al. (1993).

Note 3 Aerobic metabolic soil halftime determined by Krueger et al. (1988). Substantially longer than most field dissipation halftimes as well as the soil halftime of 14 days recommended by Knisel and Davis (2000).

Note 4 Based on photolysis coefficient of 0.018 day^{-1} recommended by USDA/ARS (1995). Actual rates of aqueous photolysis will depend on intensity of sunlight (Yu 1988b). The hydrolysis rate of dicamba is negligible (Yu 1988a).

Note 5 Based on measured values in clay loam, silt loam, and sandy loam soils (Yong et al. 1993).

Note 6 Based on values reported in USDA/ARS (1995) for clay loam, loam, and sandy loam soils.

Note 7 This estimate is the value recommended by Knisel and Davis (2000). As with all compounds, the actual proportion of foliar washed off will depend on the intensity of rainfall and values of about 0.1 to 0.7 have been noted over rainfall amounts of 1 to 60 mm (about 0.04 to 2.4 inches) (Carroll et al. 1993, Figure 2, p. 441).

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

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

Table 3-2: Summary of modeled concentrations of dicamba in streams (all units are µg/L or ppb per lb/acre applied)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
10	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
15	0.00024	0.05753	0.00000	0.00000	0.00000	0.00000
20	0.00036	0.09485	0.00000	0.00000	0.00002	0.00045
25	0.00043	0.12122	0.00000	0.00004	0.00044	0.00820
50	0.00055	0.17305	0.00129	0.02685	0.00373	0.09672
100	0.00060	0.18940	0.00361	0.09641	0.00690	0.29887
150	0.00061	0.19103	0.00416	0.13437	0.00722	0.41329
200	0.00132	0.19144	0.00411	0.14857	0.00686	0.47174
250	0.00158	0.19060	0.00388	0.15203	0.00635	0.49795

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

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
10	0.00000	0.00000	0.00000	0.00000	0.00000	0.00000
15	0.00449	0.03384	0.00000	0.00000	0.00000	0.00000
20	0.00455	0.05375	0.00000	0.00000	0.00017	0.00037
25	0.00450	0.06974	0.00001	0.00002	0.00329	0.00964
50	0.00398	0.10732	0.00525	0.02170	0.01738	0.10224
100	0.00348	0.13291	0.01106	0.07260	0.02704	0.27801
150	0.00330	0.14629	0.01174	0.09584	0.02769	0.37877
200	0.00350	0.15577	0.01118	0.10384	0.02653	0.43641
250	0.00358	0.16278	0.01037	0.10463	0.02492	0.46316

Table 3-4: Summary of monitoring data on dicamba associated with general use (USGS 2003)

Type of Site	Frequency of Occurrence	Average Concentration (µg/L)	Maximum Concentration (µg/L)
Streams			
Agricultural	1.55%	<0.04	1.14
Mixed land	0.8%	<0.035	0.39
Undeveloped land	not detected	N/A	N/A
Urban	0.33%	<0.1	0.12
Ground Water			
Agricultural	0.41%	<0.11	0.45
Mixed land	0.07%	<0.11	0.07
Undeveloped land	0	N/A	N/A
Urban	0.48%	<0.11	1.46

Table 4-1: Toxicity of dicamba in different species of mammals as well as two species of birds.

Species, sex	Dicamba preparation	LD50[a,b] (mg/kg)	Body weight[c] (kg)
Mouse, female	technical	1189 (841–1681)	0.020
Rat, male	technical	757 (449–1278)	0.375
Rat, male	formulated	1100 (925–1308)	0.375
Rats, female	technical	1414 (1017–1965)	0.241
Guinea pig, male	formulated	566 (348–923)	0.899
Pheasant, male	formulated	800 (490–1305)	1.167[d]
Chicken, female	formulated	673 (396–1142)	1.82
Rabbit, both	formulated	566 (348–923)	3.9
Sheep	not specified	353[e]	79

[a] All data from Edson and Sanderson (1965) unless otherwise specified
[b] 95% Confidence interval given in parentheses
[c] All data from U.S. EPA (1989) unless otherwise specified
[d] Altman and Dittmer (1966)
[e] Geometric mean of non-lethal dose (250 mg/kg) and lethal dose (500 mg/kg) from Palmer and Radeleff (1969).

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

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0.30003	3.99106	0.33785	3.52610	0.34050	3.52591
10	0.14817	3.99117	0.18971	3.52591	0.15704	3.52516
15	0.08084	3.99075	0.09718	3.52516	0.07596	3.52516
20	0.05324	3.99075	0.06073	3.52516	0.04700	3.52516
25	0.04006	3.99075	0.04259	3.52516	0.03363	3.52516
50	0.02036	3.99075	0.01896	3.52516	0.01762	3.52516
100	0.01521	3.99075	0.01431	3.52516	0.01376	3.52516
150	0.01474	3.99075	0.01339	3.52516	0.01268	3.52516
200	0.01451	3.99075	0.01297	3.52516	0.01217	3.52516
250	0.01438	3.99075	0.01272	3.52516	0.01187	3.52516

Table 4-3: Analyses of dose-duration relationships for the toxicity of dicamba to aquatic animals.

Species (Reference)	Intercept	Slope	r^2	p-value [1]	Acute LC_{50} [2]	Chronic LC_{50} [2]	Ratio
FISH							
Mosquito fish (Johnson 1978)	2.82	-0.075	0.83	0.26	523	335	1.6
Bluegill (Hughes and Davis 1962)	3.54	-0.55	N/A	N/A	600	23	26
Bluegill (Vilkas 1977a)	2.83	-0.37	0.86	0.082	208	23	9.1
Rainbow Trout (McAllister et al. 1985b)	2.94	-0.41	0.993	0.052	233	21	11
Coho Salmon (Bond et al. 1965)	2.63	-0.33	N/A	N/A	151	21	7.2
AMPHIBIANS							
Tadpoles, *Adelotus* (Johnson 1976)	2.52	-0.12	0.999	0.0054	220	105	2.1
Tadpoles, *Limnodynastes* (Johnson 1976)	2.99	-0.47	0.98	0.13	214	12.9	16
INVERTEBRATES							
Gammarus (Sanders 1969)	1.92	-0.67	0.996	0.058	9.8	1.62	6.0

[1] Accept as indicated by N/A, all data sets contained only 3 time points. N/A indicates that only two time points were available – i.e., zero degrees of freedom.
[2] Acute and chronic LC_{50} values estimated from log-log regression of reported LC_{50} values in Appendices 7 (fish and amphibians) and 8 (invertebrates). Acute LC_{50} values calculated at 1-day for all species. Chronic LC_{50} values calculated at 365 days for vertebrates and 14-days for invertebrates.

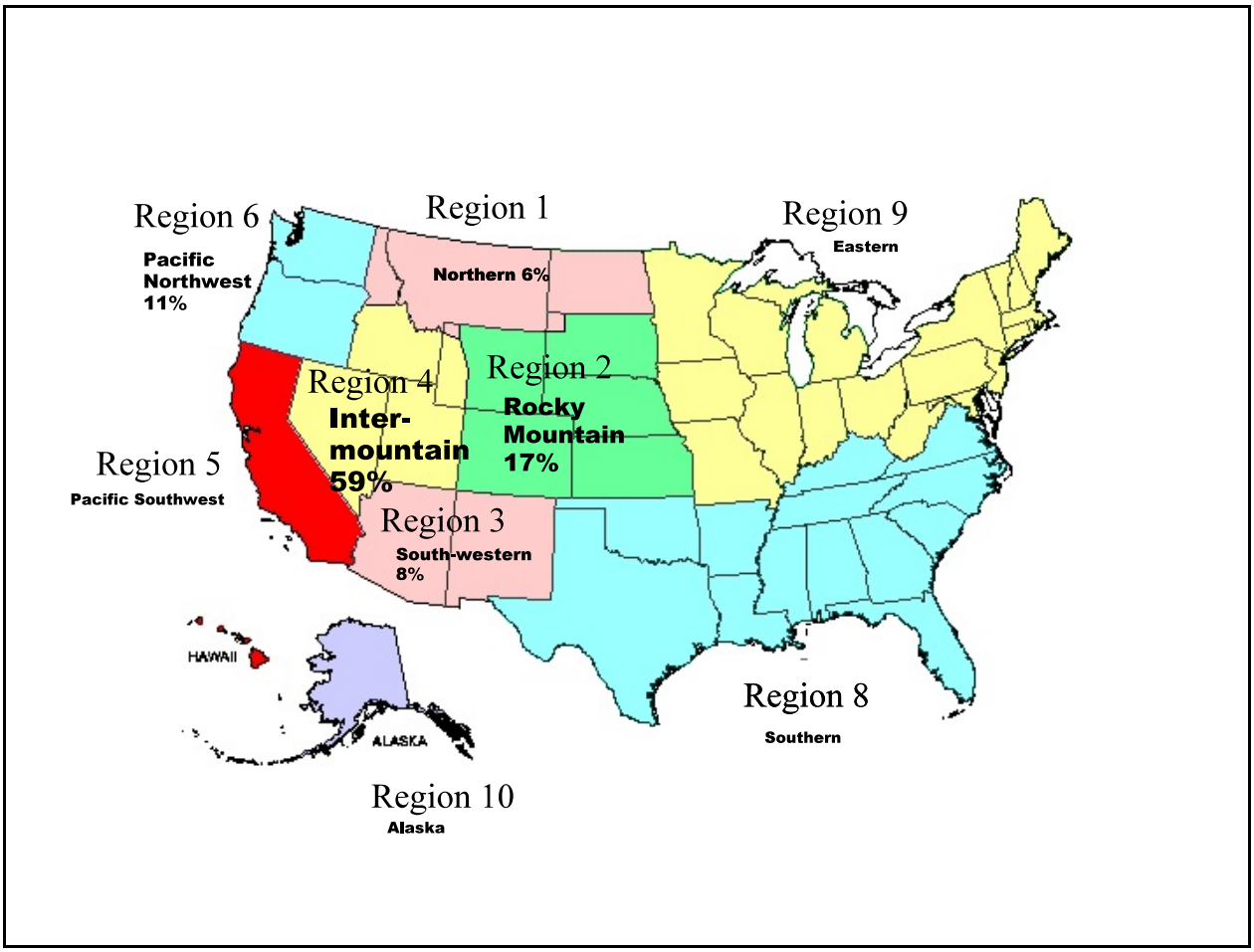


Figure 2-1: Use of Dicamba by the USDA Forest Service in various regions of the United States based on percentages of total use by FS [See Table 2-2 for data].

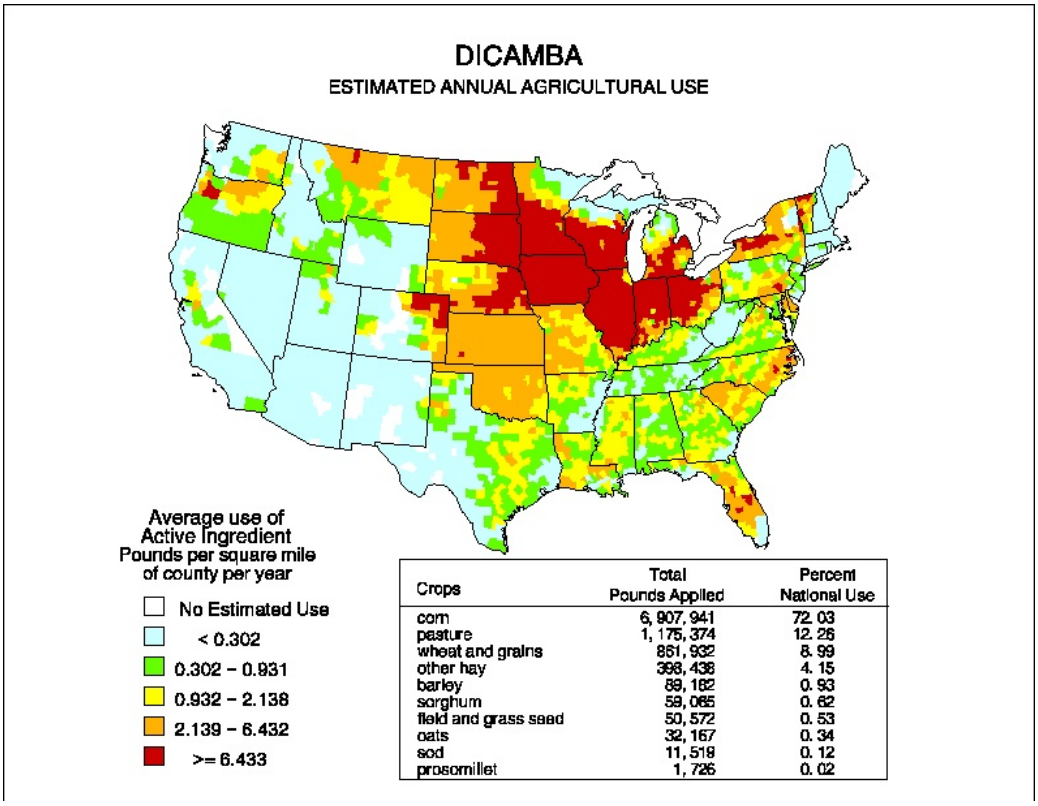


Figure 2-2:. Agricultural use of dicamba in the United States for 1992 (USGS 1998).

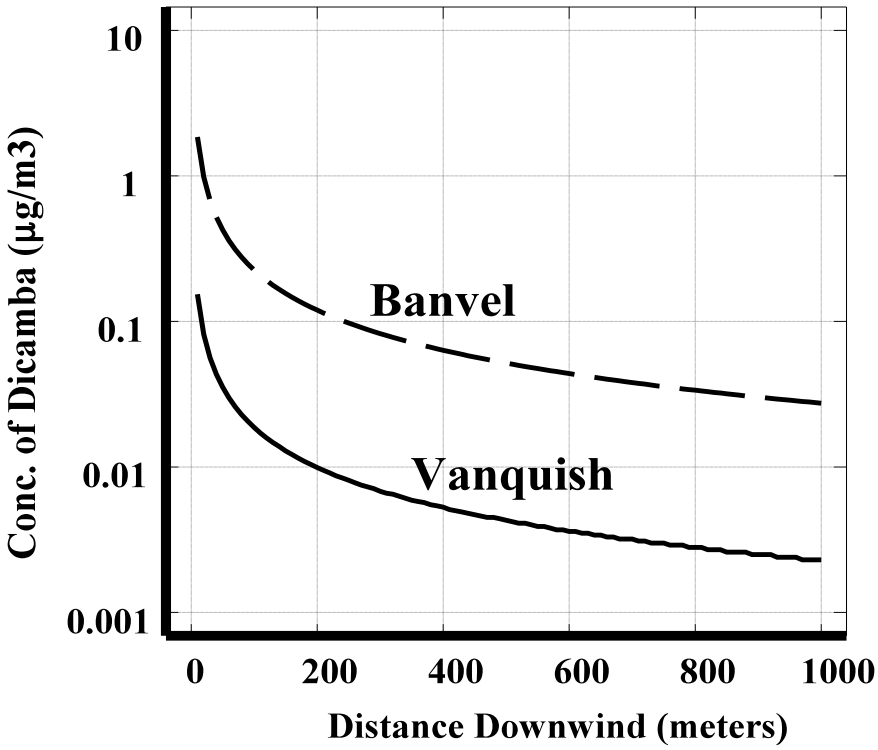


Figure 4-1: Dicamba concentrations in air after applications of Banvel (dashed line) and Vanquish (solid line). See text for details and assumptions.

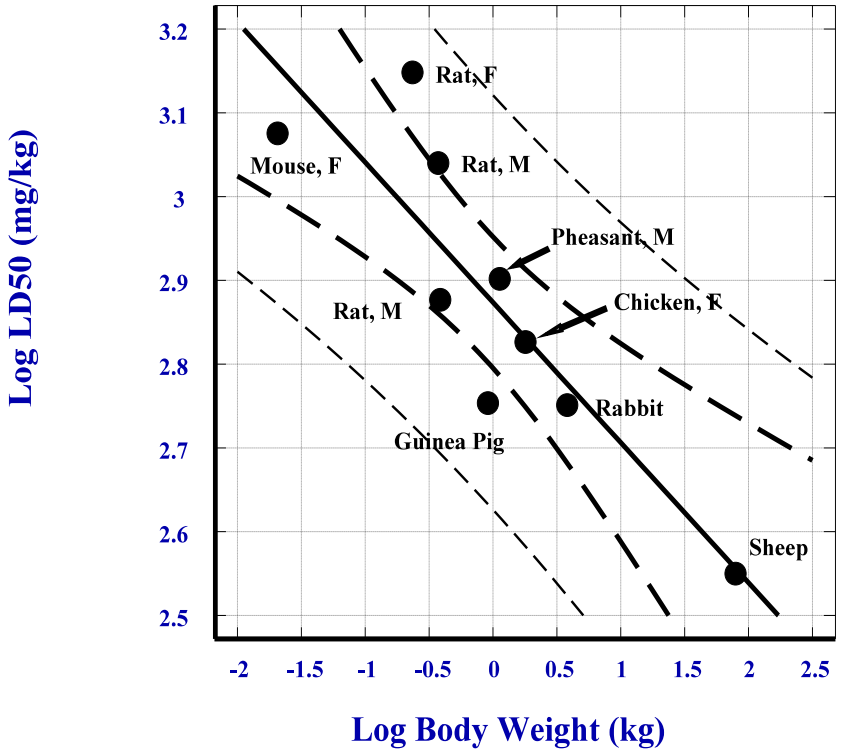


Figure 4-2: Allometric relationships for the acute toxicity of dicamba in mammals and birds (see Table 4-1 for data).

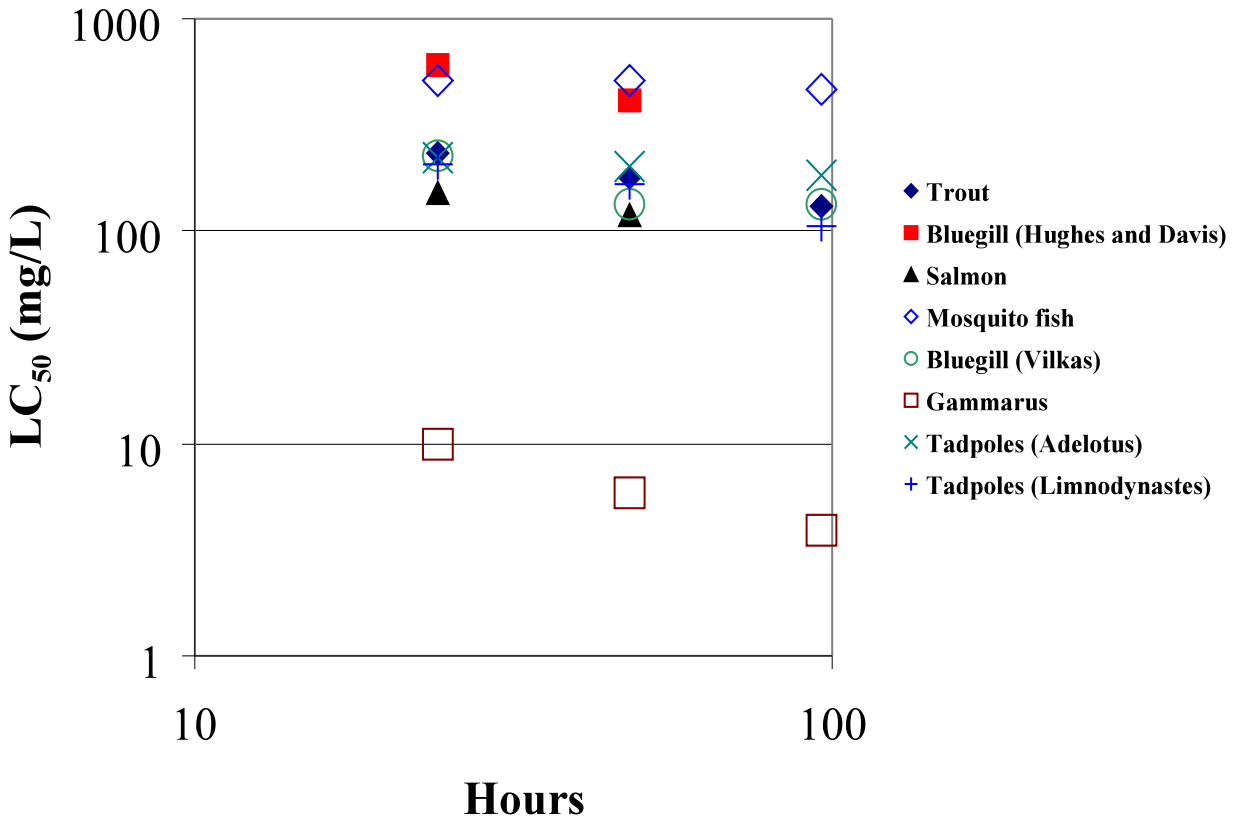


Figure 4-3: Concentration-duration relationships for dicamba in various aquatic animals (see Table 4-3 for statistical analyses).

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Appendix 1. Acute Systemic Toxicity of Dicamba to Mammals

Formulation or salt [a]	Species, Strain, Sex	Duration of Exposure (observation)	Level of Exposure	Response	Reference
Oral Exposure (mg/kg/day)					
dicamba, Pure	rat albino, F	single dose (≥7 d)	2560	LD_{50} >2560 mg/kg. In glycerol by gavage.	Edson and Sanderson 1965
dicamba, Technical, NOS	rat albino, M	single dose (≥7 d)	757 (449-1278)	LD_{50}. In glycerol by gavage. Signs of toxicity included myotonic muscular spasms, urinary incontinence and pulmonary effects (e.g., dyspnea, cyanosis, congestion, minor lung hemorrhages). Survivors had normal gross pathology.	Edson and Sanderson 1965
	rat albino, F	single dose (≥7 d)	1414 (1017-1965)		
dicamba Technical, NOS	rat Sherman, M	single dose (≥14 d)	1404 (1251-1699)	LD_{50}. In corn oil by gavage.	Gaines and Linder 1986
	rat Sherman, F	single dose (≥14 d)	1039 (905-1164)		
dicamba, Technical, NOS	rat Sherman, M	single dose (≥14 d)	3294 (2984-3650)	LD_{50}. Weanlings. In corn oil by gavage.	Gaines and Linder 1986
dicamba (Technical Banvel D, 85-90% a.i.)	rat NR, NR	single dose (NR)	2900 (± 800)	LD_{50}. In peanut oil by gavage. Effects in rats that died included reduced ambulatory motions, decreased respiratory rate and volume, weakness, terminal coma, and non-specific gross pathological changes in the liver, kidneys and lungs. The majority of deaths occurred in 3-10 hours. Clinical signs and effects on food consumption and growth were transient or not evident in rats given a sublethal dose.	???? MRID 25377
DMA salt (Technical Banvel)	rat NR, NR	single dose[b] (NR)	1707-2900 (NR)	LD_{50} (reported as range of values)[c]. Vehicle and oral method NR.	Velsicol Chem. Corp. 1979
Banvel (4 lbs DMA salt/gal)	rat NR, NR	single dose[b] (NR)	1028-2629 (NR)	LD_{50} (reported as range of values)[c]. Vehicle and oral method NR.	Velsicol Chem. Corp. 1979

Appendix 1. Acute Systemic Toxicity of Dicamba to Mammals

Formulation or salt [a]	Species, Strain, Sex	Duration of Exposure (observation)	Level of Exposure	Response	Reference
DMA salt (40.0% dicamba)	rat HSD:SD, M	single dose (14 d)	1918 (1565-2350)	LD_{50}. Undiluted by gavage. Clinical signs of neurotoxicity (e.g., decreased activity, ataxia, loss of limb coordination) on day of exposure. Gross changes in liver, kidneys and spleen of animals that died. Histology not assessed.	Kuhn (1998a) MRID 44502703
	rat HSD:SD, F	single dose (14 d)	2087 (1693-2373)		
DMA salt (99.8% m/m purity)	rat Wistar, M&F	single dose (15 d)	5000 (4398-5685)	LD_{50}. In water by gavage. 20, 50 and 80% mortality at 4000, 5000 and 6250 mg/kg, respectively. Clinical signs (mainly lethary and ataxia) on day of exposure. Body weight loss in rats that died; no clear effect on weight gain in survivors. Main gross pathologic effect was lung congestion. Histology not assessed.	Suresh (2000) MRID 45646602
Na salt (aqueous, NOS)	rat albino, M	single dose (≥7 d)	1100 (925-1308)	LD_{50}. Unspecified aqueous formulation by gavage. Signs of toxicity similar to effects described for Technical dicamba.	Edson and Sanderson 1965
Na salt (21.06% dicamba)	rat HSD:SD, M&F	single dose (14 d)	5050	1/10 deaths (LD_{50} >5050 mg/kg). Undiluted by gavage. Clinical signs (e.g., decreased activity, diarrhea, piloerection, ptosis) on day of exposure. No effect on body weight gain and no gross pathology in surviving rats. Histology not assessed.	Kuhn (1998c) MRID 44524403
Racuza 4 E.C. (methyl ester)	rat Carworth CFE, M	single dose (14 d)	3752 (3134-4493)	LD_{50}. In corn oil presumably by gavage.	Goldenthal et al. (1972) MRID 00057555
	rat Carworth CFE, female	single dose (14 d)	2979 (2246-3952)		
dicamba, Technical, NOS	mouse Tuck, F	single dose (≥7 d)	1189 (841-1681)	LD_{50}. In glycerol by gavage. Signs of toxicity similar to effects described for Technical dicamba.	Edson and Sanderson 1965
Na salt (aqueous, NOS)	guinea pig albino, M	single dose (≥7)	566[d] (348-923)	LD_{50}. Unspecified aqueous formulation by by gavage. Signs of toxicity similar to effects described for Technical dicamba.	Edson and Sanderson 1965

Appendix 1. Acute Systemic Toxicity of Dicamba to Mammals

Formulation or salt [a]	Species, Strain, Sex	Duration of Exposure (observation)	Level of Exposure	Response	Reference
dicamba, NOS	guinea pig NR, NR	1 d	3000	LD_{50}[c]. Vehicle and oral method NR.	Hayes 1982
Na salt (aqueous, NOS)	rabbit hybrid, M&F	1 d (≥7)	566[d] (348-923)	LD_{50}. Unspecified aqueous formulation by by gavage. Signs of toxicity similar to effects described for Technical dicamba.	Edson and Sanderson 1965
dicamba, NOS	rabbit NR, NR	1 d	2000	LD_{50}[c]. Vehicle and oral method NR.	Hayes 1982
Banvel D	cattle NR, NR	5 d	250	No effect	Palmer and Radeleff 1964
Banvel D	sheep NR, NR	10 d	250	No signs of toxicity at 250 mg/kg (n=1). Signs of mild toxicity (e.g., salivation, trembling and depression) but no death at 500 mg/kg (n=1). Administered as unspecified fluid dilution.	Palmer and Radeleff 1964
		2 d	500		
Dermal Exposure (mg/kg/day)					
dicamba, Pure	rat albino, F	single application (≥7 d)	1000	LD_{50} >1000. 24-hr occlusive covered contact with clipped skin. No abnormal gross pathology.	Edson and Sanderson 1965
dicamba, Technical, NOS	rat albino, M	single application (≥7 d)	1000	LD_{50} >1000. 24-hr occlusive covered contact with clipped skin. No abnormal gross pathology.	Edson and Sanderson 1965
DMA salt (99.8% m/m purity)	rat Wistar, M&F	single application aqueous paste	5000	Application site clipped, intact (not abraded) and covered for 24 hrs. LD_{50} >5000 mg/kg. 15-day observation. No mortality, clinical signs, or effects on body weight gain. No local skin irritation	Suresh (2000) MRID 45646602
Banvel, Technical	rabbit NR, NR	NR	2000	LD_{50} >2000 mg/kg[c]	Velsicol Chem. Corp. 1979
Banvel, 4 lbs/gal	rabbit NR, NR	NR	2000	LD_{50} >2000 mg/kg[c]	Velsicol Chem. Corp. 1979

Appendix 1. Acute Systemic Toxicity of Dicamba to Mammals

Formulation or salt [a]	Species, Strain, Sex	Duration of Exposure (observation)	Level of Exposure	Response	Reference
DMA salt (40.0% dicamba)	rabbit New Zealand, M&F	single application (14 d)	5050	24-hr occlusive covered contact with clipped intact skin. No mortality, clinical signs of toxicity, clear effects on body weight gain, or gross pathology. Very slight local dermal erythema found after removal of covering; not observed on days 4, 7, 11 or 14.	Kuhn (1998b) MRID 44502704
Na salt (21.06% dicamba)	rabbit New Zealand M&F	single application (14 d)	5050	24-hr occlusive covered contact with clipped intact skin. No mortality (LD_{50} >5050 mg/kg), clinical signs of toxicity, clear effects on body weight gain, or gross pathology. Very slight local dermal erythema found after removal of covering; not observed on days 4, 7, 11 or 14.	Kuhn (1998d) MRID 44524404
Racuza 4 E.C. (dicamba, methyl ester)	rabbit New Zealand, M&F	single application (14-day)	2000	24-hr occlusive contact with clipped skin that was abraded in 2/4 animals. No mortality or effects on body weight gain.	Goldenthal et al. (1972) MRID 00057555
Inhalation Exposure					
Technical Banvel DMA	rat NR, NR	4 hr (NR)	≤200 mg/L	LC_{50} >200 mg/L[c]	Velsicol Chem. Corp. 1979
Banvel 310 (4 lbs/gal DMA)	rat NR, NR	4 hr (NR)	≤200 mg/L	LC_{50} >200 mg/L[c]	Velsicol Chem. Corp. 1979
Banvel 480 (40.5 wt. % a.e. [3,6-Banvel])	rat Sprague-Dawley, M&F	4 hr (14 d)	5.4 mg/L (MMAD = 5.2μm)	No mortality (LC_{50} > 5.4 mg/L) . Decreased activity, wetting/oiliness of fur, and staining of muzzle and eyes that generally disappeared within first week. No gross pathology. No changes in lung weight or histopathology of lungs, liver, or kidneys.	Collins and Proctor (1984) MRID 00143011
dicamba DMA salt (99.8% a.i.)	rat Wistar M&F	4 hr (15 d)	3.27 mg/L (±0.49) (mean size = 0.89±0.24 μm)	Maximum attainable aerosol concentration. Nasal and eye discharge during the first 3 days of the study. No mortality, effects on body weight gain, or gross pathology. Histology not examined.	Suresh (2000) MRID 45646602

Appendix 1. Acute Systemic Toxicity of Dicamba to Mammals

Formulation or salt [a]	Species, Strain, Sex	Duration of Exposure (observation)	Level of Exposure	Response	Reference
dicamba Na salt (21.06% dicamba A.I.)	rat HSD:SD, M&F	4 hr (14 d)	2.36 mg/L (ave MMAD = 0.8 µm)	No mortality (LC_{50} > 2.36 mg/L). Decreased activity and piloerection during exposure period. No treatment-related effects on body weight gain or gross pathology.	Bennick (1998) MRID 44524405
Racuza 4 E.C. (methyl ester)	rat Carworth CFE, male	4 hr (14 d)	2 or 200 mg/L	No mortality at 2 mg/L. 70% mortality during the first 24 hours at 200 mg/L. Clinical signs observed during exposure period at both exposure levels (e.g., eye squint, dyspnea, lacrimation, erythema, decreased motor activity). No exposure-related effects on body weight gain or gross pathology at either concentration.	Goldenthal et al. (1972) MRID 00057555
Intraperitoneal administration (mg/kg/day)					
dicamba, Technical (NOS)	rat albino, M	single dose (≥7)	80 (54-119)	LD_{50}. Glycerol vehicle. Survivors had visceral adhesions	Edson and Sanderson 1965
dicamba (98% pure)	mice Swiss-Webster, M	2 d	250	50% mortality (2/4). Corn oil vehicle.	Moody et al. 1991

[a]Formulation: dicamba=3,6-dichloro-*o*-anisic acid, DMA=dimethylamine salt, Banvel=48% a.i. dicamba (DMA salt), Banvel D=48% a.i. dicamba (DMA salt) emulsifiable concentrate, Banvel 310=48% a.i. dicamba (DMA salt), Tech. Banvel=86.8% a.i. dicamba (DMA salt), Racuza 4 E.C.=dicamba methyl ester.
[b]Presumed single dose.
[c]Data from a secondary source.
[d] The values for guinea-pig and rabbit are identical in Edson and Sanderson 1965. It is not clear if this is a coincidence or a reporting error.
NOS=Not otherwise specified, NR=Not reported

Appendix 2. Skin and Eye Irritation and Allergic Sensitization Tests on Dicamba					
Formulation or Salt	**Species**	**Acute Skin Irritation**	**Acute Eye Irritation**	**Dermal Sensitization**	**Reference**
Banvel 480 (480 g/l dicamba, NOS)	rabbit	Severe			Budai et al. 1997
dicamba, Na salt Technical (79.6%, NOS)	rabbit	Moderate			Shults et al. 1995 MRID 43599101
dicamba, Na salt (21.06% dicamba)	rabbit	Slight	Minimal (unwashed)		Kuhn, 1998e, 1998f MRID 44524406 MRID 44524407
dicamba, Na salt (21.06% dicamba)	guinea pig	No irritation		No sensitization	Kuhn 1998g MRID 44524408
dicamba, DMA salt (40.0% dicamba)	rabbit	Slight	Moderate (unwashed)		Kuhn 1997, 1998a MRID 44502706 MRID 44502707
dicamba, DMA salt (40.0% dicamba)	guinea pig	No irritation		No sensitization	Kuhn 1998b MRID 44502708

Appendix 3: Systemic Toxicity of Dicamba after Repeated Oral Exposure to Mammals

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical[1] (86.8% a.i.)	rat, Charles River CD, 20/sex/dose	Exposure: 0, 1000, 5000 or 10,000 ppm in the diet for 13 weeks. Reported average chemical intake was 0, 69.4, 342 and 682 mg/kg/day in males and 0, 79.5, 392 and 751 mg/kg/day in females. Response: No compound-related effects at ≤5000 ppm as shown by assessments of general behavior and condition, body weight and food consumption, hematology, blood biochemistry, urinalysis indices, absolute and relative organ weights, gross pathology, and histopathology. At 10,000 ppm, mean body weight gain and food consumption were slightly decreased in both sexes; at week 13, weight gain was 7.5 and 6.3% less than controls, and food consumption was 9.4% and 11.1% less than controls, in males and females, respectively. Other effects at 10,000 ppm include decreased absolute kidney weight in males, increased relative liver weight in females, and histological changes in the liver of both sexes (an absence or reduction of cytoplasmic vacuolation of hepatocytes that appeared indicative of reduced glycogen storage). The organ weight and hepatic histological alterations were considered likely associated with the reduced body weight gain. Systemic NOAEL: 342 mg/kg/day (males) and 392 mg/kg/day (females) Systemic LOAEL: 682 mg/kg/day (males) and 751 mg/kg/day (females). Minimal LOAEL because liver effects were mild and appeared to be secondary to questionably adverse decreases in weight gain and food consumption.	Laveglia, 1981 (MRID 00128093)

Appendix 3: Systemic Toxicity of Dicamba after Repeated Oral Exposure to Mammals

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
Na salt (NOS)	rat, Wistar, 20M/dose	Exposure: 0, 31.6, 100, 316, 1000 or 3162 ppm in an aqueous paste diet for 15 weeks. Reported chemical intake was 0, 2.0, 6.3, 19.3, 67 or 205 mg/kg/day (0, 1.7, 5.2, 16.0, 55.6 or 170 mg/kg/day a.e.). Response: No overt signs of toxicity or exposure-related changes in body weight, food consumption or gross pathology. Absolute and relative liver weight were increased at 67 mg/kg/day (22.5 and 15.4% higher than controls) and 205 mg/kg/day (72.5 and 60.4% higher than controls). No histological examinations of liver or other tissues were performed. Systemic NOEL: 19.3 mg/kg/day (16.0 mg/kg/day a.e.). Systemic NOAEL: 205 mg/kg/day (170 mg/kg/day a.e.); low confidence due to lack of histology data.	Edson and Sanderson, 1965
dicamba, technical (90% a.i.)[2]	rat, Sprague-Dawley, 32/sex/dose	Exposure: 0, 5, 50, 100, 250 or 500 ppm in the diet for 2 years. Assuming a food factor of 0.05 kg diet/kg bw, the corresponding estimated dicamba intakes were 0, 0.25, 2.5, 5, 12.5 or 25 mg/kg/day. Response: No exposure-related effects found by evaluation of clinical signs, food consumption, body weight, hematology, organ weights, gross pathology and histopathology (14 tissues). Systemic NOAEL: 25 mg/kg/day Systemic LOAEL: Not identifed.	Davis et al. 1962 (MRID 00028248)

Appendix 3: Systemic Toxicity of Dicamba after Repeated Oral Exposure to Mammals

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical[1] (86.8% a.i.)	rat, Charles River CD, 60/sex/dose	Exposure: 0, 50, 250 or 2500 ppm in the diet for up to 27 months. Reported average intakes of the test mixture were 0, 2, 11 or 107 mg/kg/day for males (weeks 1-115) and 0, 3, 13 or 127 mg/kg/day for females (weeks 1-117). Response: No exposure-related neoplastic or non-neoplastic pathologic changes or other adverse effects were found at any dose level. Comprehensive evaluations were conducted that included appearance, behavior, survival, food consumption, body weight, hematology, blood biochemistry, urinalysis, organ weights, gross pathology and histopathology. The laboratory measurements were performed on 10 rats/sex/dose at 6, 12, 18 and 24 months, and the organ weight and pathology evaluations were performed on 10 rats/sex/dose sacrificed at 12 months and the remaining animals at terminal sacrifice. Incidences of malignant lymphoma (mixed) and thyroid parafollicular cell carcinoma were slightly increased in high-dose males, but the increases were not statistically significant in pairwise comparisons with the control group (although tests for positive dose-related trends were significant). Systemic NOAEL: 107 mg/kg/day (males) and 127 mg/kg/day (females) Systemic LOAEL: Not identified.	Goldenthal, 1985 (MRID 00146150)

Appendix 3: Systemic Toxicity of Dicamba after Repeated Oral Exposure to Mammals

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, NOS (86.8% a.i.)	mouse, Crl: CD-1 (ICR) BR, 52/sex/dose	Exposure: 0, 50, 150, 1000 or 3000 ppm in the diet for 89 weeks (males) or 104 weeks (females). Reported mean achieved intakes of the test mixture over the treatment periods were 0, 5.5, 17.2, 108 or 358 mg/kg/day for males and 0, 5.8, 18.8, 121 or 364 mg/kg/day for females. Response: No exposure-related clinical signs or effects on food consumption, efficiency of food utilization, hematology, organ weights, gross pathology, or histopathology in any dose group. Comprehensive histological examinations were limited to the control and high dose groups and mice that died in the low and intermediate dose groups; tissues routinely examined in the low and intermediate groups were limited to the liver, kidneys, lungs and gross lesions. No blood biochemistry evaluations or urinalyses were performed. Body weight gain was decreased in 3000 ppm females from approximately week 25 onwards; overall gain (weeks 0-104) was 17.0% lower than controls (P=0.07). There was a possible exposure-related decrease in survival in the 3000 ppm males; percent survival at study termination in the control to high-dose groups was 62, 46, 35, 60 and 31% in males and 58, 53, 35, 46 and 50% in females. Pairwise comparisons with controls were statistically significant ($P \leq 0.01$) for the 150 and 3000 ppm males and 150 ppm females, and there was a significant (p=0.02) positive dose-related trend in the males across all five groups (but not if the high-dose group was excluded). Toxicological interpretation of the male data is unclear due to the lack of dose-response at doses <3000 ppm, inconsistent pattern of survival between the sexes, and the lack of accompanying histopathology or any other indications of toxicity. Systemic NOAEL: 108 mg/kg/day (males) and 121 mg/kg/day (females) Systemic LOAEL: 358 mg/kg/day (males) and 364 mg/kg/day (females)	Crome et al., 1987 (MRID 40872401)

Appendix 3: Systemic Toxicity of Dicamba after Repeated Oral Exposure to Mammals

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical[1] (86.8% a.i.)	dog, beagle, 4/sex/dose	Exposure: 0, 100, 500 or 2500 ppm in the diet for one year. Reported dicamba intakes in the high dose group ranged from approximately 50-65 mg/kg/day in males and 45-55 mg/kg/day in females over the course of the study (mean data not reported). Response: No exposure-related adverse effects found by comprehensive evaluations that included clinical signs, body weight, food consumption, ophthalmic condition, hematology, blood chemistry, urinalysis indices, organ weights, gross pathology and histopathology. Food consumption and body weight gain were slightly reduced early in the study predominantly in the high dose group. These effects were transient and attributed to poor palatability of the test substance. Systemic NOAEL: 65 mg/kg/day (males) and 55 mg/kg/day (females) Systemic LOAEL: Not identified.	Drench, 1986 (MRID 40321102)
dicamba, technical (90% a.i.)[2]	dog, beagle, 3/sex/dose	Exposure: 0, 5, 25 or 50 ppm in the diet for 2 years. Assuming a food factor of 0.03 kg diet/kg bw, the corresponding estimated dicamba intakes were 0, 0.15, 0.75 or 1.5 mg/kg/day. Response: Average body weight gain was reduced in males at 25 and 50 ppm (13.5 and 28.0% less than controls) and females at 50 ppm (53.5% less than controls). There were no exposure-related changes in food consumption or other study endpoints, including clinical signs, hematology, urinalysis, organ weights (10 organs), gross pathology and histopathology (12 tissues). Systemic NOAEL: 0.15 mg/kg/day (males) and 0.75 mg/kg/day (females) Systemic LOAEL: 0.75 mg/kg/day (males) and 1.5 mg/kg/day (females)	Davis et al. 1962 (MRID 00028248)

[1]Technical Reference Standard, Velsicol Chemical Corporation
[2] The "remainder" of the formulation (Velsicol Chemical Corporation) was comprised of 3,5-dichloro isomer
NOS = Not otherwise specified.

Appendix 4: Nervous System Effects of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical (86.9%)	rat, Crl:CD BR, 10/sex/level	Exposure: A single dose in corn oil was administered by gavage in dose levels of 0 (vehicle control), 300, 600 or 1200 mg/kg. Response: Acute neurobehavioral toxicity was assessed using a Functional Observational Battery conducted within 1.5 ± 1 hours after treatment. Changes in a number of endpoints/measures occurred at all dose levels that overall were described as a stimulus- or stress-induced rigidity. The effects were generally dose-related and included rigidity in handling/body tone, increased salivation and impaired respiration, flattened and/or raised posture, impaired gait, hypoalterness, decreased rearing frequency, freezing in response to touch, abnormal righting reflex, increased tail flick latency, decreased forelimb grip strength, and decreased locomotor activity. A few of these changes also occurred in the high-dose group at 7 days after dosing, but not at day 14, indicating that there were no persistent effects. Histological examination of nervous system tissues showed no clear treatment-related alterations. Body weight gain and food consumption were reduced in the high-dose males; no other non-neurological endpoints were evaluated. Neurotoxicity NOAEL: Not identified. Neurotoxicity LOAEL: 300 mg/kg	Minnema, 1993 (MRID 42774104)

Appendix 4: Nervous System Effects of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical (86.9%)	rat, Sprague-Dawley, 10/sex/level	Exposure: 0, 3000, 6000 or 12,000 ppm in the diet for 13 weeks. Reported overall mean compound intake for the low-, mid- and high-dose groups was 197.1, 401.5 and 767.9 mg/kg/day for males and 253.4, 472.0 and 1028.9 mg/kg/day for females. Response: Subchronic neurobehavioral toxicity was assessed by a Functional Observational Battery and open-field locomotor activity during weeks 4, 8 and 13. Several effects occurred in high-dose rats of both sexes, particularly increased body tone rigidity in response to handling and touch. Additional findings of abnormal air righting reflex, mildly impaired gait, and increased latency to first step in the high dose rats were possibly related to the increased rigidity. Histological examinations of nervous system tissues and ophthalmoscopic examinations showed no treatment-related effects. Other findings included reduced body weight gain and food consumption in the high-dose males; additional non-neurological endpoints were not evaluated. Neurotoxicity NOAEL: 401.5 mg/kg/day (males) and 472.0 mg/kg/day (females) Neurotoxicity LOAEL: 767.9 mg/kg/day (males) and 1028.9 mg/kg/day (females)	Minnema, 1994 (MRID 43245210)
dicamba, technical (NOS)	rat, albino, 25F/dose	Exposure: 0 (vehicle control), 64, 160 or 400 mg/kg/day in corn oil by gavage on gestation days 0-19. Response: Clinical signs of maternal toxicity that included ataxia, salivation, body stiffening and decreased motor activity occurred in pregnant rats administered 400 mg/kg/day. Other effects at this dose level included reduced body weight gain and food consumption and several deaths. No maternal effects observed at ≤160 mg/kg/day. Other results of this study are summarized in Appendix 5. Neurotoxicity NOAEL: 160 mg/kg/day Neurotoxicity LOAEL: 400 mg/kg/day	Smith et al., 1981 (MRID 00084024)

Appendix 4: Nervous System Effects of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species Strain, Sex	Exposure/Response	Reference
dicamba, technical (NOS)	rabbit, New Zealand 19-29F/dose	Exposure: 0 (capsule control), 30, 150 or 300 mg/kg/day via gelatin capsules (once daily) on gestation days 6-18. Response: Clinical signs of maternal toxicity that included decreased motor activity, ataxia and impaired righting reflex occurred at ≥150 mg/kg/day. No maternal effects at 30 mg/kg/day. Other results of this study are summarized in Appendix 5. Neurotoxicity NOAEL: 30 mg/kg/day Neurotoxicity LOAEL: 150 mg/kg/day	Hoberman, 1992 (MRID 42429401)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
		Teratogenicity Studies	
dicamba, technical (NOS)	rat, albino, 25F/dose	Exposure: 0 (vehicle control), 64, 160 or 400 mg/kg/day in corn oil by gavage on gestation days 0-19. All animals were sacrificed on gestation day 20. Response: No maternal toxicity observed at ≤160 mg/kg/day. Dams in the 400 mg/kg/day had clinical signs of toxicity (including ataxia, body stiffening and decreased motor activity) as well as reduced body weight gain and food consumption. Three gravid and one non-gravid 400 mg/kg/day females died on or before the second day of dosing; no deaths occurred in any of the other groups. No treatment-related fetotoxicity or developmental effects at any dose level shown by assessments of numbers of pregnancies, implantation and resorption sites, and viable and dead fetuses, as well as litter weights and external, skeletal and visceral fetal examinations. Maternal toxicity NOAEL: 160 mg/kg/day Maternal toxicity LOAEL: 400 mg/kg/day Developmental toxicity NOAEL: 400 mg/kg/day Developmental toxicity LOAEL: Not identified	Smith et al., 1981 (MRID 00084024)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
dicamba, technical (87.7% a.i.)	rabbit, New Zealand, 10F/dose	Exposure: 0 (vehicle control), 0.5, 1, 3, 10 or 20 mg/kg/day in 0.5% Methocel by gavage on gestation days 6-18. Animals were sacrificed on gestation day 29. An excess number of animals were mated to provide 10 pregnant animals/group at termination. This was pilot study apparently conducted to determine dose levels for the Goldenthal et al. (1978) study summarized below. Response: No exposure-related effects on a limited number of endpoints of maternal toxicity (clinical signs, mortality, body weight gain) and developmental toxicity (viable/nonviable fetuses, early/late resorptions, total implantations, external abnormalities) at ≤3 mg/kg/day. Effects at 10 and 20 mg/kg/day included an apparent dose-related increase in mean number of post-implantation losses (250 and 600% more than controls) and decrease in mean number of live fetuses (15.1 and 17.2% less than controls), as well as slight decreases in maternal body weight gain during the treatment period that largely recovered by the end of the study. Maternal toxicity NOAEL: 3 mg/kg/day Maternal toxicity LOAEL: 10 mg/kg/day Developmental toxicity NOAEL: 3 mg/kg/day Developmental toxicity LOAEL: 10 mg/kg/day	Wazeter et al., 1977 (MRID 00025373)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
Banvel D, technical (87.7% a.i.)	rabbit, New Zealand, 31-35F/dose	Exposure: 0 (vehicle control), 1.0, 3.0 or 10.0 mg/kg/day in 0.5% aqueous methylcellulose by gavage on gestation days 6-18. Animals were sacrificed on gestation day 29. 31-35 females/dose level were mated to provide 20 pregnant animals/group at termination. Because of insufficient pregnancies, 59 additional rabbits were treated five months later to complete the groups. Response: There were no chemical-related clinical signs of toxicity in the dams, although maternal body weight was slightly reduced at 10 mg/kg/day (body weight on day 18 and 29 was 2.4 and 1.3% lower than on day 0 in the high-dose group, compared to 3.1 and 5.3% higher than day 0 in the vehicle controls). Slightly reduced mean fetal body weight (8.1% less than vehicle controls) and slightly increased number of post-implantation losses/dam (20.0% higher than controls) were also observed in the 10 mg/kg/day group, but these changes were not statistically significantly different than control values. No remarkable effects occurred at ≤3.0 mg/kg/day, including changes in numbers of early and late resorptions, total implantations, corpora lutea, viable and nonviable fetuses, fetal body weight and sex ratio, or incidences of external, visceral (including brain) or skeletal abnormalities. Maternal toxicity NOAEL: 3 mg/kg/day Maternal toxicity LOAEL: 10 mg/kg/day Developmental toxicity NOAEL: 3 mg/kg/day Developmental toxicity LOAEL: 10 mg/kg/day This study is used as the basis for the chronic RfD for dicamba (U.S. EPA, 1992a)	Goldenthal et al., 1978 (MRID 00028236)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
dicamba, technical (NOS)	rabbit, New Zealand Hra:(NZW)SPF, 19-29F/dose	Exposure: 0 (capsule control), 30, 150 or 300 mg/kg/day via gelatin capsules (once daily) on gestation days 6-18. Animals were sacrificed on gestation day 29. Response: No exposure-related effects at 30 mg/kg/day as shown by assessments of maternal toxicity (clinical observations, body weight, food consumption), abortions, premature deliveries, corpora lutea, implantations, early and late resorptions, live/dead fetuses, litter sizes, fetal sex ratio and body weight, and fetal gross external, soft tissue and skeletal alterations. Maternal toxicity occurred at ≥150 mg/kg/day, including signs of neurotoxicity (e.g., decreased motor activity, ataxia) and reduced body weight gain. Other maternal effects at 300 mg/kg/day included rales, labored breathing, impaired righting reflex, perinasal discharge, dried or no feces, reduced food consumption, and weight loss during the dosing period. Abortions occurred at the maternally toxic doses of 150 mg/kg/day (one doe) and 300 mg/kg/day (four does, significantly different from control group), but were not accompanied by any other effects on embryo-fetal viability or development. Maternal toxicity NOAEL: 30 mg/kg/day Maternal toxicity LOAEL: 150 mg/kg/day Developmental toxicity NOAEL: 30 mg/kg/day Developmental toxicity LOAEL: 150 mg/kg/day	Hoberman, 1992 (MRID 42429401)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
		Reproductive Toxicity Studies	
dicamba, technical (90% a.i.; "remainder" comprised of 3,5-dichloro isomer)	rat, Sprague-Dawley, 2M and 3F	Exposure: 500 ppm in the diet for 3 months. This dietary level corresponds to an estimated dose of 25 mg/kg/day. The treated males and females were bred twice with an identical number of unexposed rats. The rats were subgroups of control and high-dose rats taken from a two-year chronic toxicity study (Davis et al., 1962). Response: No exposure-related adverse effects on breeding success (no. females with litters/number mated), percent of live births, average number of pups/litter, or average body weight and sex distribution of pups. Reproductive NOAEL: 25 mg/kg/day Reproductive LOAEL: Not identifed.	Davis et al. 1962 (MRID 00028248)

Appendix 5: Reproductive and Developmental Toxicity of Dicamba after Repeated Oral Exposure

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference
dicamba, technical (Technical Banvel D) (87.2% a.i.)	rat, Charles River CD, 20F/dose 10M/dose	Exposure: 0, 50, 125, 250 or 500 ppm in the diet for three consecutive generations. F0 animals were exposed for 3 weeks (until 100 days old) before mating. These dietary levels correspond to estimated doses of 0, 2.5, 6.25, 12.5 or 25 mg/kg/day. The F1a litters were suckled for 7 days and then terminated. After an interval of one week the F0 dams were remated with the F0 males. The F1b litters were suckled until normal weaning at 3 weeks, and then fed the test diet until 3 months old when they were mated. Following weaning of the F2a litters the F1b rats were fed the test diet for 8 months and remated produce the F2b generation. The F2b rats (10 females and 5 males per dose level) were used to produce F3a and F3b litters using the mating/exposure schedule used to produce the two F2 generations. The F3a and F3b litters were terminated after weaning. Response: No exposure-related effects on number and size of litters as shown by determinations that included fertility index (no. pregnancies/no. matings), gestation index (no. litters with live pups/no. pregnancies), viability index (no. live pups at 7 days/no. born), lactation index (no. pups weaned/no. alive at 7 days), or pup body weight at and following birth. No exposure-related gross external or visceral abnormalities (all generations examined) or histological changes in the viscera (examinations limited to F3 generation). Reproductive NOAEL: 25 mg/kg/day Reproductive LOAEL: Not identified.	Witherup et al., 1966 (MRID 00028249)
dicamba, technical (86.9% a.i.)	Rat, Crl:CD (SD)BR VAF/Plus, 28-32 sex/dose	Exposure: 0 (diet control), 500, 1500 or 5000 ppm in the diet for two consecutive generations. Reported intakes of dicamba in the 500, 1500 and 5000 ppm groups in the F0 generation (mean of weeks 1-10) were 35.1, 105 and 347 mg/kg/day for males, and 41.1, 125 and 390 mg/kg/day for females. Intakes in the F1 generation (weeks 5-16) were 40.6, 121 and 432 mg/kg/day for males, and 44.2, 135 and 458 mg/kg/day for females. F0 animals (32/sex/group) were exposed from 6 weeks of age for 10 weeks prior to pairing and subsequently until they were terminated after all litters had weaned. The F1 generation (28/sex/group) was selected from these litters with direct diet exposure commencing at 4 weeks of age. The F1 pups were reared to maturity and paired at 16 and 25 weeks of age to produce F2a and F2b generations. The study was terminated after the F2b litters were weaned.	Masters, 1993 (MRID 43137101)

Formulation or Salt	Species, Strain, Sex	Exposure/Response	Reference

Responses Noted in Masters (1993): A comprehensive assessment of showed no effects on fertility or reproductive performance at any level of exposure. Body weight gain was significantly ($p \leq 0.05$) reduced in F1 females, mate 1, on day 14 of pregnancy at 500, 1500 and 5000 ppm, but the response did not increase with dose (22.2, 14.5 and 8.2% less than controls). Body weight gain in F1 females, mate 2, was similarly reduced on days 14 and 17 of pregnancy at ≥1500 ppm. The changes in F1 female body weight appeared to be associated with slight reductions in food and water intake, particularly at 5000 ppm. Consistent with these changes in F1 females was significantly reduced mean pre-weaning body weight gain in F2a and F2b pups at 1500 ppm (10-14% less than controls) and F1, F2a and F2b pups at 5000 ppm (24-30% less than controls). Other effects at 5000 ppm included significantly delayed sexual maturation in F1 males (45.6 days old vs. 43.7 in controls; likely related to the initial reduced growth rate), signs of neurotoxicity (increased body tone and slow righting reflex) in F1 females (both matings) during the latter part of lactation, slightly increased (non-significant) F2b pup pre-weaning mortality, and increased relative liver weight in all adults and weanlings in all generations except F0 males. Histological examinations (liver and reproductive tissues) and sperm examinations (number, motility, mobility) showed no treatment-related changes in adults or weanlings in any generation.
Reproductive NOAEL: 35-44 mg/kg/day (500 ppm)
Reproductive LOAEL: 105-135 mg/kg/day (1500 ppm)

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
dicamba DMA, technical (86.93% a.i.)	Bobwhite quail (*Colinus virginianus)*	acute oral (gavage, corn oil)	single dose (14 d)	LD50 = 216 mg/kg (95% CI = 162-288) Equiv to 187 mg a.e./kg No mortality level = 62.5 mg/kg LOEL = 31.2 mg/kg (signs of neurotoxicity) Equiv to 27 mg a.e./kg NOEL = 15.6 mg/kg [13.6 mg a.e./kg]	Campbell et al., 1993 (MRID 42918001)

Note on Campbell et al. 1993: Signs of neurotoxicity were seen in two of five animals at the LOEL. Effects included lethargy, wing droop, loss of coordination, weakness and rigidity in the legs, and abnormal gait. Effects were transient in one animal but persisted for four days after dosing in the other animal.

dicamba, DGA salt, see note below	Bobwhite quail	acute oral (gavage, dispersed in water)	single dose (14 d)	LD50 = 968 mg/kg (95% CI = 644-1615) corresponding to 372 mg a.e./kg No mortality level = Not identified LOEL = 292 mg/kg [112 mg a.e./kg] NOEL = Not identified (<292 mg/kg)	Grimes, 1986a (MRID 00162070)
dicamba, DGA salt, see note below	Bobwhite quail	subacute dietary	5 days (3 d)	LD50 > 5620 ppm NOEL = 5620 ppm (highest level tested, no deaths or overt signs of toxicity) Ave food intake and body weight during dosing period at NOEL were 9 g food/bird/day and 30g bw.	Grimes, 1986b, 1986c (MRID 00162071, 00162072)

Note on Grimes 1986b: The test material is identified on label as 4 lb/gal diglycolamine salt of dicamba (percent a.i. not reported). This is presumably Vanquish, which is 56.8% a.i. and 38.5% a.e. Signs of toxicity at the LOEL were mainly neurotoxic and included lower limb weakness and rigidity, loss of coordination, reduced reaction to external stimuli, lethargy and/or prostate posture; surviving birds recovered by days 4-6. The NOAEL of 5620 ppm corresponds to a dose of 1686 mg/kg/day based on food consumption data or 650 mg a.e./kg.

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
dicamba, IPA salt (32.3% a.e.)	Bobwhite quail	acute oral (gavage, dispersed in water)	single dose (14 d)	LD50 = 1373 mg/kg (95% CI = 1105-1716) corresponding to about 440 mg/kg a.e. No mortality level = 810 mg/kg [261 mg a.e./kg] LOEL = 292 mg/kg [signs of neurotoxicity] [94 mg a.e./kg] NOEL = Not identified (<292 mg/kg)	Beavers, 1986 (MRID 00164105)
Banvel technical (86.8% a.i.)	bobwhite quail (*Colinus virginianus*) (14 days old)	subacute oral dietary (dissolved in corn oil and mixed with diet)	5 days (3 d)	NOEL = 1000 ppm LOEL = 2150 ppm. Abnormal feeding behavior (toe picking) with no clear effect on body weight gain. Overt signs of toxicity (e.g., loss of coordination and wing droop) at ≥4640 ppm. Mortality at 10,000 ppm (highest tested level). Note: ave food intake/body weight was 80g food-day/39g bw at 1000 ppm and 78g food-day/36g bw at 2150 ppm	Fink 1977a (Accession No. 232965) *
dicamba, DMA salt (Technical Banvel) (86.8% a.i.)	bobwhite quail	subacute dietary	8 days (NR)	LD50 > 10,000 ppm diet	Velsicol Chemical Corporation 1979
dicamba, free acid (Banvel XP) (10% a.i.)	bobwhite quail	subacute dietary	8 days (NR)	LD50 > 10,000 ppm diet. Secondary data source.	Velsicol Chemical Corporation 1979

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
dicamba, technical (86.9% a.i.)	Bobwhite quail (*Colinus virginianus)*	1-generation reproduction dietary (corn oil diluent added to diet)	21 weeks (photoperiod increased during week 8 to induce egg laying)	NOEL = 1600 ppm (highest level tested). No exposure-related deaths, overt signs of toxicity, or effects on body weight, feed consumption or reproductive endpoints (egg production and quality, embryo viability, and hatchling health and 14-day survivability). Based on measured food consumption (about 10.5% of body weight), the dietary NOAEL corresponds to a dose of 170 mg/kg bw.	Beavers et al., 1994b (MRID 43814004)
Na salt (aqueous, NOS)	chicken (hen, hybrid commercial)	acute oral (gavage)	single dose (NR)	LD_{50} = 673 mg/kg (95% CI = 396-1142). Unspecified aqueous formulation. Neurotoxicity indicated by salivation.	Edson and Sanderson, 1965
dicamba (NOS)	domestic chicken (hen)	acute oral (gavage, corn oil)	single dose (14 d)	LD50 = 316 mg/kg (95% CI = 72-443)	Roberts et al. 1983 (MRID 00131290)
dicamba (NOS)	domestic chicken (hen)	acute oral delayed neurotoxicity (gavage, corn oil)	single dose (21 d)	316 mg/kg: Inability to stand from days 1-19. Sciatic nerve damage that appeared to be secondary to the prolonged recumbency rather than a direct chemical effect. No ataxia or other typical signs of neurotoxicity. Decreased body weight. 158 mg/kg: Recumbent for <1 day but no histopathological changes in nervous system. Initial decrease in body weight followed by partial recovery. 79 mg/kg: No neurotoxic or other effects.	Roberts et al. 1983 (MRID 00131290)

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
dicamba, technical (89.3% a.i.)	Japanese quail (*Coturnix japonica)*, chicks	subacute dietary (corn oil diluent added to diet)	5 days (≥3 d)	NOEL = 5000 ppm (highest level tested). No mortality, overt signs of toxicity, or effects on food consumption. Note: Food consumption ranged from 10.5-13.1 g/bird/day. 14-day-old chicks; bw NR	Hill and Camardese, 1986
dicamba, technical (86.93% a.i.)	Mallard duck (*Anos platyrhynchos)*	acute oral (gavage, corn oil)	single dose (14 d)	LD50 = 1373 mg/kg (95% CI = 1105-1716) No mortality level = 810 mg/kg LOEL = 175 mg/kg (signs of toxicity)[3] NOEL = Not identified (<175 mg/kg)	Campbell and Beavers, 1993 (MRID 42774106)
dicamba, DMA salt (Technical Banvel) (86.8% a.i.)	Mallard duck	acute oral	presumed single dose (NR)	LD50 = 2000 mg/kg	Velsicol Chemical Corporation 1979
dicamba (NOS)	Mallard duck	acute oral (NOS)	NR	LD50 = 2009 mg/kg. Additional data NR.	Bryant, 1993 (MRID 4279400)
Banvel technical (86.8% a.i.)	mallard duck (*Anas platyrhynchos*) (14 days old)	subacute oral dietary (dissolved in corn oil and mixed with diet)	5 days (3 d)	NOEL = 2150 ppm LOEL = 4640 ppm. Overt signs of toxicity including lethargy, loss of coordination and lower limb weakness; CNS effects more severe and varied at higher concentrations. No deaths at ≤10,000 ppm (highest tested level). Note: ave food intake/body weight was 884g food-day/330g bw at 2150 ppm and 572g food-day/319g bw at 4640 ppm	Fink 1977b (Accession No. 232965) *

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
Banvel technical (86.8% a.i.)	mallard duck (*Anas platyrhynchos*) (14 days old)	subacute oral gavage (dissolved in corn oil and intubated into crop)	8 days (0 d)	NOEL = not identified LOEL = 215 mg/kg/day. Overt signs of toxicity including reduced reaction to external stimuli, depression, loss of coordination and lower limb weakness; CNS effects more severe and varied at higher doses. Surviving birds appeared to have loss of motor function. LD50 = 2009 mg/kg/day (95% CI = 1523-2649)	Fink 1977c (Accession No. 232965) *
dicamba (NOS)	Mallard duck	subacute dietary	8 days (NR)	LC50 > 10,000 ppm. Additional data NR.	Bryant, 1993 (MRID 4279400)
dicamba, DMA salt (Technical Banvel) (86.8% a.i.)	Mallard duck	subacute dietary	8 days (NR)	LD50 > 10,000 ppm diet	Velsicol Chemical Corporation 1979
Banvel, NOS	Mallard duck, fertile eggs	embryotoxicity (egg immersion, aqueous emulsion)	30 seconds on day 3 of development	200 lb/acre (highest tested level; lower concentrations not specified): Reduced growth and stunted eye development. LC50 >200 lb/acre. Effects observed by external examination of embryos on day 18 of egg development. Quantitative data (incidence or magnitude of effects) not reported.	Hoffman and Albers, 1984

Appendix 6: Toxicity of Dicamba to Birds

Formulation or Salt	Species	Type of Study	Exposure Time (Observation)	Response	Reference
dicamba, technical (86.9% a.i.)	Mallard duck	one-generation reproduction dietary (diluted in acetone/corn oil and added to feed)	21 weeks (photoperiod increased at week 9 to induce egg laying)	LOEL = 1600 ppm (highest level tested). Slightly reduced hatchability indicated by non-statistically significant ($p>0.05$) reductions in percentages of hatchlings/eggs set (24.2% less than controls), hatchlings/maximum eggs set (27.1%), 14-day-old survivors/eggs set (26.7%) and 14 day-old survivors/maximum eggs set (31.3%). NOEL = 800 ppm. No exposure-related deaths, overt signs of toxicity, or effects on body weight, feed consumption or reproductive endpoints (egg production and quality, embryo viability, and hatchling health and 14-day survivability). Based on measured body weights and food consumption, the birds consumed food at a rate of about 11.5% of body weight per day. Thus, the LOEL corresponds to a dose of about 184 mg/kg/day and the NOEL corresponds to a dose of about 92 mg/kg/day.	Beavers et al., 1994a (MRID 43814003)
dicamba, (aqueous, NOS)	pheasant (male, hybrid commercial)	acute oral (gavage)	single dose (NR)	LD_{50} = 800 mg/kg (95% CI = 490-1305). Unspecified aqueous formulation.	Edson and Sanderson, 1965
dicamba (NOS)	Quail (NOS)	subacute dietary	8 days (NR)	LC50 > 10,000 ppm. Additional data NR.	Bryant, 1993 (MRID 4279400)

Appendix 7: Toxicity of Dicamba to Fish and Amphibians

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference
FISH					
dicamba, technical (88% a.i.)	Bluegill sunfish (*Lepomis macrochirus*)	static unmeasured	96 hr	LC50 > 50 mg/L note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
dicamba, technical (88% a.i.)	Rainbow trout (*Oncorhynchus mykiss*)	static unmeasured	96 hr	LC50 = 28 mg/L (95% CI not reported) note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
dicamba, technical (88% a.i.)	Cutthroat trout (*Oncorhynchus clarki*)	static unmeasured	96	LC50 > 50 mg/L. note: LC50 of dicamba was >50 mg/L alone or in 1:1 combination with picloram, 2,4-D butyl ester or 2,4-D isooctyl ester. 50 mg/L dicamba did not significantly alter the toxicity of these herbicides.	Woodward 1982
Banvel technical (86.82%)	Bluegill sunfish (*Lepomis macrochirus*)	static unmeasured	24 hr 48 or 96 hr 24 - 96 hr	LC50 = 227.3 mg/L (95% CI 202.5-255.1) LC50 = 135.3 mg/L (95% CI not reported) NOEC = 56.0 mg/L (No abnormal behavior or dark discoloration)	Vilkas 1977a (Accession No. 232965)
dicamba (Banvel) (38% [4 lb/gal] potassium salt of dicamba)	Bluegill sunfish (*Lepomis macrochirus*)	static unmeasured	96 hr 96 hr	LC50 = 230 mg/L (95% CI 180-320) No effect level: 100 mg/L (no mortality or other abnormal effects – i.e, surfacing, loss of equilibrium, dark discoloration, quiescence and/or fish on the bottom of the test vessel). 24- and 48-hour LC50 and 95% CI were the same as the 96-hour values. Test concentrations "prepared based on total compound" Test material (CN 10-6471) identified as Banvel Herbicide in EPA citation.	McAllister et al. 1985a (MRID 00153150)

Appendix 7: Toxicity of Dicamba to Fish and Amphibians

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference
dicamba (Banvel) (38% potassium salt of dicamba)	Rainbow trout (*Salmo gairdneri*)	static unmeasured	24 hr 48 hr 96 hr 96 hr	LC50 = 230 mg/L (95% CI 180-320) LC50 = 180 mg/L (95% CI 100-320) LC50 = 130 mg/L (95% CI 100-180) No effect level: 56 mg/L (no mortality or other abnormal effects[3]). Test concentrations "prepared based on total compound". Test material (CN 10-6471) identified as Banvel Herbicide in EPA citation.	McAllister et al. 1985b (MRID 00153151)
dicamba (Banvel)	Coho salmon (*Oncorhynchus kisutch)* (yearling)	static renewal, measured	144 hr, freshwater[a] 268 hr, seawater[a]	100% survival at ≤110 mg/L (highest level tested) in both fresh and salt water. Histological examination of fish exposed to 100 mg/L for 144 hours showed alterations in the liver (foci of peripheral and/or peribiliary bile necrosis, apparently regarded as not toxicologically significant by investigators), but not in kidneys or gills. Fish in other exposure groups not examined.	Lorz 1979
dicamba (Banex)	Mosquito fish (*Gambusia affinis*)	static unmeasured	24 hr 48 hr 96 hr	LC50 = 516 mg/L LC50 = 510 mg/L LC50 = 465 mg/L	Johnson 1978
dicamba, NOS	Bluegill sunfish (*Lepomis macrochirus*)	NR	48 hr	LC50 = 130 mg/L	Hurlbert, 1975
Banvel technical (reference standard, 86.82%)	Sheepshead minnow (*Cyprinodon variegatus*)	static unmeasured	24 hr 48 hr 96 hr	LC50 > 180 mg/L (highest level tested) for all exposure times. No mortality or abnormal behavior.	Vilkas 1977c (Accession No. 232965) *

Appendix 7: Toxicity of Dicamba to Fish and Amphibians

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference
dicamba DMA salt (Banvel D), liquid	Bluegill sunfish (*Lepomis macrochirus*)	static unmeasured	24 hr 48 hr	LC50[b] = 600 ppm (a.e.) LC50[b] = 410 ppm (a.e.)	Hughes and Davis 1962
dicamba DMA salt (Banvel D), granular	Bluegill sunfish (*Lepomis macrochirus*)	static unmeasured	24 hr 48 hr 24 hr 48 hr	LC50[b] = 20 ppm (a.e.) on vermiculite granules LC50[b] = 20 ppm (a.e.) on vermiculite granules LC50[b] = 67.5 ppm (a.e.) on attapulgite granules LC50[b] = 67.5 ppm (a.e.) on attapulgite granules	Hughes and Davis 1962
dicamba DMA salt (Banvel D)	Bluegill sunfish (*Lepomis macrochirus*)	NR	48 hr	LC50 = 130.0 mg/L ("estimated" LC50, secondary data)	Bohmont 1967
dicamba DMA salt (Banvel D)	Coho salmon (*Oncorhynchus kisutch)* (juvenile)	static unmeasured	24 hr 48 hr	LC50[b] = 151 ppm LC50[b] = 120 ppm	Bond et al. 1965
dicamba DMA salt (Banvel D)	Rainbow trout (*Oncorhynchus mykiss)*	static unmeasured	72 hr	LC50[b] > 320 ppm	Bond et al. 1965
dicamba DMA salt (Banvel D)	Rainbow trout (*Oncorhynchus mykiss*)	NR	48 hr	LC50 = 35.0 mg/L ("estimated" LC50, secondary data)	Bohmont 1967
AMPHIBIANS					
dicamba (Banel)	Frog (tadpole) (*Adelotus brevis*)	static unmeasured	24 hr 48 hr 96 hr	LC50 = 220 mg/L LC50 = 202 mg/L LC50 = 185 mg/L	Johnson 1976
dicamba (Banel)	Frog (tadpole) (*Limnodynastes peroni*)	static unmeasured	24 hr 48 hr 96 hr	LC50 = 205 mg/L LC50 = 166 mg/L LC50 = 106 mg/L	Johnson 1976

Appendix 7: Toxicity of Dicamba to Fish and Amphibians

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference

[a] Survival was assessed after exposure in freshwater for 144 hours and subsequently, following transfer, in seawater for 268 hours.
[b] Reported as MTL (median tolerance limit)
[c] Abnormal effects included surfacing, loss of equilibrium, dark discoloration, quiescence and/or fish on the bottom of the test vessel.

Appendix 8: Toxicity of Dicamba to Aquatic Invertebrates

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference
Cladocera					
dicamba, technical (88% a.i.)	Waterflea *Daphnia magna*	static unmeasured	48 hr	LC50 > 100 mg/L note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
dicamba (40.15% a.i.)	Waterflea *Daphnia magna*	static unmeasured	24 hr 48 hr 48 hr	LC50 > 1000 mg/L LC50 > 1000 mg/L No effect level: 1000 mg/L (no mortality, surfacing, clumping or lying on vessel bottom). Test concentrations "prepared based on total compound." Test material identified as CN-11-4962 (Velsicol) with purity of 40.15% dicamba.	Forbis et al. 1985 (MRID 00153152)
dicamba (Banvel) (38% potassium salt of dicamba)	Waterflea *Daphnia magna*	static unmeasured	24 hr 48 hr 48 hr	LC50 = 780 mg/L (95% CI 560-1000) LC50 = 750 mg/L (95% CI 560-1000) NOEC: 560 mg/L (no mortality, quiescence or lying on vessel bottom). Test concentrations "prepared based on total compound." Test material (CN 10-6471) identified as Banvel Herbicide in EPA citation.	Forbis et al. 1985 (MRID 00153152)
dicamba, NOS	Waterflea *Daphnia magna*	static unmeasured	48 hr	LC50 > 100 mg/L	Sanders 1969
dicamba, NOS	*Daphnia pulex*	NR	48 hr	EC50 = 11 mg/L	Hurlbert 1975

Appendix 8: Toxicity of Dicamba to Aquatic Invertebrates

Formulation or Salt	Species	Type of Exposure	Exposure Time	Response	Reference
Amphipoda					
dicamba, technical (88% a.i.)	*Gammarus fasciatus*	static unmeasured	96 hr	LC50 > 100 mg/L note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
dicamba, NOS	*Gammarus lacustris*	static unmeasured	24 hr 48 hr 96 hr	LC50 = 10 mg/L LC50 = 5.8 mg/L LC50 = 3.9 mg/L	Sanders 1969
dicamba, NOS	*Gammarus lacustris*	NR	96 hr	LC50 = 3.8 mg/L	Hurlbert, 1975
Decapoda					
dicamba, technical (88% a.i.)	*Palaemonetes kadiakensis*	static unmeasured	96 hr	LC50 > 56 mg/L note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
Isopoda					
dicamba, technical (88% a.i.)	*Asellus brevicaudus*	static unmeasured	96 hr	LC50 > 100 mg/L note: "calculated concentrations were based on percent active ingredients" - p.2, paragraph 1	Johnson and Finley 1980
Banvel technical (86.82% a.i.) with acetone as solvent	Grass Shrimp *Palaemonetes pugio* sea water	static unmeasured	24 or 48 hr 96 hr 96 hr	NOEC = 100 mg/L (highest level tested) NOEC = 56 mg/L LOEC= 100 mg/L (highest level tested[2]). 10% mortality.	Vilkas 1978 (Accession No. 232965, MRID 00034702)
Banvel technical (86.82% a.i.)	Fiddler Crab *Uca pugilator* sea water	static unmeasured	24, 48 or 96 hr	NOEC = 180 mg/L (highest level tested[2]). No mortality or abnormal appearance.	Vilkas 1977b (Accession No. 232965, MRID 00034704)

Appendix 9: Toxicity of Dicamba to Aquatic Plants

Form	Species	Type of Assay	Exposure Time	Response[2]	Reference
Algae, freshwater					
dicamba technical (89.5% a.i.)	*Anabaena flos-aquae*	static, measured	5 days	$EC10^4$ = 0.0049 mg/L a.i. (95% CI = 0.0005-0.030) EC50 = 0.061 mg/L a.i. (95% CI = 0.0096-0.55) reported as a.i.; based on initial measured test concentrations (no renewal)	Hoberg 1993c (MRID 42774109)
dicamba technical (89.5% a.i.)	(diatom) *Navicula pelliculosa*	static, measured	5 days	$EC10^4$ = 0.51 mg/L a.i. (95% CI = 0.26-0.95) EC50 = 2.3 mg/L a.i. (95% CI = 1.2-4.5) reported as a.i.; based on initial measured test concentrations (no renewal)	Hoberg 1993d (MRID 42774108)
dicamba technical (89.5% a.i.)	*Selenastrum capricormutum*	static, measured	5 days (120 hours)	NOEC = 3.7 mg/L a.i. (only level tested)[3]. reported as a.i.; based on initial measured test concentrations (no renewal)	Hoberg 1993e (MRID 42774107)
dicamba, sodium salt (technical grade, NOS)	*Selenastrum capricormutum*	static, unmeasured	4 days (96 hours)	NOEC = 12.5 mg/L LOEC = 25 mg/L EC50 = 36.375 mg/L (95% CI = 31.309-41.440) Assessment endpoint: biomass (flourescence)	Fairchild et al. 1997
dicamba, analytical[1]	*Chlamydomonas agloeformis*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Chlamydomonas terricola*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Chlorella ellipsoidea*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Chlorella pyrenoidosa*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Chlorella vulgaris*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975

Appendix 9: Toxicity of Dicamba to Aquatic Plants

Form	Species	Type of Assay	Exposure Time	Response[2]	Reference
dicamba, analytical[1]	*Coccomyxa subellipsoidea*	static, unmeasured	5-30 days	EC50 = 0.2-0.5 ppm)[5] EC100 = 0.9 ppm)[5]	Cullimore 1975
dicamba, analytical[1]	*Haematococcus lacustris*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Hormidium barlowi*	static, unmeasured	5-30 days	EC50 = 0.1-0.5 ppm)[5] EC100 = 2.0 ppm)[5]	Cullimore 1975
dicamba, analytical[1]	*Hormidium flaccidum*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Hormidium stoechidium*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Mesotaenium caldariorum*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Scenedesmus quadricauda*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Spongiochloris excentrica*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975
dicamba, analytical[1]	*Stichococcus bacillaris*	static, unmeasured	5-30 days	NOEC = 10 ppm (highest level tested)[5]	Cullimore 1975

Appendix 9: Toxicity of Dicamba to Aquatic Plants

Form	Species	Type of Assay	Exposure Time	Response[2]	Reference
Algae, marine					
dicamba technical (89.5% a.i.)	(diatom) *Skeletonema costatum*	static, measured	5 days	EC10[4] = 0.0097 mg/L a.i. (95% CI = 0.0011-0.063) EC50 = 0.58 mg/L a.i. (95% CI = 0.090-4.1) reported as a.i.; based on initial measured test concentrations (no renewal)	Hoberg 1993f (MRID 42774110)
Vascular plants, freshwater					
dicamba technical (89.5% a.i.)	duckweed *Lemna gibba*	static, measured	14 days	NOEC = 0.25 mg/L a.i. (frond density) LOEC = 0.51 mg/L a.i. (frond density) NOEC = 3.8 mg/L a.i. (frond biomass [dry weight]) (highest level tested)[3] reported as a.i.; based on initial measured test concentrations (no renewal); measured concentration for 4 highest test levels averaged 61% of nominal conc.	Hoberg 1993b (MRID 42774111)
dicamba, sodium salt (technical grade, NOS)	duckweed *Lemna minor*	static, unmeasured	4 days (96 hours)	NOEC =100 mg/L (highest level tested) Assessment endpoint: biomass (frond count)	Fairchild et al. 1997

[1]analytical grade, NOS
[2]Assessment endpoint: inhibition of cell growth (culture density), unless otherwise specified.
[3]Testing at a higher concentration was not performed because FIFRA guidelines do not require testing at levels above the equivalency of the maximum application rate (2.9 mg a.i./L, equivalent to a recommended maximum application rate of 4 lb a.i./A) to develop an EC50 value.
[4]Investigators considered the EC10 to be a NOEC.
[5]*In vitro* assay system in which algae were impregnated on filter paper discs and exposed to agar or liquid medium containing the chemical.

Appendix 10: Effects of dicamba on various terrestrial plants[a]

Formulation or salt[b]	Species	Life stage[c]	Application rate	Effect	Reference
CROPS: Pre-emergence					
dicamba, technical grade	Seedling emergence assay in cabbage, corn, cucumber, lettuce, oat, onion, ryegrass, soybean, tomato, turnip		application rates of 0.0021 to 2.1 lbs/acre. Different rates used for different species	NOEC values in lb/acre: cabbage: 0.53 corn: 0.25 cucumber:0.25 lettuce: 0.13 oat: 0.25 onion: <0.032 ryegrass: 0.25 soybean: <0.0022 tomato: 0.032 turnip: 0.016	Hoberg 1993a MRID 43538501
Note on Hoberg 1993a pre-emergence assay: NOEC values were not determined in onion or soybean. The EC_{25} values for these species were 0.0044 and 0.00027 lb/acre, respectively. For the most sensitive species for which an NOEC was determined – i.e., tomato with an NOEC of 0.032 lb/acre – the EC_{25} was 0.054 lb/acre. Taking the ratio of the EC_{50} values as an estimate of relative potency, the estimated NOEC for the onion is 0.0026 lb/acre [0.032 × 0.0044/0.054] and the estimated NOEC for soybean is 0.00016 lb/acre[0.032 × 0.00027/0.054].					
dicamba	soybean	PE	1.1	decrease in total yield	Magnusson and Wyse 1987
CROPS: Post-emergence					
dicamba, technical grade	Vegetative vigor assay in cabbage, corn, cucumber, lettuce, oat, onion, ryegrass, soybean, tomato, turnip		application rates of 0.00055 to 2 lbs/acre. Different rates used for different species	NOEC values in lb/acre: cabbage: 0.13 corn: 3.9 cucumber: 0.016 lettuce: 0.016 oat: 1.0 onion: 0.26 ryegrass: 1 soybean: <0.004 tomato: 0.016 turnip: 0.0047	Hoberg 1993a MRID 43538501
Note on Hoberg 1993a post-emergence assay: The relative potency method cannot be used to estimate an NOEC for soybean because the EC_{25} for soybean was higher than the EC_{25} for the most sensitive species with an NOEC.					
dicamba	cotton	PB	0.014 lb/acre [0.016 kg/ha]	no effect on total yield	Hamilton and Arle 1979
dicamba	cotton	PB	0.029 lb/acre [0.032 kg/ha]	13% decrease in total yield	Hamilton and Arle 1979

Appendix 10: Effects of dicamba on various terrestrial plants[a]

Formulation or salt[b]	Species	Life stage[c]	Application rate	Effect	Reference
dicamba	cotton	BL	0.0071 lb/acre [0.008 kg/ha]	12% decrease in total yield	Hamilton and Arle 1979
dicamba	corn	spike	0.892 lb/acre [1 kg/ha]	40+% increase in total yield	Minotti et al. 1980
dicamba	corn	8"	0.892 lb/acre [1 kg/ha]	18% increase in total yield	Minotti et al. 1980
dicamba	corn	12"	0.892 lb/acre [1 kg/ha]	13% decrease in total yield	Minotti et al. 1980
dicamba	wheat	30-d	0 [control]	no adverse effects	Ivany and Nass 1984
dicamba	wheat	30-d	0.11 lb/acre [0.12 kg/ha]	34% increase in deformed heads	Ivany and Nass 1984
dicamba	white clover	6-mon	0 [control]	no adverse effects	Griffin et al. 1984
dicamba	white clover	6-mon	0.12 lb/acre [0.14 kg/ha]	24% decrease in total yield	Griffin et al. 1984
dicamba	crimson clover	6-mon	0 [control]	no adverse effects	Griffin et al. 1984
dicamba	crimson clover	6-mon	0.25 lb/acre [0.28 kg/ha]	41% decrease in total yield	Griffin et al. 1984
dicamba	red clover	6-mon	0 [control]	no adverse effects	Griffin et al. 1984
dicamba	red clover	6-mon	0.12 lb/acre [0.14 kg/ha]	74% decrease in total yield	Griffin et al. 1984
dicamba	soybean	EB	0 [control]	no adverse effects	Auch and Arnold 1978
dicamba	potatoes		0.02 lb/acre [0.022 kg/ha]	reduced total tuber yield by 75%	Wall 1994
dicamba	soybean	EB	0.01 lb/acre [0.011kg/ha]	47% decrease in total yield	Auch and Arnold 1978
dicamba	soybean	EP	0.01 lb/acre [0.011kg/ha]	no adverse effects	Auch and Arnold 1978
dicamba	soybean	EP	0.025 lb/acre [0.028kg/ha]	45% decrease in total yield	Auch and Arnold 1978
dicamba	peanut	NR	0 [control]	no adverse effects	Banks et al. 1977

Appendix 10: Effects of dicamba on various terrestrial plants[a]

Formulation or salt[b]	Species	Life stage[c]	Application rate	Effect	Reference
dicamba	peanut	NR	3 lb/acre [3.36kg/ha]	virtually eliminated	Banks et al. 1977
dicamba	sunflower	PE	0 [control]	no adverse effects	Magnusson and Wyse 1987
dicamba	sunflower	PE	1 lb/acre [1.1kg/ha]	decrease in total yield	Magnusson and Wyse 1987
dicamba	sunflower	2-L	0.0014 lb/acre [0.0016kg/ha]	no effect on total yield	Derksen 1989
dicamba	sunflower	2-L	0.0029 lb/acre [0.0032kg/ha]	42% decrease in total yield	Derksen 1989
DMA	rapeseed	25-d	0.1 lb/acre [0.11kg/ha]	no effect on total yield	O'Sullivan and Kossatz 1984
DMA	rapeseed	25-d	[0.14kg/ha]	53% decrease in total yield	O'Sullivan and Kossatz 1984
CROPS: Application in irrigation water					
DMA	cotton	PE	50 µg/L/day[d]	no effect on fresh weight	Scifres et al. 1973
DMA	cotton	PE	100 µg/L/day[d]	67% decrease in fresh weight	Scifres et al. 1973
DMA	sorghum	PE	100 µg/L/day[d]	no effect on fresh weight	Scifres et al. 1973
DMA	sorghum	PE	500 µg/L/day[d]	70% increase in fresh weight	Scifres et al. 1973
DMA	cucumber	PE	50 µg/L/day[d]	no effect on fresh weight	Scifres et al. 1973
DMA	cucumber	PE	100 µg/L/day[d]	40% decrease in fresh weight	Scifres et al. 1973
dicamba	cotton	90-d	0.068	no effect on total yield	Bruns et al. 1972
dicamba	cotton	90-d	0.285	19% decrease in 1st yield	Bruns et al. 1972
TREES					
dicamba	white ash	8 m	2 lb/acre [2.2 kg/ha]	no injury	Neely and Crowley 1974
dicamba	white ash	8 m	3 lb/acre [3.4kg/ha]	slight phytotoxicity	Neely and Crowley 1974
dicamba	pin oak	8 m	1 lb/acre [1.1kg/ha]	no injury	Neely and Crowley 1974

Appendix 10: Effects of dicamba on various terrestrial plants[a]

Formulation or salt[b]	Species	Life stage[c]	Application rate	Effect	Reference
dicamba	pin oak	8 m	2 lb/acre [2.2kg/ha]	very slight phytotoxicity	Neely and Crowley 1974
dicamba	honey locust	8 m	0 [control]	no injury	Neely and Crowley 1974
dicamba	honey locust	8 m	1 lb/acre [1.1kg/ha]	very slight phytotoxicity	Neely and Crowley 1974
dicamba	blue spruce	3 m	1 lb/acre [1.1kg/ha]	no injury	Neely and Crowley 1974
dicamba	blue spruce	3 m	2 lb/acre [2.2kg/ha]	very slight phytotoxicity	Neely and Crowley 1974
AS	cherry	30.5 cm	0 [control]	no adverse effects	Johnson 1985
AS	cherry	30.5 cm	0.25 lb/acre [0.3kg/ha]	5% decrease in growth	Johnson 1985
AS	cherry	30.5 cm	0.75 lb/acre [0.85kg/ha]	100% mortality	Johnson 1985
AS	juniper	30.5 cm	0.27 lb/acre [0.3kg/ha]	no effect on growth	Johnson 1985
AS	juniper	30.5 cm	0.75 lb/acre [0.85kg/ha]	29% decrease in growth	Johnson 1985
AS	holly (Japanese)	30.5 cm	0 [control]	no adverse effects	Johnson 1985
AS	holly (Japanese)	30.5 cm	0.25 lb/acre [0.3kg/ha]	29% decrease in growth	Johnson 1985
AS	holly (Japanese)	30.5 cm	0.75 lb/acre [0.85kg/ha]	32% decrease in growth	Johnson 1985

[a] Modified and expanded from Caux et al. 1993. Units reported in Caux as kg/ha. Reported values are in brackets [] and are converted to approximate lb/acre.
[b] Formulation: dicamba = 3,6-dichloro-*o*-anisic acid, DMA = Dimethyl salt of dicamba; AS = 3,6-dichloro-2-methoxybenzoic acid - Al salt.
[c] Life stage: PE = preemergence, PB = prebloom, BL = bloom, EB = early bloom, EP = early pod, 2-L = 2- to 4-leaf stage, 30-d = 30 day postemergence, NR = not reported.
[d] These are 30-d greenhouse studies whereby 50mL of aqueous solutions of 50, 100, or 500 µg/L/day DMA were used as single preemergence irrigation treatments.