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Carbaryl

Human Health and Ecological Risk Assessment

Revised Final Report

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Acronyms, Abbreviations, and Symbols

ACGIH	American Conference of Governmental Industrial Hygienists
AChE	acetylcholinesterase
ADD	average daily dose
AEL	adverse-effect level
a.i.	active ingredient
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
$BMDL_{10}$	lower limit of the benchmark dose for 10% reponse
bw	body weight
calc	calculated value
CBI	confidential business information
ChE	cholinesterase
CI	confidence interval
cm	centimeter
CNS	central nervous system
DAA	days after application
DAT	days after treatment
DER	data evaluation record
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
ED_{10}	dose causing 10% response
EHE	2-ethylhexyl ester
EFED	Environmental Fate and Effects Division (U.S. EPA/OPP)
ExToxNet	Extension Toxicology Network
F	female
FH	Forest Health
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
FOB	function observation battery
FQPA	Food Quality Protection Act
g	gram
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient
IARC	International Agency for Research on Cancer
IgG	serum immunoglobulin G
IgM	serum immunoglobulin M
IRED	Interim Reregistration Eligibility Decision
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
LADD	lifetime average daily dose
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
mg	milligram
mg/kg/day	milligrams of agent per kilogram of body weight per day
mL	milliliter
mM	millimole
mPa	millipascal, (0.001 Pa)
MOS	margin of safety
MRID	Master Record Identification Number
MSDS	material safety data sheet
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
NEPA	National Environmental Policy Act
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
Pa	Pascal
PBPK	physiologically-based kinetic
ppm	parts per million
RBC	red blood cells
RED	re-registration eligibility decision
RfD	reference dose
SERA	Syracuse Environmental Research Associates
TEP	typical end-use product
t.g.i.a.	Technical grade active ingredient
TRED	Tolerance Reassessment Eligibility Decision
UF	uncertainty factor
U.S.	United States
USDA	U.S. Department of Agriculture
U.S. EPA	U.S. Environmental Protection Agency
USGS	U.S. Geological Survey
WHO	World Health Organization

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

OVERVIEW

Carbaryl is an insecticide that kills insects by inhibiting the activity of acetylcholinesterase (AChE), an enzyme that is important in the regulation of the nervous system of insects as well as other invertebrate and vertebrate species. While carbaryl is more toxic to insects and other arthropods than to vertebrates, carbaryl may be hazardous to humans as well as a several groups of nontarget organisms.

This risk assessment considers two uses of carbaryl: leaf beetle control and bark beetle prevention. The risk characterization for bark beetle prevention is not fully characterized because of the highly variable and program specific applications that may be made. The risk characterization for leaf beetle control indicates that accidental exposures of workers, members of the general public, and a several groups of nontarget organisms would exceed the level of concern. Under general conditions of exposure anticipated in Forest Service programs, workers can apply carbaryl in a manner that will not lead to any significant toxic effect, so long as care is exercised to minimize exposure. For members of the general public, the greatest potential risks are associated with the consumption of contaminated vegetation. For nontarget species, both aquatic and terrestrial arthropods as well as some sensitive amphibians appear to be groups of organisms that are at greatest risk. Nonetheless, risks to mammals, birds, and fish are plausible, and some plants might also be adversely affected.

As with any generic risk assessment, the risk characterization given in this document is highly dependent on a set of generic and conservative assumptions. This limitation is particularly important in interpreting the risk characterization. For example, applications of carbaryl in Forest Service programs may be made in areas where the consumption of contaminated vegetation by humans is unlikely, particularly over a prolonged period of time. Similarly, all of the exposure assessments based on contaminated water will not be directly applicable to areas with no surface water or surface water with substantially different characteristics than the bodies of water modeled in this risk assessment. Consequently, the large number of hazard quotients that exceed the level of concern under the generic exposure assumptions used in this document clearly suggest a need for a careful program-specific review of carbaryl applications but they do not necessarily indicate that all applications of carbaryl will pose an unacceptable risk to human or nontarget species.

PROGRAM DESCRIPTION

Carbaryl is used in Forest Service programs for the control of leaf beetles on poplars and the prevention of bark beetle infestations in pines. Both types of uses involve the application of various formulations of Sevin, all of which are produced by Bayer CropScience. The formulations are registered for forestry and other non-agricultural applications as well as for applications to numerous agricultural crops. In every other respect, the application of carbaryl to control leaf beetles is substantially different from its application for the prevention of bark beetles.

Application methods for controlling leaf beetles involve relatively standard ground or aerial broadcast application methods in which the leaves of the tree are treated directly over a relatively narrow range of application rates – i.e., from 0.1 to 1.0 lb a.i./acre. Applications for preventing bark beetle infestations involve direct application of carbaryl solutions to tree bark in which the application rate is most meaningfully expressed in units of lb a.i. per tree. The recommended labeled rate is 0.0031 lb a.i./ft^2 of tree bark. Depending on the size of the tree, the labeled rate can range from about 0.1 to more than 1.0 lb a.i./tree. In Forest Service programs, applications are typically made to only high value trees that may be interspersed over a relatively wide range within an overall treated area. Consequently, functional application rates in terms of lbs/acre will depend on the number of trees treated, the size of the trees, and the total treated area of concern.

Based on national data from USGS and the U.S. EPA as well as data from California, it appears that the use of carbaryl in Forest Service programs is extremely small relative to the total amount of the insecticide used in agriculture and in other non-Forest Service applications. Based on a comparison of Forest Service use statistics and agricultural use statistics, the use of carbaryl by the Forest Service is about 4 million times less than agricultural use.

HUMAN HEALTH RISK ASSESSMENT

Hazard Identification – Carbaryl inhibits AChE activity in mammals as well as insects. Unlike AChE inhibition in insects, however, AChE inhibition in mammals is rapidly reversible. Carbaryl is rapidly absorbed after oral exposure and more slowly absorbed after dermal exposure. Since carbaryl is also rapidly metabolized and eliminated from the body, its potential to accumulate with repeated exposure is low.

The consequence of AChE inhibition is wide ranging from mild signs of toxicity (e.g., salivation or lacrimation) to convulsions and death. Neurotoxicity is considered to be the critical effect of carbaryl exposure, and all other signs of toxicity appear to be secondary effects. Therefore, if exposure levels are below those associated with neurotoxicity, the risk of other adverse effects is unlikely, with the possible exception of effects on immune function. Some of the available studies regarding carbaryl toxicity indicate that effects on immune function may occur at doses that are very close to the NOAEL for neurotoxicity.

In addition to effects on the nervous system and immune function, carcinogenicity is the only other endpoint of major concern. The U.S. EPA determined that carbaryl is a likely human carcinogen, and this endpoint is considered quantitatively in this risk assessment. While there is some uncertainty concerning the mechanism of carcinogenicity – i.e., genetic or epigenetic – this endpoint is treated conservatively as a non-threshold response.

Exposure Assessment – All exposure assessments for carbaryl are summarized in the EXCEL workbooks that accompany this risk assessment: Attachment 1 for applications associated with leaf beetle control and Attachment 2 for applications associated with bark beetle prevention. In these workbooks, Worksheet E01 summarizes exposures for workers and Worksheet E03 summarizes exposures for the general public.

For workers applying carbaryl for leaf beetle control, three types of application methods are modeled: directed ground spray, broadcast ground spray, and aerial spray. In non-accidental scenarios involving the normal application of carbaryl, central estimates of exposure for workers are approximately 0.001 mg/kg/day for aerial and backpack workers and about 0.002 mg/kg/day for broadcast ground spray workers. Upper bounds of exposures are approximately 0.011 mg/kg/day for broadcast ground spray workers and 0.006 mg/kg/day for backpack and aerial workers.

For workers involved in applying carbaryl to tree bark for bark beetle prevention, the estimates of exposure are somewhat less: 0.0025 (0.000042 to 0.026) mg/kg bw/day. These exposure estimates, as well as corresponding exposure estimates for the general public, are unit estimates based on the treatment of a single tree with a average diameter of 4 feet and treated along 35 feet of bark. Depending on the number of trees that are treated and the size of the trees being treated, exposures may be higher or lower.

All of the accidental exposure scenarios for workers involve dermal exposure. The accidental exposure scenarios lead to dose estimates that are substantially greater than the general exposure levels estimated for workers. The greatest exposure is estimated as 5.6 (3.8-8.2) mg/kg bw and is associated with wearing contaminated gloves for 1 hour.

For the general public (Worksheet E03), acute levels of exposures range from minuscule (e.g., $5x10^{-5}$ mg/kg/day) to about 67 mg/kg bw at the typical broadcast application rate of 0.75 lb a.i./acre. The upper bound of exposure, 67 mg/kg bw, is associated with the accidental direct spray of a child. This exposure scenario is extreme. The next higher estimated dose is 10.5 mg/kg bw, which is associated with the consumption of contaminated fish after an accidental spill. This exposure scenario is both extreme and also implausible in that an accidental spill would likely lead to signs of toxicity in fish and possible fish mortality. Thus, the probability that humans would consume the fish is low. The highest dose associated with a plausible exposure scenario is about 0.1 (0.03 – 1.0) mg/kg bw, which is associated with the consumption of contaminated vegetation after a broadcast application for leaf beetle control. The exposure estimates in the workbook for bark beetle prevention are lower than those in the corresponding scenario for leaf beetle control. This discrepancy, however, is an artifact of the unit exposure approach taken for applications associated with bark beetle prevention – i.e., the treatment of a single tree.

The chronic or longer-term exposure levels are much lower than the estimates of corresponding acute exposure levels. For leaf beetle control, the highest longer-term exposure levels are associated with the consumption of contaminated vegetation, and the upper bound for this scenario is about 0.06 mg/kg/day. That scenario is followed by the scenario for the longer-term consumption of contaminated fruit with an upper bound of 0.008 mg/kg/day. As with the acute exposures, longer-term exposures associated with the consumption of surface water or contaminated fish are much lower than those associated with the consumption of contaminated vegetation.

Dose-Response Assessment – While the hazard identification for carbaryl is somewhat complex, the dose-response assessment for systemic toxicity is relatively simple. The recent U.S. EPA risk assessment derives an acute RfD of 0.01 mg/kg bw/day based on neurotoxicity. Because of the rapid reversibility of AChE inhibition, the EPA does not derive a chronic RfD. For the current Forest Service risk assessments, the acute RfD of 0.01 mg/kg bw is used to characterize risks associated with both acute and chronic exposure. The primary reservation with this approach concerns the effects of carbaryl on immune function. While there is little doubt that carbaryl can cause changes, including inhibition, in immune function, most studies suggest that neurotoxicity is the critical effect and that changes in immune function are most likely to occur at doses above the threshold for neurotoxicity. One immunotoxicity study, however, suggests that endpoints associated with immune suppression may occur at doses that are only modestly above the animal dose for neurotoxicity used as the basis for EPA's acute RfD. This consideration is addressed further in the risk characterization.

The U.S. EPA has determined that carbaryl is a likely human carcinogen and derived a cancer potency factor for carbaryl. This cancer potency factor is used in the current risk assessment to derive a dose of 0.02774 mg/kg bw/day which is associated with a risk level of one in one-million.

Because many of the hazard quotients discussed in the risk characterization exceed a value of one by a substantial margin, dose-severity relationships for carbaryl are considered. Hazard quotients of up to 10 might not be associated with detectable or clinically significant adverse effects. It is likely that hazard quotients between 10 and 20 would be associated with adverse effects on the kidneys althought it does not appear that overt signs of toxicity would be apparent. The poentail effects associated with hazard quotients between 20 and about 250 cannot be well-characterized. Single oral doses corresponding to hazard quotients of 50, 100, and 200 have not been associated with signs or symptions of toxicity in humans. Hazard quotients in the range of about 250 to 500 could be associated with overt signs and symptoms of cholinesterase inhibition – i.e., salivation, lacrimation, sweating, contraction of the pupil, increased peristalsis with abdominal pain, and muscular fasciculation (twitching). Without medical attention, it is possible that these exposures could also involve effects such as decreased heart rate, decreased blood pressure, increased respiratory rate, and involuntary urination and defecation, and convulsions. As hazard quotients increase above 500, concern for lethality would increase. Death due to the suicidal ingestion of carbaryl has been demonstrated at a dose of about 5,700 mg/kg bw. This death occurred despite emergency medical treatment. It is plausible that much lower doses, perhaps as low as 100 mg/kg bw (corresponding to a hazard quotient of 10,000), could present a risk of death in the absence of medical intervention.

Risk Characterization – Although carbaryl is more toxic to insects than to mammals, including humans, carbaryl effectively inhibits enzyme activity essential to the regulation of the human nervous system – i.e., AChE activity. Consequently exposure to carbaryl is potentially hazardous to workers as well as members of the general public.

Virtually all accidental exposure scenarios for workers and members of the general public lead to hazard quotients that are clearly unacceptable. Hazard quotients for accidental exposures exceed 7000 for workers and 9000 for members of the general public. By definition, all of the accidental exposure scenarios should be regarded as extreme. In addition, all of the accidental exposure scenarios are highly implausible because members of the general public are excluded from treated areas during and immediately after application. Nonetheless, these implausible scenarios are used consistently in Forest Service risk assessments to identify which types of accidental exposures may present a risk that exceeds the level of concern. For carbaryl, all of the accidental exposures fall into this category and the exclusion of members of the general public from the treated area during application is a prudent and necessary practice.

Because of the different methods used to assess exposures associated with carbaryl applications for leaf beetle control and bark beetle prevention, the risk characterizations of non-accidental exposures for the two uses are interpreted differently. Broadcast applications for leaf beetle control are relatively standard, and interpreting the resulting hazard quotients is relatively simple. Applications for bark beetle prevention, however, are based on unit exposure assumptions – i.e., the application to a single high-value tree of a fixed size. Consequently, the hazard quotients for bark beetle applications are relative, and the risk characterization for bark beetle applications has to be assessed at the program level, once the details of the application can be specified – i.e., the number and size of the trees to be treated and the area over which the treatments will be applied.

Under general conditions of exposure anticipated in Forest Service programs, workers can apply carbaryl in a manner that will not lead to any significant toxic effect, so long as care is exercised to minimize exposure. If, however, care is not exercised, the level of exposure is likely to exceed the level of concern at all but the lowest application rate. At the typical application rate for leaf beetle control, hazard quotients for systemic toxicity range from 6 to 11 at the upper bound of exposures. At the highest anticipated application rates, the corresponding hazard quotients range from 8 to 15.

For members of the general public, many of the hazard quotients associated with acute non-accidental exposures are greater in magnitude than those for workers. The greatest hazards are associated with the consumption of contaminated vegetation (HQ values up to 135) and swimming in contaminated surface water (HQ values up to 62). For longer-term exposures, the hazard quotients are lower, and the level of concern – i.e., an HQ greater than 1 – is exceeded only for those exposures associated with the consumption of contaminated vegetation.

ECOLOGICAL RISK ASSESSMENT

Hazard Identification – The endpoints of concern in the ecological risk assessment are similar to those discussed in the human health risk assessment – i.e., AChE inhibition. Vertebrates including mammals, birds, reptiles, amphibians, and fish may be adversely affected by exposure to carbaryl because of its well-characterized neurotoxicity. Although standard toxicity studies may demonstrate other toxicological endpoints, neurotoxicity is the critical effect on which the ecological risk assessment is based. For mammals, there is no apparent systematic relationship between toxicity and body size. For birds, however, there is a weak relationship between

sensitivity and body size, suggesting that smaller birds may be more sensitive than larger birds. As with mammals, studies in fish indicate that neurotoxicity, although rapidly reversible, is the most sensitive endpoint. Thus, this risk assessment differs from most Forest Service risk assessments, in that acute sublethal neurotoxic effects, rather than longer-term reproductive effects, dominate the hazard identification for fish. Although the available studies on amphibians are far fewer than those on fish, they provide adequate evidence that certain amphibians (i.e., some species of salamanders) may be even more sensitive than some sensitive fish to the effects of carbaryl. The very limited amount of information on reptiles qualitatively suggests that their response to carbaryl exposure is like that of other vertebrates and that neurotoxicity is the endpoint of primary concern.

Terrestrial arthropods appear to be much more sensitive than vertebrates to carbaryl exposure. Based on the arthropod species tested in standard laboratory toxicity studies, the honey bee appears to be the most sensitive terrestrial arthropod. Nevertheless, some field studies suggest that carbaryl may have a substantial impact on ground spiders. It is unclear, however, whether the impact can be attributed to greater exposure levels, greater inherent susceptibility, or both. Standard toxicity studies on other terrestrial invertebrates are restricted to earthworms. These studies as well as more general field studies suggest that non-arthropod terrestrial invertebrates – i.e., worms and snails – are much less sensitive than arthropods to the effects of carbaryl exposure.

Like terrestrial arthropods, aquatic arthropods tend to be more sensitive than non-arthropod invertebrates and most aquatic vertebrates to the effects of carbaryl exposure. Sensitive amphibians are the exception. The open literature regarding the effects of carbaryl on the numerous species of aquatic invertebrates is diverse and in some instances very old. While most of the open literature is reasonably consistent with the data used by the U.S. EPA, one study suggests that dragonfly nymphs (*Brachythermis contaminata*) may be much more sensitive than other species to the effects of carbaryl exposure. Given, however that the study on dragonflies involves exposure to a poorly characterized formulation, the study on dragonflies is classified as an outlier and not otherwise used in the current risk assessment.

The direct effects of carbaryl on plants are not well or clearly documented. The available standard laboratory toxicity studies suggest that terrestrial plants are relatively tolerant. Nonetheless, incident reports cited by the U.S. EPA suggest that carbaryl may damage certain crops, particularly citrus. The available toxicity studies on aquatic plants suggest that algae are not highly sensitive to carbaryl. In fact, the major impact of carbaryl applications on aquatic plants might be the algal blooms secondary to adverse effects on the aquatic invertebrates that graze on the plants.

Exposure Assessment – Terrestrial animals might be exposed to any applied pesticide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation. The exposure scenarios for terrestrial species are summarized in Worksheet G01 of the EXCEL workbooks that accompany

this risk assessment for the typical application rate used in leaf beetle control (Attachment 1) and the unit application rate used in bark beetle prevention (Attachment 2).

In acute exposure scenarios, the highest exposure for terrestrial vertebrates involves the consumption of contaminated fish by a predatory bird after an accidental spill which could amount to approximately 460 mg/kg. There is a wide range of exposure levels anticipated from the consumption of contaminated vegetation by terrestrial animals: central estimates range from 1 mg/kg for a small mammal consuming fruit to 20 mg/kg for a large bird. Upper bound estimates for the consumption of contaminated vegetation range from about 2 mg/kg for a small mammal consuming fruit and 57 mg/kg for a large bird consuming grasses. The consumption of contaminated water based on expected environmental concentrations will generally lead to much lower levels of acute exposure – i.e., in the range of about 0.002-0.004 mg/kg. The accidental spill scenario leads to much higher estimates of exposure – i.e., about 0.5-10 mg/kg. A similar pattern is seen for chronic exposures.

The central estimate for daily doses for a small mammal from the longer-term consumption of contaminated vegetation at the application site is about 0.003 mg/kg/day, with an upper estimate of about 0.024 mg/kg/day. Dose estimates associated with the consumption of contaminated water are in the range from 0.00001 to 0.0002 mg/kg bw/day for a small mammal. Based on general relationships of body size to body volume, larger vertebrates, relative to small vertebrates, will be exposed to lower doses, under comparable exposure conditions.

Exposures of aquatic organisms to carbaryl are based on essentially the same information used to assess the exposure of terrestrial species to contaminated water. The peak estimated rate of contamination of ambient water associated with the application of carbaryl for leaf beetle control is 0.02 (0.002 to 0.033) mg a.i./L at a normalized application rate of 1 lb a.i./acre. For longer-term exposures, the estimated rate of contamination of ambient water is 0.0003 (0.0001 to 0.002) mg a.i./L at a normalized application rate of 1 lb a.i./acre. For the assessment of potential hazards to aquatic species, these water contamination rates are adjusted based on the application rates considered in this risk assessment.

As in the exposure assessment for human health, the unit application rate used in bark beetle prevention (Attachment 2) leads to substantially lower estimates of exposure than the corresponding exposure estimates based on broadcast applications for leaf beetle control. Actual exposures associated with applications for bark beetle prevention will depend on the number and size of the treated trees as well as the acreage that is treated.

Dose-Response Assessment –The available toxicity data on nontarget species support separate dose-response assessments in seven groups of organisms: terrestrial mammals, birds, nontarget terrestrial invertebrates, fish, amphibians, aquatic invertebrates, and aquatic algae. Different units of exposure are used for different groups of organisms depending on how exposures are likely to occur and how the available toxicity data are expressed.

For mammals, birds, and fish, separate toxicity values are not derived for acute and chronic exposures. As with the dose-response assessment for human health, the rationale for this approach is the rapid reversibility of AChE inhibition. For mammals, an NOEC of 4 mg/kg bw/day is used from a reproduction study. The same approach is used for birds with an NOEC of 21 mg/kg bw/day from a reproduction study. A somewhat different approach is used for fish. While the U.S. EPA uses a reproductive NOEC of 0.21 ppm, the current risk assessment identifies the inhibition of brain AChE as a more sensitive sublethal effect and uses an NOEC 0.03 ppm d for tolerant fish species and a LOEC of 0.006 ppm for sensitive fish species.

The U.S. EPA uses toxicity values from fish studies to assess risks to amphibians. This approach appears to be justified with the exception of longer-term risks to sensitive species of amphibians. Based on a recent toxicity study in salamanders from the open literature that is not cited in the U.S. EPA, the longer-term risks to sensitive amphibian species is based on a NOEC of 0.0005 ppm.

Arthropods are much more sensitive than vertebrates to carbaryl exposure. For terrestrial arthropods, the LD_{50} value of 1.2 mg/kg bw is adopted from the recent EPA risk assessment. For aquatic arthropods, a NOEC of 0.0035 ppm is used for acute exposures and a reproductive NOEC of 0.0015 is used for longer-term exposures. Other groups of aquatic invertebrates – e.g., mollusks and aquatic worms – are much more tolerant of exposure to carbaryl. For characterizing risks in these groups, an acute EC_{50} of 2.7 mg/L is used for acute exposures and a NOEC of 0.5 mg/L is used for longer-term exposures.

Risks to terrestrial plants are not considered quantitatively but are addressed qualitatively in the risk characterization. No data are available on aquatic macrophytes. For aquatic algae, an NOEC of 0.29 ppm is used to characterize risks after both acute and longer-term exposures.

Risk Characterization – As with the human health risk assessment, the risk characterization for nontarget species focuses primarily on broadcast applications for leaf beetle control, because the exposure assessments that underlie the development of the hazard quotients are relatively standard – i.e., they represent exposures that can be reasonably anticipated in programs for leaf beetle control. For bark beetle prevention, exposures are based on treatment unit assumptions, specifically the treatment of a single high-value tree. Because of this limitation, the hazard quotients for bark beetle applications are relative, and the risk characterization for bark beetle applications must be assessed at the program level, once the number and size of the trees to be treated as well as the area over which the treatments will be applied can be specified. Qualitatively, the general identification of the nontarget organisms at greatest risk may be similar in applications for both leaf beetle control and bark beetle prevention.

While carbaryl is more toxic to insects and some other arthropods, terrestrial vertebrates may be at risk at all but the lowest anticipated application rate. At 0.1 lb a.i./acre, the consumption of contaminated grasses by large and small mammals leads to hazard quotients that marginally exceed the level of concern (1.1 to 1.2) and only at the upper range of plausible exposures. The only other risk quotients that exceeds the level of concern at the lowest application rate is the

upper bound of the risk quotient for a predatory bird consuming contaminated fish after an accidental spill (an HQ of 3) and the upper bound of the risk upper bound of the quotient for a small mammal consuming insects (an HQ of 1.7).

The typical application rate (0.75 lb a.i./acre) and the highest application rate (1 lb a.i./acre) do not differ remarkably, and the risk characterizations for birds and mammals are similar. Hazard quotients associated with acute exposures exceed the level of concern for both accidental scenarios (i.e., direct spray and a spill into a pond) as well as expected exposures based on the consumption of contaminated vegetation and prey. No hazard quotients for the longer-term exposure scenarios exceed the level of concern.

Carbaryl is an effective insecticide. Accordingly, adverse effects, including mortality, are likely to be observed in terrestrial insects exposed to carbaryl during direct spray applications. This does not mean, however, that the consequences of broadcast or directed applications of carbaryl will lead to significant environmental harm (i.e., wide-spread mortality in all insect species). The environmental impact of carbaryl applications will vary in degree according to the timing of the applications as well as which insects and other arthropods are exposed. The available data suggest that the impact of carbaryl exposure is not likely to be substantial or significant with respect to terrestrial non-arthropods.

As with terrestrial invertebrates, the available data on aquatic invertebrates indicate that arthropods are generally more sensitive than non-arthropods to the effects of carbaryl. While the differences in sensitivity among arthropods are not substantial for acute exposures, longer-term studies suggest that some arthropods (e.g., midges) may be more tolerant than others (e.g., daphnids) to the effects of carbaryl exposure.

Based on the standard accidental spill scenario used in this risk assessment as well as other Forest Service risk assessments, spills of field solutions of carbaryl in the range of application rates considered in this risk assessment could adversely impact most groups of aquatic organisms. The only exception involves tolerant invertebrates (e.g., mollusks) at the lowest application rate. In fact, the consequence of a serious accidental spill is likely to be substantial mortality among exposed fish, invertebrates, amphibians, and aquatic plants. Secondary effects, such as algal blooms, could be part of the recovery process and be interconnected with population shifts among invertebrate grazers and predators.

Based on expected environmental concentrations – i.e., carbaryl concentrations anticipated from the normal application of the insecticide – the risk characterization is highly dependant on the application rate. At the lowest anticipated application rate (0.1 lb a.i./acre), no adverse effects are anticipated in any group of organisms. At the typical and upper bound of the application rate (i.e., 0.75 and 1 lb a.i./acre), expected peak concentrations could have adverse effects on sensitive species of fish, invertebrates, and amphibians. Based on the acute hazard quotients, sensitive invertebrates may be the group of aquatic organisms at greatest risk. For longer-term effects, the group at greatest risk appears to be amphibians. Except for the accidental spill

scenario, the adverse effects would probably be sublethal rather than lethal in all aquatic vertebrates.

1. INTRODUCTION

The USDA Forest Service uses carbaryl to control numerous insects that cause severe damage in forests. This document assesses the human health effects and ecological and environmental effects as a consequence of carbaryl use in forestry programs sponsored by the USDA. Specifically, this risk assessment addresses the use of commercial formulations of carbaryl to control cottonwood leaf beetles (*Chrysomela scripta*) on hybrid poplar trees in the South and Midwest and various pine bark beetles (e.g., the pine engraver, *Ips pini*; the southern pine bark beetle, *Dendroctonus frontalis*; black turpentine beetle, *Dendroctonus terebrans*; western pine beetle, *Dendroctonus brevicomis*) in western coniferous forests.

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 carbaryl and its commercial formulation, an assessment of potential exposure to the product, an assessment of the dose-response relationships, and a characterization of the risks associated with plausible levels of exposure. These are the basic steps recommended by the National Research Council of the National Academy of Sciences (NRC 1983) for conducting and organizing risk assessments.

Although this is a technical support document and addresses some specialized technical areas, an effort was made to ensure that the document can be understood by individuals who do not have specialized training in the chemical and biological sciences. Certain technical concepts, methods, and terms common to all parts of the risk assessment are described in plain language in a separate document (SERA 2006a).

The series of human health and ecological risk assessments prepared for the USDA Forest Service are not, and are not intended to be, comprehensive summaries of all of the available information. This statement is particularly true with respect to carbaryl, for which numerous published studies are available. For instance, a cursory search of Toxline, a commonly used database provided by the National Library of Medicine, identified a total of 6875 citations relating to carbaryl. In addition, 3462 unpublished studies were submitted to the U.S. EPA/OPP to support the pesticide registration and re-registration of this compound. It is beyond the scope of and resources available for the preparation of this risk assessment to cover all of the available literature in detail. Instead, the risk assessment is guided by existing reviews in the open literature (e.g., Arbuckle and Sever 1998; Bakke 2004; Cox 2005; Cranmer 1986; FAO/WHO 2001; Grue et al. 1997; Hastings et al. 2001; Mount and Oehme 1981; NPIC 2003; O'Malley 1997; USDA/FS 1989b; WHO 1994) as well as the recent series of reviews and risk assessments produced by the U.S. EPA as part of the reregistration of carbaryl (i.e., a total of 7 citations from U.S. EPA/OPP 2003a-e, 2004a,b, 2007a,b).

The 1994 review by the World Health Organization (WHO 1994) is a comprehensive and critical review of the open literature (as well as some unpublished studies) up to 1993 which summarizes and reviews 735 citations. The information from this review is used directly in many instances

in the current human health and ecological risk assessment as an alternative to consulting the vast amount of literature on carbaryl published prior to 1994. Nonetheless, key studies from the published literature up to 1993 were obtained and reviewed as necessary to prepare the current Forest Service risk assessment. Likewise, most citations published after 1993 were obtained and reviewed for incorporation into the current risk assessment. The citations that were not obtained in preparation of the risk assessment are identified in Chapter 5 (References) by the phrase, "Cited in …" at the end of the citation. The more recent reviews (e.g., Cox 2005; FAO/WHO 2001) were used primarily to identify references not discovered during the literature search and screening processes. Again, all key studies – i.e., studies that impact critical components of the hazard identification, exposure assessment, or dose-response assessment – from the open literature were obtained and reviewed in the conduct of the current risk assessment.

As noted above, numerous (i.e., 3462) unpublished studies were submitted to the U.S. EPA in support of the registration of carbaryl. These studies are treated by the U.S. EPA as confidential business information (CBI), and full copies of these studies were not available for the current risk assessment. The key information from these studies, however, is summarized in the U.S. EPA/OPP citations noted above. The key citations used in the preparation of this risk assessment are the Reregistration Eligibility Decision (RED) for Carbaryl (U.S. EPA/OPP 2007a), the Interim Registration Eligibility Decision or IRED (U.S. EPA/OPP 2004a) as well as the science chapters prepared by the U.S. EPA/OPP Health Effects Division (U.S. EPA/OPP 2003e) and the U.S. EPA/OPP Environmental Fate and Effects Division (U.S. EPA/OPP 2003d). In addition to these documents, *cleared reviews* pertaining to carbaryl were obtained from the U.S. EPA in response to a Freedom of Information Act (FOIA) request. Cleared reviews consist primarily of detailed summaries of registrant submitted studies (referred to as Data Evaluation Records or DERs), internal analyses and reviews conducted by the U.S. EPA, and correspondence between the U.S. EPA and the registrant. A total of 107 cleared reviews (as electronic files) were kindly provided by U.S. EPA/OPP.

In addition to reviews published in the open literature, there is an immense amount of information about carbaryl on the Internet – e.g., over 675,000 hits at http://www.google.com/. For the most part, however, data derived from the Internet is not used unless the information is well documented. The most useful database for the risk assessment is the ECOTOX database compiled and reviewed by the U.S. EPA (U.S. EPA/ORD 2006). ECOTOX is also the main ecotoxicity database used by the Pesticide Action Network (PAN 2006).

The Forest Service will update this and other similar risk assessments on a periodic basis and welcomes input from the general public on the selection of studies included in the risk assessment. This input is helpful, however, only if recommendations for including additional studies specify why and/or how the new or not previously included information would be likely to alter the conclusions reached in the risk assessments.

Almost no risk estimates presented in this document are given as single numbers. Usually, risk is expressed as a central estimate and a range, which is sometimes quite large. Because of the need to encompass many different types of exposure as well as the need to express the uncertainties in the assessment, this risk assessment involves numerous calculations, most of are relatively simple. The relatively simple calculations are included in the body of the document.

Some of the calculations, however, are cumbersome. For those calculations, an EXCEL workbook, consisting of a set of worksheets, is included as an attachment to the risk assessment. The worksheets provide the detail for the estimates cited in the body of this document. The worksheets are divided into the following sections: general data and assumptions, chemical specific data and assumptions, exposure assessments for workers, exposure assessments for the general public, and exposure assessments for effects on nontarget organisms. SERA (2005) provides documentation governing the use of EXCEL workbooks. Because of differences in the application methods for leaf beetle control and bark beetle prevention, two sets of worksheets are provided as attachments. Attachment 1 provides the worksheets for leaf beetle control. These worksheets are standard for most Forest Service risk assessments involving broadcast applications. Attachment 2 provides the worksheets for bark beetle prevention. These worksheets are customized for the application of carbaryl to tree bark, and are discussed further in Section 2.4.2. Details for using these worksheets are given in Worksheet A1 of Attachment 2.

2. PROGRAM DESCRIPTION

2.1. OVERVIEW

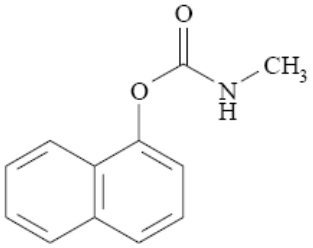
Carbaryl is an insecticide that kills target insects by inhibiting acetylcholinesterase (AChE) activity. Carbaryl is used in Forest Service programs for the control of leaf beetles on poplars and the prevention of bark beetle infestations in pines. Both types of uses involve the application of various formulations of Sevin, all of which are produced by Bayer CropScience. The formulations are registered for forestry and other non-agricultural applications as well as for applications to numerous agricultural crops. In every other respect, the application of carbaryl to control leaf beetles is substantially different from its application for the prevention of bark beetles.

Application methods for controlling leaf beetles involve relatively standard ground or aerial broadcast application methods in which the leaves of the tree are treated directly over a relatively narrow range of application rates – i.e., from 0.1 to 1.0 lb a.i./acre. Applications for preventing bark beetle infestations involve direct application of carbaryl solutions to tree bark in which the application rate is most meaningfully expressed in units of lb a.i. per tree. The recommended labeled rate is 0.0031 lb a.i./ft^2 of tree bark. Depending on the size of the tree, the labeled rate can range from about 0.1 to more than 1.0 lb a.i./tree. In Forest Service programs, applications are typically made to only high value trees that may be interspersed over a relatively wide range within an overall treated area. Consequently, functional application rates in terms of lbs/acre will depend on the number of trees treated, the size of the trees, and the total treated area of concern.

Based on national data from USGS and the U.S. EPA as well as data from California, it appears that the use of carbaryl in Forest Service programs is extremely small relative to the total amount of the insecticide used in agriculture and in other non-Forest Service applications. Based on a comparison of Forest Service use statistics and agricultural use statistics, the use of carbaryl by the Forest Service is about 4 million times less than agricultural use.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

Carbaryl is the common name for 1-naphthalenyl methylcarbamate and consists of a naphthalene ring (two fused aromatic rings) and methylcarbamate (-OCO-NH-CH_3) moiety:



Carbaryl is a systemic and contact (dermal or topical) insecticide that acts by inhibiting acetylcholinesterase (AChE), an enzyme important in the functioning of the nervous system in

both invertebrates, such as insects, and mammals, including humans. Carbaryl has been used as an insecticide since 1959 and is registered for use in more than 400 types of applications (U.S. EPA/OPP 2004a). Selected chemical and physical properties of carbaryl are summarized in Table 1.

As listed in Table 1, several commercial formulations of carbaryl are available. Most of the formulations listed in Table 1, however, are marketed overseas and are not used in the United States. The formulations of carbaryl that may be used in Forest Service programs are listed in Table 2. Each of these formulations is marketed under the general trade name of Sevin and produced by Bayer CropScience. Furthermore, each product is registered for forestry and other non-agricultural applications as well as application to many agricultural crops. Other formulations of carbaryl were registered in the United States; however, most of those registrations have been canceled. Other active commercial formulations of carbaryl – e.g., Adios – are registered primarily for domestic use and do not have forestry applications.

The publicly available information about the inert ingredients contained in carbaryl formulations is provided in Table 3. This information is discussed further in Section 3.1.14 (Inerts and Adjuvants). Information submitted to the U.S. EPA on formulations – including information on impurities, inerts, and manufacturing processes – cannot be released under FOIA and was not obtained for the current risk assessment.

2.3. APPLICATION METHODS

The application methods used for carbaryl vary according to the target pest: leaf beetle or bark beetle. Application methods for controlling leaf beetles involve relatively standard ground or aerial broadcast application methods in which the leaves of the tree are treated directly. Applications for preventing bark beetle infestations involve direct application by high-pressure spray to a section of the tree trunk. Aerial applications are not used for preventing bark beetle infestations.

2.3.1. Leaf Beetles

For leaf beetles, carbaryl formulations are applied to trees by standard broadcast foliar application methods. All carbaryl formulations that may be used in Forest Service programs (Table 2) are labeled for both ground and aerial application methods. Although the Forest Service generally tries to avoid using aerial application methods, both ground and aerial broadcast application methods are included in the current risk assessment in the event that the Forest Service needs to consider aerial applications of carbaryl. The product labels for the Sevin formulations summarized in Table 2 discuss small scale applications that might be conducted with backpacks – i.e., selective foliar application. Forestry applications involving backpack applications would probably be limited to small trees. For these types of applications, a worker treats approximately 0.5 acre/hour, with plausible rates ranging from 0.25 to1.0 acre/hour.

Ground applications to larger trees will use high pressure hoses. For the current risk assessment these application are assessed as hydraulic sprays. Spray equipment mounted on tractors or trucks is used to apply insecticide to the trees. By analogy to herbicide hydraulic sprays, it is

assumed that this application rate ranges from about 8 to 21 acres/hour (USDA/FS 1989a, p 2-9 to 2-10).

In aerial applications, liquid formulations are applied through specially designed spray nozzles and booms. The nozzles are designed to reduce turbulence and maintain a large droplet size, both of which contribute to a reduction in spray drift. Aerial applications may only be made under meteorological conditions that minimize the potential for spray drift. In aerial applications, approximately 40–100 acres may be treated per hour.

2.3.2. Bark Beetles

Carbaryl treatment to prevent or suppress bark beetle damage to trees is made prior to beetle flight and infestation of the host trees. Carbaryl is applied to the tree trunk (rather than the leaves) from the base of the tree – i.e., ground level – and upward until the tree diameter is less than 5 inches. For protections against the elm bark beetle, all bark surfaces including trunk, limbs, and twigs must be treated. Most Forest Service applications involve a high-pressure sprayer, which can typically be used to apply carbaryl formulations up to a height of 30-35 feet from the ground. If the target application height needs to exceed 30-35 feet, the applicator must use a bucket-lift to allow treatment of the higher areas of the tree. Since this is a labor and material intensive application method, it is used primarily for preventive treatment to high-value trees, such as those in a campground or trees of high genetic or other intrinsic value (Bakke 2004).

2.4. MIXING AND APPLICATION RATES

The two uses of carbaryl covered in this risk assessment – i.e., the control of leaf beetles and bark beetles – involve very different types of applications that lead to qualitative differences in how application rates are expressed at the field level. For the control of leaf beetles, standard broadcast applications are used, and application rates are readily expressed in units of lb a.i. (active ingredient) per acre. For the prevention of bark beetle damage, however, carbaryl is applied directly to tree trunks, and application rates are expressed in units of lb a.i./ft^2 of bark.

2.4.1. Leaf Beetles

As indicated in Table 2, the carbaryl formulations that may be used in Forest Service programs have labeled broadcast application rates ranging from 0.25 to 16 lbs a.i./acre. The upper bound of this range, however, applies only to the control of California red scale (*Aonidiella aurantii*) and Yellow scale (*Aonidiella citrina*) on citrus trees in California.

Since the current risk assessment does not encompass the control of scale on citrus trees, the maximum labeled broadcast application rate of 16 lbs a.i./acre is not considered further. Also, as summarized in Table 2, the product labels specify maximum application rates of 5-8 lb a.i./acre for various other pest species and crops. Like the maximum application rate for red and yellow scale, these relatively high broadcast application rates are not considered further in this risk assessment because they are not used in Forest Service programs (Section 2.5).

As specified in the last column of Table 2, forestry application rates to control leaf beetles encompass a very narrow range – i.e., 0.75- 1.0 lb a.i./acre. The upper range of this application rate is consistent with the maximum broadcast application rate for forestry uses designated by the U.S. EPA in the Interim Registration Eligibility Decision document for carbaryl (U.S. EPA/OPP 2004a, p. 104). The Forest Service does attempt to limit the amount of pesticides applied to the minimum effective application rate. As discussed in Section 2.5, some Forest Service programs have used broadcast application rates in the range of 0.1 lb a.i./acre.

For this risk assessment, the typical broadcast application rate for carbaryl is taken as 0.75 lb a.i./acre, which is the lower bound of the range of labeled application rates for forestry uses (Table 2). The maximum application rate is taken as 1.0 lb a.i./acre, the maximum labeled broadcast application rate for forestry uses as well as the maximum broadcast application rate for forestry specified by U.S. EPA (U.S. EPA/OPP 2004a, p. 104). The lower range of the application rate is taken as 0.1 lb a.i./acre. As discussed in Section 2.5, this lower bound is near the lowest broadcast application rates used in Forest Service Programs (Table 5).

In addition to considering application rates, this risk assessment considers specific application volumes – i.e., the number of gallons of material, including carbaryl and the material (primarily water) in which the carbaryl is mixed. For this risk assessment, the extent to which these formulations are diluted prior to application primarily influences dermal and direct spray scenarios, both of which are dependent on the 'field dilution' (i.e., the concentration of carbaryl in the applied spray). The greater the concentration of carbaryl in the field solution, the greater is the risk of adverse human health and ecological effects.

Based on the information in the product labels for the formulations specified in Table 2, application volumes ranging from 1 to 20 gallons/acre used in this risk assessment with the central estimate taken as10 gallons/acre. Application volumes of 2-10 gallons/acre are recommended for aerial application, and application volumes of 1-20 gallons/acre are recommended for ground spray applications.

Notably, the selection of application rates and dilution volumes in this risk assessment is intended to reflect typical or central estimates as well as plausible lower and upper bounds. In the assessment of specific program activities, the Forest Service may use program-specific application rates to modify the worksheets included with this report (Attachment 1) to assess any potential risks for a proposed application.

2.4.2. Bark Beetles

As noted in Table 2, carbaryl applications made to prevent bark beetle infestations are not expressed in units of lb a.i./acre. The product labels for the formulations used by the Forest Service or used in Forest Service programs (Table 2) typically express the application rate in terms of the volume of a field solution (typically a 2 % solution) per 50 square feet of tree bark.

It should be noted that the "2% solution" specified on the product label is a somewhat imprecise reference to a 1.8% w/v rather than a 2% w/v solution when the amount of carbaryl and the

volume of the solution is converted to metric units. For example, the label for Sevin XLR Plus, a liquid formulation, calls for mixing 5 fluid ounces of the formulation per gallon of field solution. Since one gallon (128 ounces) of the formulation contains 4 lbs of carbaryl, the field solution will have a concentration of about 0.16 lb a.i./gallon [5 oz formulation x (4lbs a.i./128 oz formulation) / 1 gallon field solution = 0.15625 lbs/gallon]. Converting pounds to kilograms (1 lb = 0.4536 kg) and gallons to liters (1 gal = 3.785 L), a concentration of 0.15625 lbs/gallon corresponds to a concentration of about 0.018 kg/L or 1.8% w/v solution [(0.15625 lbs x 0.4536 lb/kg) / (1 gal x 3.785 L/gal) = 0.01872 kg/L].

Similar calculations can be made for granular formulations, such as Sevin 80 WSP, which are distributed in 1.25 lb packets that contain 80% w/w carbaryl or 1 lb a.i./packet. Mixing directions for the granular formulations specify mixing 1 packet in 6.67 gallons of water, equivalent to about 0.15 lb a.i./gallon [1 lb a.i./6.67 gallons = 0.1499 lb a.i./gallon]. This, in turn, is also equivalent to a concentration of about 0.018 kg/L or about a 2% w/v solution [(0.1499 lbs x 0.4536 lb/kg) / (1 gal x 3.785 L/gal) = 0.01796 kg/L].

In the recent Interim Registration Eligibility Decision document for carbaryl (U.S. EPA/OPP 2004a) and the Reregistration Eligibility Decision for Carbaryl (U.S. EPA/OPP 2007a), the U.S. EPA does not specifically address applications to tree bark. Moreover, tree bark applications are not addressed in the U.S. EPA/OPP Science Chapters for Carbaryl (U.S. EPA/OPP 2003d,e, 2007c) or in the other related U.S. EPA/OPP documents cited in the bibliography of the current risk assessment (Section 5). This omission is important to the current risk assessment because, as noted above, the product labels that concern applications for controlling bark beetles express the application rate only in units of field solution per 50 square feet of bark and do not specify a maximum rate for applications to tree bark in terms of lbs a.i./acre.

Expressing the application rate for carbaryl in lbs a.i./acre for bark beetle prevention does not represent the same type of exposure as for leaf beetle control because of the spot nature of applications for bark beetle prevention. As specifically noted by Gibson (2007), a 10-acre campground that is treated with carbaryl for bark beetle prevention could involve applications that would directly deposit carbaryl over a much smaller area of about 0.1 acre. Thus, while the application rate within the canopy or immediate area of the tree might involve a very high application rate in terms of lbs a.i./acre, the impact on the larger area would not be equivalent to this high application rate because only a small fraction of the area of concern would be treated.

An additional complicating factor in developing exposure assessments for bark beetle applications involves differences among the trees at different sites. As discussed in Section 2.5 and summarized in Table 4, application rates expressed in units of lbs a.i./tree may differ by more than an order of magnitude – i.e., reported rates of about 0.1 lb a.i./tree in Region 2 of the Forest Service (Rocky Mountain Region) to more than 1 lb a.i./tree in Region 5 of the Forest Service (Pacific Southwest Region). These differences are a consequence of carbaryl applications made to trees of differing sizes.

This type of variability is difficult to accommodate in a general risk assessment. For the exposure assessments that are conducted as part of this risk assessment (Sections 3.2 and 4.2), application rates need to be converted to units of lbs a.i./acre in terms of the affected area. As with the exposure assessments for leaf beetle control as well as U.S. EPA and Forest Service risk assessments in general, the affected area is taken as a 10-hectare plot (about a 24.7-acre plot). Most of the exposure scenarios require an estimate of the application rate in lbs a.i./acre. For this generic risk assessment, exposures are based a unit exposure, specifically, the treatment of one large high-value tree in the affected area, apparently similar to the trees to be treated in Region 5 – i.e., a resulting application rate of about 1 lb/tree. Thus, the resulting risk quotients derived from exposure assessments based on lb/acre application rates have a different interpretation than those given in this risk assessment for leaf beetle control. For bark beetle prevention, the risk quotients must be interpreted in the context of the number of trees that might be treated in a given affected area, and this interpretation is discussed further in the risk characterizations for human health (Section 3.4) and ecological effects (Section 4.4).

In terms of practical significance in the assessment of specific Forest Service applications, this unit exposure approach has little impact. Typically, the Forest Service will prepare assessments (often termed Environmental Assessments or EAs) prior to a specific application of carbaryl or other pesticides. To facilitate such a program-specific assessment, this risk assessment is accompanied by a set of worksheets (Attachment 2) that are customized to applications for bark beetle prevention. In the evaluation of a specific program, the Worksheet A01 allows the user to enter the average height and radius of the trees, the concentration of carbaryl to be used, the number of trees to be treated in the affected area, and the size of the affected area. In Worksheet A01 for bark beetle applications (Attachment 2), all exposure assessments are based on a tree with an average diameter of 4 feet and a treated area that is 35 feet high.

Another factor that must be considered in the assessment of carbaryl applications to tree bark is the proportion of carbaryl that is actually applied to the tree bark relative to the proportion that misses the tree (through splashing or misapplication) during application. When carbaryl is applied directly to tree bark, it is readily absorbed by the bark, and this is the basis for the efficacy of the treatment. While risks to nontarget insects or other organisms in close contract with the tree bark are plausible, risks to other organisms will be minimal, as discussed further in Section 4.4. Because of the nature of the application method, however, some carbaryl will be applied to surrounding vegetation or soil. Very little quantitative information is available on application efficiency. Hoy (1980) reports that a good applicator can apply 90% of a pesticide solution to the tree bark during a bark treatment. A more recent study by Fettig et al. (2007) suggests that an application efficiency of 80% may approximate worst-case application efficiency. For this risk assessment, the unit exposures are based on the somewhat more conservative assumption that the typical application efficiency is 80% and that a plausible range of application efficiencies is 75-90%. These application efficiencies are used in this risk assessment to estimate the amount of carbaryl that is applied to soil or nontarget vegetation. The worksheets that accompany this risk assessment (Attachment 2) allow for the specification of different application efficiencies for the assessment of specific program applications.

2.5. USE STATISTICS

Based on information from the USDA/Forest Service, the U.S. EPA, the USGS, and the state of California, the use of carbaryl in forestry is very small relative to agricultural uses.

The USDA Forest Service tracks and reports its use of pesticides by management use objectives and by geographical areas referred to as "*Regions*". The Forest Service classification divides the United States into nine regions designated from Region 1 (Northern) to Region 10 (Alaska) (Figure 1). [Note: There is no *Region 7* in the Forest Service system.]

As illustrated in Figure 1 and detailed further by region in Table 4, the use of carbaryl in terms of total pounds applied in Forest Service programs during 2004, the most recent year for which statistics are available, is almost equally divided among the Pacific Southwest Region 5 (California and Hawaii with 38% of total use), the Intermountain Region 4 (Nevada, Utah, and parts of Idaho and Wyoming with 31%), and Rocky Mountain Region (South Dakota, Nebraska, Colorado, and parts of Wyoming with 32%). Less than 1% of total Forest Service use occurred in the Northern Region 1 (North Dakota, Montana, and parts of Idaho). No carbaryl use was reported in other regions. The total amount of carbaryl used in all regions in 2004 was 5517.6 pounds, and this use was almost equally divided between applications expressed in units of pounds and acres (45% of the total that probably reflect broadcast applications) and applications expressed in units of pounds per tree (55% of the total that probably reflect applications to tree bark).

The average broadcast application rate used by the Forest Service in 2004 was about 0.5 lbs a.i./acre. As discussed in Section 2.4.1, the broadcast application rates considered in this risk assessment encompass these rates.

Application reported rates expressed as lb a.i./tree differ substantially in Region 5 compared with Regions 2 and 4. Region 5 reports bark application rates of about 1.22 lb a.i./tree. This application rate appears to be consistent with plausible applications to trees like the Ponderosa pine. For example, typical diameters for mature Ponderosa pine are about 4 feet (Burns and Honkala 1990). If the average treatment height is assumed to be 35 feet with an average diameter of about 4 feet, the treated area of bark would be about 440 ft^2 (SA = π x diameter x height). At the recommended application rate of 0.003125 lb a.i./ft^2 of bark, the amount of carbaryl applied would be about 1.4 lbs a.i./tree.

The application rates reported for Regions 2 and 4 range from about 0.06 to 0.1 lb a.i./tree. The application rate of 0.1 lb a.i./tree is very close to rates reported by Caissie (2007) from the Arapaho Roosevelt National Forest in Region 2. The rate of 0.06 lb a.i./tree is very close to the rate of 0.047 lb a.i./tree [40 lbs a.i./851 trees] reported by Jungck (2007). Other reports from Region 2, however, indicate application rates of about 0.24 lb a.i./tree (Waugh 2007). As noted in the previous section, Green (2007) summarized bark applications in the White River National Forest (Region 2) that resulted in application rates of 4 gallons of a 2% solution per tree. This rate corresponds to approximately 0.32 lb a.i./tree [0.02 gallons formulation/gallons field

solution x 4 lbs a.i./gallon of formulation x 4 gallons field solution/tree], somewhat higher than the 0.1 lb a.i./tree application rate for Region 2 based on 2004 statistics.

The use pattern by region given in Table 4 and illustrated in Figure 1 may not be predictive of uses in all Forest Service regions for the coming years. As noted in Section 1, this risk assessment explicitly considers the use of carbaryl for the control of insect pests in the south (Region 8) and Midwest (Regions 8 and 9), Forest Service regions that have not used carbaryl in the past 5 years.

Carbaryl is used on a number of crops, and a summary of the agricultural uses of carbaryl is presented in Figure 2 (USGS 1998). These use statistics are for 1997, the most recent year for which data are available from the U.S. Geological Survey. As indicated in this figure, more than 3.7 million lbs of carbaryl were applied primarily to wheat (23.13%) and other hay (20.83%). The geographical distribution of the agricultural uses of carbaryl for 1997 are broader than those of the Forest Service (Figure 1), with substantial agricultural use occurring in the east (FS Regions 8 and 9) as well as in California (FS Region 5) but relatively little agricultural use occurring in the areas of greatest Forest Service use – i.e., FS Regions 2 and 4 as illustrated in Figure 1. For 2004, the use of carbaryl in all Forest Service programs was approximately 0.06% of the amount used in agriculture in 1997 [2517.6 pounds / 3,700,000].

It should be noted that the statistics given for the Forest Service apply only to applications made on National Forests managed by the Forest Service and may not reflect the total use of carbaryl in all forestry applications. The U.S. EPA (U.S. EPA/OPP 2004a) compiled statistics on all uses of carbaryl from 1992 to 2001. Based on these statistics, the U.S. EPA estimated that the average annual use of carbaryl in the United States is about 1,919,500 pounds per year and that forestry applications – termed woodland in the U.S. EPA analysis – accounts for only 28,000 pounds or about 1.4% (U.S. EPA/OPP 2002a; U.S. EPA/OPP 2004a, p. 11). Thus, total national forestry uses of carbaryl are minor, relative to total national agricultural uses.

The California Department of Pesticide Regulation provides very detailed pesticide use statistics (CDPR 2006). For 2004, the most recent year for which data are available for California, the total use of carbaryl in California was 240,071 lbs. Forestry and related uses included applications to timberland (990 lbs) and rights-of-way (236 lbs) for a total of 1226 lbs or about 0.5% of total use. The use of carbaryl in California declined substantially between 1997 and 1998 and declined gradually from 1998 to 2003 with only a slight increase in use from 2003 to 2004 (Figure 3).

3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

Carbaryl is a direct neurotoxin that inhibits acetylcholinesterase (AChE) activity. This inhibition, however, is rapidly reversible in mammals. Carbaryl is rapidly absorbed after oral exposure and more slowly absorbed after dermal exposure. Since carbaryl is also rapidly metabolized and eliminated from the body, its potential to accumulate with repeated exposure is low.

The consequence of AChE inhibition is wide ranging from mild signs of toxicity (e.g., salivation or lacrimation) to convulsions and death. Neurotoxicity is considered to be the critical effect of carbaryl exposure, and all other signs of toxicity appear to be secondary effects. Therefore, if exposure levels are below those associated with neurotoxicity, the risk of other adverse effects is unlikely, with the possible exception of effects on immune function. Some of the available studies regarding carbaryl toxicity indicate that effects on immune function may occur at doses that are very close to the NOAEL for neurotoxicity.

In addition to effects on the nervous system and immune function, carcinogenicity is the only other endpoint of major concern. The U.S. EPA determined that carbaryl is a likely human carcinogen, and this endpoint is considered quantitatively in this risk assessment. While there is some uncertainty concerning the mechanism of carcinogenicity – i.e., genetic or epigenetic – this endpoint is treated conservatively as a non-threshold response.

3.1.2. Mechanism of Action

The mechanism of action of carbaryl, which is relatively well understood, is reviewed in some detail in the published literature (Cranmer 1986; WHO 1994) and in documents prepared by the U.S. EPA in support of the reregistration of carbaryl (U.S. EPA/OPP 2003e, 2004a).

The primary mechanism of action of carbaryl involves a direct effect on the nervous system. As with many carbamates and organophosphate insecticides, exposure to carbaryl can result in the inhibition acetylcholinesterase (AChE) activity. The U.S. EPA (e.g., U.S. EPA 2007a) uses AChE inhibition as the endpoint of concern for most dose-response assessments of carbaryl, and a similar approach is taken in this risk assessment. Depending on the degree of AChE inhibition, clinical effects of exposure can range from mild signs of toxicity (e.g., salivation or lacrimation) to convulsions and death. A characteristic of carbaryl as well as other N-methyl carbamates is the rapid reversibility and consequent rapid recovery from cholinesterase inhibition. As discussed further in Section 3.1.5, this characteristic has a major impact on the assessment of potential long-term consequences of exposure.

The biochemical basis for the toxic effects of carbaryl as well as other inhibitors of AChE activity is related to the normal function of AChE. In the cholinergic system, neural impulses are transmitted between nerve cells or between nerve cells and an effector cell (such as a muscle

cell) by the acetylcholine. When the acetylcholine reaches a certain level, the receptor cell is stimulated. Normally, the acetylcholine is rapidly degraded to inactive agents (acetate ion and choline) by AChE. Carbaryl as well as many other carbamate and organophosphate pesticides will inhibit AChE activity. When AChE activity is inhibited, acetylcholine persists and continues to accumulate at the synapse (the space between the two cells). Initially, this accumulation causes continuous stimulation of the cholinergic system, which may be followed by paralysis because of nerve cell fatigue.

There are two types of AChE, one occurring in nerve tissue and the other in red blood cells (RBC). In addition, plasma contains cholinesterases (ChE) that are different from and have broader substrate specificity, compared with RBC or nerve tissue AChE (Abou-Donia 1995). Although plasma ChE and RBC AChE are most often used as indices of exposure to cholinesterase inhibitors, these enzymes are not the receptors that lead to signs of toxicity (Anwar 1997; Ecobichon 1991, 1994; Gage 1967; Thompson 1999; Wills 1972); moreover, there is a poor correlation between plasma ChE inhibition and the signs and symptoms of toxicity (Peedicayil et al. 1991).

Toxic effects are induced by the inhibition of AChE in nerve tissue (Abou-Donia 1995; Gage 1967; Wills 1972). The physiological functions, if any, of plasma ChE and RBC AChE have not been identified (Abou-Donia 1995). The inhibition of RBC AChE is generally regarded as a more clinically significant index of cholinesterase inhibition in the nervous system, compared with inhibition of plasma ChE (ATSDR 1993).

The effects of carbaryl due to AChE inhibition are similar in all species of mammals (Cranmer, 1986). While there is some indication that carbaryl and other carbamates may impact nicotinic acetylcholine receptors (Smulders et al. 2003, 2004), the effects are predominantly due to the accumulation of acetylcholine at synaptic sites in specific divisions of the peripheral autonomic nervous system, specifically all of the parasympathetic nerves, some post-ganglionic fibers and the neuro-muscular junction of skeletal muscle fibers. Acetylcholine also has a role as a neurotransmitter in the central nervous system, but this role is not as well defined as its actions in the peripheral nervous system (Weiner and Taylor 1985). The consequences of the accumulation of acetylcholine at synaptic sites first result in a stimulation, followed by a depression or paralysis. The effects of AChE inhibition are intimately linked to the known functions of acetylcholine. They include: salivation, increased bronchial secretions, lacrimation, sweating, contraction of the pupil, decreased heart rate, decreased blood pressure, increased respiratory rate, increased peristalsis, involuntary urination and defecation, muscular fasciculation (twitching), convulsions, death is usually due to respiratory arrest.

This mechanism, in turn, can affect the regulation of the respiratory system by the brain. At sufficiently high doses, carbaryl can impair respiration to the point of asphyxiation in animals. In general, respiratory failure in humans occurs only at extraordinarily high levels of plasma cholinesterase inhibition (i.e., about 95%), and acute signs of neurotoxicity in cases of carbaryl poisoning are associated with brain AChE inhibition that causes a 2- to 3-fold increase in brain acetylcholine (Cranmer 1986).

Many inhibitors of AChE show a consistent increase in toxicity with increasing temperature (e.g., Grue et al. 1997). While carbaryl appears to behave in this manner in some wildlife species (e.g., Almar et al. 1998), information suggesting a more complex relationship in which carbaryl is more toxic to mammals at extreme, relative to moderate temperatures is limited (Ahdaya et al. 1976). In addition to the impact of temperature on carbaryl toxicity, AChE inhibition and the consequent increase in acetylcholine can affect body temperature by stimulating the hypothalamus (Gordon et al. 2006).

The nervous system has an impact on many other important physiological processes. As detailed in the remainder of this hazard identification carbaryl may elicit a broad range of responses as exposures increase in intensity and duration – e.g., cardiovascular, immunological, and reproductive effects. Mechanistically, these responses may occur subsequent to effects on many different physiological or biochemical processes; nonetheless, the effects all appear to be related to the neurotoxicity of carbaryl.

One mechanism of action that may be independent of neurotoxicity, however, involves the induction of mixed function oxidases. Mixed function oxidases (i.e., the cytochrome P-450 enzyme system) are enzymes or enzyme systems involved in the metabolism of a broad range of naturally occurring chemicals (e.g., steroids) as well as xenobiotics – i.e., man-made chemicals that do not typically occur in nature. In general, any compound that serves as a substrate for or is metabolized by a mixed function oxidase may inhibit or alter the metabolism of other compounds that also serve as substrates for the mixed function oxidase. Furthermore, substrates for mixed function oxidases can often induce the production of mixed function oxidases, thereby enhancing their own metabolism as well as that of other substrates (Hodgson and Rose 2006). There are many different forms of mixed function oxidase, and there is some disagreement in the literature regarding the specific forms that carbaryl may induce (e.g., Dension et al. 1998 vs Delescluse et al. 2001). Nonetheless, carbaryl is metabolized by mixed function oxidases, a class of enzymes that are involved in the metabolism of many chemicals, both naturally occurring and man-made (e.g., Cress and Strother 1974; Ledirac et al 1997; Hodgson and Rose 2006; U.S. EPA/OPP 2003e). As with most chemicals that are metabolized by mixed function oxidases, carbaryl can also induced the synthesis of mixed function oxidases. As discussed further in Section 3.1.16 (Toxicological Interactions), this mechanism is related to the toxicological interactions of carbaryl with other compounds.

Most information suggests that the toxic effects of carbaryl are secondary to neurotoxic mechanisms. In other words, neurotoxicity is considered to be the critical effect. If exposure levels are less than those associated with neurotoxicity, it is unlikely that other adverse effects will result from exposure, with the possible exception of immunotoxicity. As discussed in Section 3.1.7, some of the available studies regarding carbaryl toxicity indicate that effects on immune function may occur at doses that are very close to the NOAEL for neurotoxicity.

3.1.3. Pharmacokinetics and Metabolism

3.1.3.1. General Considerations

Pharmacokinetics involves the quantitative study of the absorption, distribution, and excretion of a compound. Pharmacokinetics is important to this carbaryl risk assessment for three reasons. First, many of the most plausible and quantitatively most significant exposure assessments (Section 3.2) involve dermal exposure, although most of the dose-response assessments (Section 3.3) used to interpret the consequences of dermal exposure involve oral exposure levels. Accordingly, it is necessary to understand the kinetics of both oral and dermal absorption so that dermal exposure assessments can be appropriately compared with oral dose-response assessments. Second, the exposure scenarios considered in this risk assessment encompass a wide range of durations. Therefore, it is important to understand how the duration of exposure affects the level of carbaryl in the body. Last, most carbaryl toxicity studies involve experiments with laboratory mammals. Understanding the differences between animals and humans with respect to the absorption, distribution, and excretion of carbaryl, helps to interpret better the consequences of carbaryl exposure for both workers and members of the general public.

The pharmacokinetics of carbaryl have been well studied and are reviewed in a number of sources (e.g., Cranmer 1986; Dorough and Casida 1964; Ehrich et al. 1992; FAO/WHO 2001; Ross et al. 2004; U.S. EPA/OPP 2003e; WHO 1994) . Carbaryl is readily absorbed after oral and inhalation exposure and is widely distributed in tissues (Tol-Luty et al. 2001b). Dermal absorption occurs more slowly. Because dermal exposure is a predominant route in many of the exposure scenarios considered in this risk assessment, the kinetics of dermal absorption are discussed in more detail in Section 3.1.3.2. Carbaryl is metabolized rapidly via hydroxylation, hydrolysis, epoxidation, and conjugation. After hydrolysis, the major metabolites include 1-naphthol, carbon dioxide, and methylamine (NH_2CH_3). Other metabolites of carbaryl include hydroxylated derivatives of carbaryl and carbaryl methylol (Tang et al. 2002). Shrewsbury et al. (1997) report that about one half of the breakdown of carbaryl to1-napththol may be due to hydrolysis and the other half due to P-450 mediated metabolism. There are no remarkable species or sex differences in the distribution of carbaryl (Ross et al. 2004; WHO 1994).

3.1.3.2. Dermal Absorption

Most of the occupational exposure scenarios and many of the exposure scenarios for the general public involve the dermal route of exposure. For these exposure scenarios, dermal absorption is estimated and compared to an estimated acceptable level of oral exposure based on subchronic or chronic toxicity studies in animals. Hence, it is necessary to assess the consequences of dermal exposure relative to oral exposure and the extent to which carbaryl is likely to be absorbed from the surface of the skin.

Two types of dermal exposure scenarios are considered: immersion and accidental spills. As detailed in SERA (2006), the calculation of absorbed dose for dermal exposure scenarios involving immersion or prolonged contact with chemical solutions uses Fick's first law and requires an estimate of the permeability coefficient (K_p) expressed in cm/hour. For exposure scenarios like direct sprays or accidental spills, which involve deposition of the compound on the

surface of the skin, dermal absorption rates (k_a) expressed as a proportion of the deposited dose that is absorbed per unit time are used in the exposure assessment.

As summarized in U.S. EPA/OPP (2003e, Appendix 1/Table 1), there are two available studies that investigate dermal absorption in rats. Each study measures absorption over a 10-hour period after dermal exposure to different doses of carbaryl. In one study (MRID 43552901), rats were dosed at 35.6, 403, and 3450 μg/cm^2, and the measured proportion of absorbed carbaryl was 12.7%, 7.44% and 1.93% of the applied dose, respectively. In the other study (MRID 43339701), rats were dosed at 63, 626, and 3410 μg/cm^2, and the measured proportion of absorbed carbaryl was 8.9%, 0.62% and 0.48% of the applied dose, respectively.

In the recent RED for carbaryl, the U.S. EPA/OPP (2007a, p. 7) uses the highest percentage of absorbed dose (i.e., 12.7% at a dose of 35.6 μg/cm^2) as a conversion factor for calculating oral equivalent dermal doses for longer-term exposure. Implicit in this use of the 12.7% absorption factor is the assumption that the exposure is occurring over a 10-hour period.

In the current Forest Service risk assessment, several of the dermal exposure scenarios involve accidental exposure over a short period of time – i.e., one to several hours. This risk assessment uses the same data used by the U.S. EPA but uses the experimental data to derive a first-order dermal absorption rate in units of hours^{-1}. This conversion involves a rearrangement of the basic equation for first-order absorption, $P = 1 - e^{-k \times t}$, where P is the proportion absorbed after a given time (t) and k is the first-order dermal absorption rate. Solving for k, this equation rearranges to $k = \ln(t)/t$. Using this rearrangement, the first-order dermal absorption rate based on 12.7% (P=0.127) absorption over a 10-hour period is equal to 0.08962 hour^{-1}. The other data regarding the dermal absorption of carbaryl summarized by U.S. EPA/OPP (2003e) can be similarly used to calculate first-order dermal absorption rates. Incidentally, all of these absorption rates are higher than the 0.08962 hour^{-1} rate. The highest rate is about 0.232 hour^{-1} based on 0.48% absorption over a 10-hour period at a dose of 3410 μg/cm^2.

Chang et al. (1994) developed a 4-compartment model to describe the pharmacokinetics of carbaryl and other pesticides. Based on this model, the absorption rate for the transfer from the skin surface to the outer dermal compartment (K_{42} in the Chang designation) is estimated at 0.0007 hour^{-1}. While the Chang et al. (1994) study is useful for comparing differences in dermal absorption kinetics, the absorption rates from the study are not comparable to the rates used by the U.S. EPA and this risk assessment – i.e., a simple first-order absorption model.

In instances where experimental data on dermal absorption are not available, quantitative structure activity relationships, detailed in SERA (2006a), are often employed to estimate dermal absorption rates. These calculations are given in Worksheet B06 of the EXCEL workbooks that accompany this risk assessment. As indicated in this worksheet, the calculated first-order dermal absorption rate coefficient is 0.00814 hour^{-1} with a 95% confidence interval of 0.00312-0.0212 hour^{-1}. The central estimate in this worksheet is about a factor of 10 below the dermal absorption rate for carbaryl based on the 12.7% absorption factor. The upper range in this worksheet is about a factor of 10 below the dermal absorption rate based on the 0.48% absorption factor.

Thus, for carbaryl, the structure activity relationships appear to grossly underestimate the dermal absorption rate from the experimental data used by the U.S. EPA, and the rates based on structure activity relationships are not used directly in this risk assessment.

For the current risk assessment, the central estimate of the first-order dermal absorption rate is taken as 0.08962 $hour^{-1}$ and the upper bound of the first-order dermal absorption rate is taken as 0.2319 $hour^{-1}$. Both of these values are based on the experimental data on carbaryl as described above. The lower bound of the first-order dermal absorption rate is taken as 0.0312 $hour^{-1}$. This lower bound is based on a 10-fold increase in the lower bound estimate from Worksheet B06.

There appear to be no experimental data on the permeability coefficient for carbaryl. Typically, the data gap is filled by using quantitative structure activity relationships to estimate a dermal permeability coefficient. As discussed in SERA (2006a), the structure activity relationships were developed by the U.S. EPA (1992) and are similar to the relationships used to estimate the first-order dermal absorption rate – i.e., both algorithms are based on the molecular weight and K_{ow} of the compound. The application of the EPA algorithm to carbaryl is given in Worksheet B05 of the EXCEL workbooks that accompany this risk assessment.

Based on the EPA algorithm, the estimated dermal permeability coefficient for carbaryl is 0.00487 cm/hour with a 95% confidence interval of 0.00333-0.00713 cm/hour. Given that the algorithm for calculating the k_a results in a substantial underestimation, the EPA algorithm for estimating K_p is not used directly in this risk assessment. Because the algorithms for estimating the k_a and k_p are similar to each other and because the algorithm for estimating the k_a appears to underestimate the dermal absorption rates based on experimental data by a factor of about 10, the estimates of k_p based on the EPA algorithm is multiplied by a factor of 10. Accordingly, for this risk assessment, the dermal permeability coefficient for carbaryl is 0.0487 cm/hour with a 95% confidence interval of 0.0333-0.0713 cm/hour.

3.1.3.3. Excretion

While excretion rates are not used directly in either the dose-response assessment or risk characterization, excretion half-lives can be used to infer the effect of longer-term exposures on body burden based on the *plateau principle* (e.g., Goldstein et al. 1974). The concentration of the chemical in the body after a series of doses (X_{Inf}) over an infinite period of time can be estimated based on the body burden immediately after a single dose, X_0, by the relationship:

$$X_{Inf}/X_0 = 1 / (1- e^{-ke\ t^*)})$$

where t* is the interval between dosing.

The U.S. EPA/OPP (2003e, p. 27) review of the pharmacokinetics of carbaryl, cites an approximate whole body half-life of 24 hours (1 day), which is similar to carbaryl half-lives cited in other reviews for both mammals and birds (Cranmer 1986; Ehrich et al. 1992; Ross et al. 2004; WHO 1994). The half-life of 1 day corresponds to a first-order whole body k_e of 0.693 [$ln(2)/t_{50}$]. Using this k_e and a 1-day interval between doses (i.e., daily dosing), results in an

increased body burden with infinite exposure, relative to the body burden after a single dose, of about 2. This value is a relatively modest increase over time and is consistent with the identical values used for the acute RfD and chronic RfD for carbaryl (Section 3.3).

3.1.4. Acute Oral Toxicity

One type of acute toxicity information involves time-specific LD_{50} or LC_{50} values (i.e., doses or concentrations of a toxicant that result in or are estimated to result in 50% mortality of the test species during a specified exposure or observation period). These values can be viewed as an index of acute lethal potency. Information is also available on the acute neurological effects of carbaryl (Section 3.1.6) as well as acute dermal toxicity (Section 3.1.12) and acute inhalation toxicity (Section 3.1.13).

The lowest acute oral LD_{50} cited by the U.S. EPA is 307 mg/kg in rats (U.S. EPA/OPP 2003e, p. 24). This value is a composite of LD_{50} values for males (302.6 mg/kg bw) and females (311.5). As with the pharmacokinetics of carbaryl (Section 3.1.3.1), sensitivity to carbaryl does not appear to be gender specific. In terms of labeling requirements, this LD_{50} value is used to classify carbaryl as a Category II pesticide, resulting in a Warning signal word on the product label (see SERA 2007a, Table 3-2). As discussed further in Section 4.1 (Hazard Identification for Ecological Effects), this LD50 value is also used to classify carbaryl as moderately toxic (see SERA 2007a, Table 4-1).

The rat $LD_{50\ of}$ 307 mg/kg bw used by the U.S. EPA is in the central range of published LD_{50} values in rats – i.e., about 90-850 mg/kg bw (Cranmer 1986; FAO-WHO 2001; WHO 1994). Cats appear to be the most sensitive mammals with an oral LD_{50} of 150 mg/kg bw, while monkeys appear to be the least sensitive species with an oral LD_{50} of more than 1000 mg/kg bw (WHO 1994). Interspecies differences are considered further in the ecological risk assessment (Section 4.1). For the human health risk assessment, the relative insensitivity of monkeys to carbaryl supports the use of toxicity data on rodents in the dose-response assessment (Section 3.3). Cranmer (1986, p. 268) notes that: *Females are occasionally slightly more susceptible than males*. This remark appears to refer to studies conducted in the USSR in the late 1960s. As noted above, however, more recent studies do not suggest substantial gender-related differences in sensitivity to carbaryl.

As summarized in Appendix 2, the effects of acute toxicity induced by carbaryl are primarily and clearly related to neurotoxicity (Section 3.1.6) – e.g., salivation, respiratory distress, muscle tremors, and weakness (Moser 1995). Sublethal exposures to carbaryl are associated with decreased body temperature in mice (Ahdaya et al. 1976) and rats (Gordon et al. 2006), and impacts on body temperature are noted as well in subchronic toxicity studies (Section 3.1.5). While changes body temperature may occur at doses below those associated with frank signs of neurotoxicity, the effects are attributable to increased cholinergic activity (Section 3.12.).

As discussed in Section 3.1.5 (Subchronic or Chronic Systemic Toxic Effects) and in greater detail in the dose-response assessment (Section 3.3), the U.S. EPA/OPP (2007a,c) based the

acute RfD for carbaryl on neurotoxicity. Furthermore, the EPA determined that a separate chronic RfD is not required for carbaryl because of the rapid reversibility of AChE inhibition.

In assessing the acute toxicity of carbaryl, the U.S. EPA relied on the results of a neurotoxicity screening battery (U.S. EPA-PPTS 1998a). This battery is similar to standard toxicity study in terms of dosing but involves a large number of neurological and behavioral observations. As detailed in U.S. EPA/OPP (2007c), the acute neurotoxicity study used for carbaryl (MRID # 43845201-43845204) involves administering gavage doses of 10, 50, or 125 mg/kg bw/day to rats for 14 days. All exposure levels were associated with dose-related decreases in brain AChE as well as decreases in red blood cell AChE and plasma ChE. As discussed further in Section 3.3, the dose-response relationships for brain AChE inhibition served as the basis for deriving the acute RfD for carbaryl.

3.1.5. Subchronic or Chronic Systemic Toxic Effects

There are numerous subchronic and chronic toxicity studies on carbaryl. Many of the published studies are reviewed in some detail by WHO (1994), FAO/WHO (2001) and Cranmer (1986). Several of the longer-term bioassays as well as the more recent literature summarized in Appendix 3 are focused on specific forms of toxicity – e.g., neurotoxicity, reproductive effects, and immune function. These studies are discussed in the subsections below.

In terms of the practical impact of subchronic and chronic effects on the risk assessment of carbaryl, a key determination is the recent position by the U.S. EPA/OPP (2007a, p. 9 ff) that endpoints for longer-term exposure to carbaryl are not of primary concern for two reasons. First, the most important and sensitive endpoint for carbaryl involves AChE inhibition. Second, AChE inhibition is rapidly reversible. Consequently, if exposure levels are below the level of concern based on the acute toxicity of carbaryl, then longer-term exposures will also be below the level of concern.

This position was recently adopted U.S. EPA/OPP (2007a). In previously conducted assessments, the U.S. EPA purposely considered longer-term toxicity studies and derived chronic RfDs. The current chronic RfD for carbaryl listed on the U.S. EPA IRIS web site (http://www.epa.gov/iris/subst/0019.htm) is based on the chronic toxicity study by Carpenter et al. (1961) in which rats were given dietary concentrations of 50, 100, 200, or 400 ppm carbaryl over a 2-year period. The only reported signs of toxicity included mild histopathological changes in the liver and kidneys (i.e., cloudy swelling of the renal tubules and hepatic cords) of rats in the high dose group. Based on food consumption and body weight data, the dietary concentration of 400 ppm (LOAEL) corresponds to an average daily dose of 15.6 mg/kg bw/day, and the dietary concentration of 200 ppm (NOAEL) corresponds to an average daily dose of 9.6 mg/kg bw/day. The U.S. EPA/ORD (2002) applied a standard uncertainty factor of 100 – i.e., multiplicative factors of 10 for interspecies extrapolation and 10 for sensitive individuals – to derive an RfD of 0.1 mg/kg/day.

More recently and in support of the reregistration of carbaryl, the U.S. EPA/OPP (2003e, p. 15) used a chronic feeding study in dogs to derive a 10-fold lower chronic RfD of 0.01 mg/kg/day. In this study, the lowest dose tested, 3.1 mg/kg/day, was associated with AChE inhibition, and the RfD was derived using an uncertainty factor of 300 – i.e., multiplicative factors of 10 for interspecies extrapolation, 10 for sensitive individuals, and 3 for the use of a LOAEL rather than a NOAEL.

As discussed in Section 3.3, the current risk assessment explicitly and purposely considers both acute and chronic exposures. Nevertheless, this consideration is consistent with the approach taken by the U.S. EPA in that the acute RfD recommended in the most recent EPA assessment (U.S. EPA/OPP 2007a) is identical to the previously derived chronic RfD of 0.01 mg/kg/day (U.S. EPA/OPP 2003e). Both RfDs are based appropriately on the most sensitive endpoint in the most sensitive species. That both RfDs are identical supports EPA's position that focusing on acute exposure levels is protective of chronic exposure levels as well (U.S. EPA/OPP 2007a).

3.1.6. Effects on Nervous System

As discussed in Durkin and Diamond (2002), a neurotoxicant is a chemical that disrupts the function of nerves, either by interacting with nerves directly or by interacting with supporting cells in the nervous system. This definition of neurotoxicant distinguishes agents that act directly on the nervous system (direct neurotoxicants) from those agents that might produce neurological effects that are secondary to other forms of toxicity (indirect neurotoxicants). Virtually any chemical will cause signs of neurotoxicity in severely poisoned animals and can be classified as an indirect neurotoxicant. For carbaryl, there is ample indication of direct neurotoxic effects (Section 3.1.2).

With the exception of carcinogenicity (Section 3.1.10), the toxicity values used in this human health risk assessment and in the EPA's recent risk assessment on carbaryl (U.S. EPA/OPP 2007a) are based on neurotoxicity. The key toxicity value is the dose of 1.1 mg/kg bw selected by the U.S. EPA as the basis for the acute RfD for carbaryl. This toxicity value is based on benchmark dose analysis of a rat developmental toxicity study in which 1.1 mg/kg bw dose is the lower limit on the ED_{10} for the inhibition of brain cholinesterase in rats pups on postnatal Day 11 (U.S. EPA/OPP 2007a, p. 9, Table 3).

The quantitative use of this study is discussed further in Section 3.4 (Dose-Response Assessment). In terms of the hazard identification, the most important points are whether or not the above study is the most sensitive endpoint in the most sensitive species.

The neurotoxicity of carbaryl is well studied and well reviewed (Cranmer 1986; FAO/WHO 2001; WHO 1994). None of studies covered in these reviews or encountered elsewhere in the open literature (Appendix 3) suggests a lower or more conservative value on which to base the dose-response assessment for carbaryl. As noted by Cranmer (1986), most published studies regarding the neurotoxicity of carbaryl suggest that sublethal doses ranging from 10 to 100 mg/kg bw cause adverse effects in several mammalian species. This dose range is consistent with the other reviews on carbaryl.

The lowest dose associated with an adverse effect after exposure to carbaryl is reported by Singh (1973). An acute intraperitoneal injection of 0.54 mg/kg bw administered to rats caused a transient (60 minute) decrease in their spontaneous activity (running wheel) by a factor of about 45%. Singh (1973) interprets this decrease in activity as suggestive of a cholinergic effect, but the effect was not statistically significant ($p > 0.05$). Cranmer (1986) suggests that the transient decrease in activity may have been associated with a more general distress response induced by administering the carbaryl by injection. On the other hand, Singh (1973) did use a saline control and noted a decrease in activity of only about 6%. In any event, intraperitoneal injection is not an appropriate route of exposure for quantitative use in the current risk assessment.

3.1.7. Effects on Immune System

There are various methods for assessing the effects of chemical exposure on immune responses, including assays of antibody-antigen reactions, changes in the activity of specific types of lymphoid cells, and assessments of changes in the susceptibility of exposed animals to resist infection from pathogens or proliferation of tumor cells (Durkin and Diamond 2002).

With the exception of skin sensitization studies (Section 3.1.11.2), specific studies regarding the effects of pesticides on immune function are not required for pesticide registration. Accordingly, the U.S. EPA human health risk assessment of carbaryl (U.S. EPA/OPP 2007a,c) does not address the potential effects of exposure on immune function.

The effects of carbaryl on immune function are well documented in standard reviews (Cranmer 1986; FAO/WHO 2001; WHO 1994). While there is little doubt that exposure to carbaryl can affect immune function, many immunological functions are mediated through neurological mechanisms, and effects on immune function often occur secondary to other toxic effects. As noted by Cranmer (1986, p. 253): *Most studies in rabbits, mice and rats, at doses permitting survival, have not produced significant effects on the immune system. Carbaryl does not appear to represent a risk factor to the human immune system*.

As with the numerous studies on neurotoxicity (Section 3.1.6), the primary concern with effects on the immune function involves the extent to which adverse effects occur at doses lower than 1.1 mg/kg bw, which is the basis for the acute RfD for carbaryl (U.S. EPA 2007a). In that respect, the toxicity studies by Street and Sharma (1975) and Dong et al. (1998) are of concern.

Street and Sharma (1975) report a decrease in IgG and IgM antibodies as well as atrophic effects on the spleen and thymus in rabbits in response to sheep red blood cells (SRBC) after 4 weeks of exposure to 4, 20, 45, or 150 ppm carbaryl in the diet (corresponding to daily average doses of 0.23, 1.08, 2.3, or 8.38 mg/kg bw/day). The decrease in the two types of antibodies as well as the atrophic effects on the spleen and thymus are general responses that suggest an impairment in normal immune function. Nonetheless, the effects noted by Street and Sharma (1975) were inconsistent at low doses and were not dose related. Street and Sharma (1975) attribute the effects to physiological stress rather than viewing them as a direct toxic effect.

Dong et al. (1998) exposed groups of 10 rats to carbaryl by gavage at doses of 0, 2, 10, or 50 mg/kg bw for 2 weeks. Details of this study are summarized in Appendix 3. The animals were sensitized with subcutaneous injections of house dust mite antigen starting 3 days after the onset of carbaryl dosing. The rats were then challenged with the antigen by tracheal instillation 1 day after the last dose of carbaryl. Two days after this challenge, a statistically significant increase was noted in the 50 mg/kg dose group in terms of antigen-specific cell proliferation in the lymph nodes of the lung and a dose-related decrease was noted in antigen-specific splenocyte proliferation and macrophage number in bronchoalveolar fluid. The decreases in splenocyte proliferation were statistically significant at all dose levels, but the effect on macrophage numbers is significant only at the two higher dose levels.

3.1.8. Effects on Endocrine System

The direct effects of chemical exposure on endocrine function are most often assessed in mechanistic studies concerning estrogen, androgen, or thyroid hormone systems (i.e., assessments on hormone availability, hormone receptor binding, or post-receptor processing). Also, changes in the structure of major endocrine glands (i.e., the adrenal, hypothalamus, pancreas, parathyroid, pituitary, thyroid, ovary, and testis) may be indicative of chemical effects on the endocrine system. Disruption of the endocrine system during development may give rise to effects on the reproductive system that can be expressed only after maturation. Consequently, multigeneration exposures are recommended for toxicological assessment of suspected endocrine disruptors (Durkin and Diamond 2002).

U.S. EPA/OPP (2007c) addresses the potential effects of carbaryl on endocrine function based on the results of a 2-generation reproduction study in rats, which was submitted to the Agency in support of the reregistration of carbaryl (MRID 45448101), as well as the results of one study published in the open literature (Pant et al. 1995). In the MRID study, a dietary concentration of 1500 ppm, corresponding to a dose of about 125 mg/kg bw/day in male rats, caused a dose-related but statistically insignificant increase in the frequency of abnormal sperm. As discussed in Section 3.1.9, the observed increase was not associated with any treatment related effects on reproduction. Details about the Pant et al. (1995) study are provided in Appendix 3. At gavage doses of 50 or 100 mg/kg bw, Pant et al. (1995) observed statistically significant increases in the frequency of abnormal sperm. Based on this information, the U.S. EPA/OPP (2007c) concluded that:

> *…although there was possible toxicity to endocrine tissue (testes and thyroid), there was no indication of these effects occurring via an endocrine-mediated mechanism and the points of departure in the risk assessment are lower than doses at which these effects occurred and are protective from toxicity to these organs.* (U.S. EPA/OPP 2007c, p. 22)

A follow-up study by the Pant et al. (1996) supports the EPA's position and identifies a NOAEL of 25 mg/kg bw for effects on sperm morphology. The NOAEL is consistent with the study by Chapin et al. (1997) which reports no effects on sperm at 25 mg/kg bw/day.

Notwithstanding the above assessment, there are some studies suggesting that carbaryl has the potential to impact endocrine function. *In vitro*, carbaryl has been shown to compete with β-estradiol in binding to human estrogen receptors (Klotz et al. 1997) and inhibit progesterone production (Cheng et al. 2006). In addition, as discussed in Section 4.1, there are some studies suggesting that carbaryl may have endocrine mediated effects in fish and amphibians. While these studies are considered in this risk assessment, the effects of carbaryl on endocrine function appear to have a NOAEL (i.e., 25 mg/kg bw) that is substantially greater than the NOAEL for neurotoxicity (i.e., 1.1 mg/kg bw). Thus, unlike potential effects on immune function, potential effects on endocrine function are not a primary concern in the human health risk assessment.

3.1.9. Reproductive and Teratogenic Effects

3.1.9.1. Developmental (Teratology) Studies

Developmental studies are used to assess whether a compound has the potential to cause birth defects as well as other effects during development or immediately after birth. These studies typically entail gavage administration to pregnant rats or rabbits on specific days of gestation. Teratology assays as well as studies on reproductive function (Section 3.1.9.2) are generally required by the EPA for the registration of pesticides. Very specific protocols for developmental studies are established by U.S. EPA/OPPTS and are available at http://www.epa.gov/opptsfrs/publications/ OPPTS Harmonized.

A major distinction in the interpretation of developmental studies concerns the presence or absence of maternal toxicity, because maternal toxicity can and often does lead to adverse fetal effects. Based on acceptable guideline studies in rats (MRID 44732901) and rabbits (MRID 44904202), the U.S. EPA/OPP (2007c) found no indication of teratogenic effects associated with carbaryl exposure. At maternally toxic doses (i.e., decreased weight gain and decreased plasma and red blood cell cholinesterase activity) the only observed fetal effects were decreased fetal body weight and incomplete ossification.

In the recent open literature and the reviews concerning the toxicity of carbaryl (Cranmer 1986; FAO/WHO 2001; WHO 1994), the preponderance of studies in rodents, rabbits, swine, and primates provide no indication that carbaryl induces birth defects. Dogs, however, may be more sensitive than other species. There are two teratogenicity studies in which birth defects were observed in beagles exposed to carbaryl (Imming et al. 1969; Smalley et al. 1968). The NOAEL in dogs is 2 mg/kg bw/day, and the LOAEL is 5 mg/kg bw/day (Imming et al. 1969). Notably, both of the teratogenicity studies are associated with maternal toxicity. As discussed by Cranmer (1986), the effects in dogs may be associated with a unique metabolic pathway in dogs, relative to other species.

Panciera (1967) observed cardiac anomalies in 2 of 23 offspring from sheep exposed to a dietary concentration of 250 ppm carbaryl. No abnormalities were observed in the offspring of sheep exposed to a dietary concentration of 100 ppm. In control sheep, the incidence of cardiac anomalies was 0 of 44. Based on the Fisher Exact text, the 2/23 response is not statistically significant from 0/44 (p=0.1144). Robens (1969) observed teratogenic effects in guinea pigs at a

dose of 300 mg/kg bw. This dose, however, was associated with maternal toxicity including death.

3.1.9.2. Reproduction Studies

Reproduction studies involve exposing one or more generations of the test animal to the compound. The general experimental method involves dosing the parental (P) generation (i.e., the male and female animals used at the start of the study) to the test substance prior to mating, during mating, after mating, and through weaning of the offspring (F_1). In a 2-generation reproduction study, this procedure is repeated with male and female offspring from the F_1 generation to produce another set of offspring (F_2). During these types of studies, standard observations for gross signs of toxicity are made. Additional observations often include the length of the estrous cycle, assays on sperm and other reproductive tissue, and number, viability, and growth of offspring.

U.S. EPA/OPP (2007c) includes the review of one standard 2-generation reproduction study (MRID 45448101) in rats in which the parent generations were exposed to dietary concentrations of 75, 300, or 1500 ppm carbaryl. The dietary concentration of 1500 ppm is classified as a LOAEL for parental effects based on decreased body weight, weight gain, and feed consumption. No adverse effects on reproduction were observed (i.e., effects on estrous cycle, sperm motility, mating, and fertility index etc). The dietary concentration of 300 ppm is classified as a LOAEL in F_2 pups, based on decreased pup survival. Based on food consumption and body weight measurements, the LOAEL in pups corresponds to a dose of about 23.4-36.3 mg/kg bw/day in male pups and 26.9-36.3 mg/kg bw/day in female pups.
Cranmer (1986) summarizes several 2- and 3-generation reproduction studies in which adverse effects consistent with those noted in MRID 45448101 are reported – i.e., fetal mortality and decreased body weight. None of these studies, however, report adverse effect levels below the levels in the study used by U.S. EPA.

3.1.9.3. Developmental Neurotoxicity

A developmental neurotoxicity study is a specialized toxicity test designed to assess the effect of direct neurotoxins on fetal development (U.S. EPA/PPTS 1998b). These studies are similar to standard reproduction studies (Section 3.1.9.2) in that pregnant animals are dosed with the neurotoxin, and exposure to the offspring occurs *in utero*. Developmental neurotoxicity studies differ from standard reproduction studies in that offspring are subject to a number of specific observations and tests designed to evaluate the effect of the neurotoxin on several neurological and behavioral endpoints.

As summarized in U.S. EPA/OPP (2007c, p. 14), a developmental neurotoxicity study was conducted on rats at doses of 0.1, 1, or 10 mg/kg bw/day (MRID 44393701). In the high dose group, adverse effects were observed in both dams (ChE inhibition, behavior, and body weight gain) and offspring (alterations in morphometric measurements of components of the brain). The 1 mg/kg bw/day exposure level was classified as a NOAEL for the dams and their offspring.

3.1.10. Carcinogenicity and Mutagenicity

Carbaryl has been assayed for mutagenicity in numerous test systems, including bacterial assays, mammalian cell cultures for mutagenicity and DNA or gross chromosomal damage, unscheduled DNA synthesis, and *in vivo* test systems using both *Drosophila* and mice. The U.S. EPA requires a battery of mutagenicity assays for pesticide registration. As indicated in Section 3.1.3.1, carbaryl undergoes epoxidation as part of its metabolism in mammals. Epoxides are highly reactive and can cause DNA damage. These effects were observed in the studies submitted to the U.S. EPA for pesticide registration (U.S. EPA/OPP 2007c) as well as in studies in the open literature (e.g., Cranmer 1986; Meeker et al. 2004b; Xia et al. 2005). DNA damage and effects on cell division have all been noted.

In terms of a quantitative significance to the human health risk assessment, carcinogenicity is an issue only if the data are adequate to support the derivation of a cancer potency factor. For carbaryl, the U.S. EPA determined that carbaryl is a likely human carcinogen based on the induction of malignant tumors in mice (MRID 42786901) and rats (MRID 42918801). As summarized in U.S. EPA/OPP (2007c), the bioassay in mice was used to derive a cancer potency factor (Q_1^*) based on an increase in hemangiosarcomas in mice at a dietary concentration of 8000 ppm. Thus, cancer is considered an endpoint of concern in this risk assessment; in addition, cancer risks are considered quantitatively for longer-term exposures (Section 3.3).

Bigot-Lasserre et al. (2003) suggest that the tumor induction observed in the studies used by the U.S. EPA to derive the cancer potency factor may have occurred through a non-genotoxic mechanism. This point is germane to this risk assessment because the dose-response model used by the U.S. EPA is a non-threshold model that is most clearly applicable to carcinogens that act through genotoxic mechanisms – i.e., direct interaction with DNA. For carcinogens that act by non-genotoxic mechanisms, a case can be made for using a less conservative threshold model – i.e., the NOAEL approach. While this argument has merit, Forest Service risk assessments defer to the approach and methods used by the U.S. EPA.

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

Based on standard studies for assessing eye and skin irritation, carbaryl does not appear to be an irritant to skin or eyes and was given a Category IV classification – i.e., the lowest classification used by the U.S. EPA – for these endpoints (U.S. EPA/OPP 2007c). In addition, the U.S. EPA determined that carbaryl is not a skin sensitizer based on a standard assay in guinea pigs (U.S. EPA/OPP 2007c). Nonetheless, the U.S. EPA does note a number of case reports involving human exposure in which irritant effects to the eyes and skin as well as presumptively allergic reactions are documented. Based on these reports, the Agency recommended warning statements on product labels for carbaryl concerning the potential for sensitization in humans.

Apparently, Cranmer (1986) reviewed a larger group of unpublished studies than is covered in U.S. EPA/OPP (2007c). Cranmer cites a 1983 study in which Sevin XLR, a formulation proposed for use by the Forest Service, caused transient iritis and conjunctival irritation. This effect is not noted in the more recent review by U.S. EPA/OPP (2007c). Pesticide formulations may change over time and it is not clear whether the specific XLR formulation used in 1983 is

the same as the more recent formulation. Some older petroleum-based carbaryl formulations – i.e., Sevin Oil –were reported to cause skin sensitization. This formulation, however, is not proposed for use by the Forest Service. Similarly, Sevin RP-2, another formulation that is not proposed for use by the Forest Service, is reported to cause mild irritant effects. In a more recent study among banana plantation workers in Panama exposed to an unspecified formulation of carbaryl, skin patches worn by the workers tested positive for exposure (Penagos et al. 2004). The extent to which case reports of skin and eye irritation and/or skin sensitization after exposure to carbaryl involves formulations used or proposed for use by the Forest Service cannot be determined.

3.1.12. Systemic Toxic Effects from Dermal Exposure

As with many pesticides, acute dermal LD_{50} values for carbaryl are substantially greater than acute oral LD_{50} values. Most of the studies reporting dermal LD_{50} values are unpublished studies conducted in the 1970s and 1980s. Based on these studies, the acute dermal LD_{50} for carbaryl is greater than 2000 mg/kg bw (Cranmer 1986; FAO/WHO 2001; WHO 1994). More recent studies by Tos-luty et al. (2001a,b) discuss dermal LD_{50} values in which levels of exposure are expressed in units of mg/cm^2 and do not provide sufficient detail to convert the levels of exposure to units of mg/kg bw.

Of the three subchronic (28-day) dermal toxicity studies submitted to the U.S. EPA in support of the reregistration of carbaryl, only one study (MRID 45630601) was classified as acceptable (U.S. EPA/OPP 2007c, p. 79). In the study, male and female rats were treated with repeated dermal doses of 20, 50, or 100 mg/kg/day. Consistent with the low potential of carbaryl to cause skin irritation (Section 3.1.11), no effects on the skin were noted over the 28-day exposure period. The dose of 50 mg/kg/day is classified as a LOAEL based on observed decreases in brain and RBC AChE in males and decreases in RBC AChE in females. On the basis of these findings, the U.S. EPA classifies the dermal toxicity of carbaryl as low (Category III).

3.1.13. Inhalation Exposure

The U.S. EPA/OPP (2007c) cites an acute inhalation LC_{50} value for rats of greater than 3.4 mg/L (MRID 00148502). The report of a "greater than" value typically indicates that less than 50% mortality occurred at the specified exposure concentration. Based on this study, the inhalation toxicity of carbaryl is classified as low (Category IV). Nonetheless, the U.S. EPA/OPP (2007c) identifies the inhalation toxicity of carbaryl as a data gap and indicates that an acute inhalation study monitoring the time course of cholinesterase inhibition should be conducted.

Cranmer (1986) reviews a number of unpublished studies from the 1970s regarding the inhalation toxicity of carbaryl and reports acute LC_{50} values ranging from 5 to 23 mg/L. While few details are given by Cranmer (1986), it appears that some carbaryl formulations may be less toxic than carbaryl itself. WHO (1994) provides a somewhat more detailed assessment of the inhalation toxicity of carbaryl and carbaryl formulations; however, most of these studies are concerned with dust formulations that involve veterinary uses. One useful comparison, however, involves a minimal lethal dose (1/5 rats) after a 4-hour exposure to Sevin XLR at a concentration

of 792 mg/m^3. This concentration is equivalent to 7.92 mg/L, suggesting that the Sevin XLR formulation is similar in toxicity to technical grade carbaryl.

The open literature includes only one subchronic inhalation toxicity study. As summarized in Appendix 3, Ladics et al. (1994) exposed rats to concentrations of 36, 137, or 355 mg/m^3 carbaryl, 6 hours/day, 5 days/week for 2 weeks. Consistent with the adverse effects observed after oral exposure to carbaryl, signs of neurotoxicity as well as decreases in humoral immune function (antibody titers and spleen cell number) were observed in rats after inhalation exposure to the compound.

3.1.14. Inerts and Adjuvants

The U.S. EPA is responsible for regulating the incidence of inerts and adjuvants in pesticide formulations. As implemented, these regulations affect only pesticide labeling and testing requirements. As part of this regulatory activity, U.S. EPA classifies inerts into four lists based on the available toxicity information: toxic (List 1), potentially toxic (List 2), unclassifiable (List 3), and non-toxic (List 4). List 4 is subdivided into two categories, 4A and 4B. List 4A constitutes inerts for which there is adequate information to indicate a minimal concern. List 4B constitutes inerts for which the use patterns and toxicity data indicate that use of the compound as an inert is not likely to pose a risk. These lists as well as other updated information regarding pesticide inerts are maintained by the U.S. EPA at the following web site: http://www.epa.gov/opprd001/inerts/.

As summarized in Table 3, carbaryl formulations used in Forest Service programs contain a number of inert ingredients. Some inerts - i.e., those listed under SARA Title III, Section 313 – must be and are specified on the product material safety data sheets. The identity of other inerts was obtained by through a FOIA by the Northwest Coalition for Alternatives to Pesticides (NCAP), and these inerts are listed at the NCAP web site: http://www.pesticide.org/FOIA/inertslinks.html. As indicated in Table 3, all of the inerts listed on the material safety data sheets for carbaryl formulations are either on List 4A or List 4B. Three of the inerts listed by NCAP for Sevin 80S are not on the EPA inerts list – i.e., sodium dialkyl naphthalene sulfonate, naphthalene sulfonic acid formaldehyde condensate, ammonium and sodium salt, and Surfynol TG-E, a surfactant.

The potential toxicity of inerts in pesticide formulations can sometimes impact the risk assessment. This statement applies specifically to herbicide formulations for which the active ingredient poses a minimal risk to humans. There is little doubt that carbaryl is the toxic agent of primary concern in formulated products. The EPA classification of the inert ingredients in the carbaryl formulations used by the Forest Service suggests they do not pose a substantial risk of exposure, relative to carbaryl. Accordingly, the inerts do not have an impact on the hazard identification for potential health effects in humans.

3.1.15. Impurities and Metabolites

3.1.15.1. Metabolites

As discussed in SERA (2007, Sections 3.1.3.1), two types of metabolites may be considered in a risk assessment, *in vivo* metabolites and environmental metabolites. *In vivo* metabolites refer to compounds that may form within an animal after a chemical agent is absorbed. Environmental metabolites refer to compounds that may form in the environment as the result of biological and chemical processes, including breakdown in soil or water or breakdown by sunlight (photolysis).

1-Naphthol is the major *in vivo* and environmental metabolite of carbaryl (Section 3.1.3.1). In the recent U.S. EPA risk assessment on carbaryl (U.S. EPA/OPP 2007a,c), the Agency's evaluation of 1-napthol involves combining exposures to 1-naphthol with exposures to carbaryl itself. This is an inherently conservative position in that 1-naphthol does not have the specific neurotoxic properties of carbaryl. This conservative approach is adopted in the current Forest Service risk assessment.

3.1.15.2. Impurities

Virtually no chemical synthesis yields a totally pure product. Technical grade carbaryl, like other technical grade products, undoubtedly contains impurities. To some extent, concern for impurities in technical grade carbaryl is limited because the existing toxicity studies on carbaryl were conducted with the technical grade product. Thus, if toxic impurities are present in the technical grade product, they are likely to be encompassed by the available toxicity studies on the technical grade product.

Impurities can be a substantial concern in a risk assessment if the impurities pose risks that are qualitatively different from those of the active ingredient. No such impurities were identified in the open literature on carbaryl or in the U. S. EPA's assessments of carbaryl.

3.1.16. Toxicological Interactions

The major metabolic pathway for carbaryl involves hydrolysis, which can be mediated by albumin, cytochrome P-450, or other esterases (Cranmer 1986; Shrewsbury et al 1997). Like many agents metabolized by cytochrome P-450, carbaryl can induce cytochrome P-450 – i.e., cause an increase in cytochrome P-450 levels in the liver (Cress and Strother 1974). The ability of carbaryl to induce cytochrome P-450 has implications for toxicological interactions because the cytochrome P-450 enzyme system is involved in the metabolism of many xenobiotics as well as many naturally occurring compounds – e.g., steroids. Consequently, carbaryl may competitively inhibit the interaction of other agents with cytochrome P-450 and other agents may competitively inhibit the interaction of carbaryl with cytochrome P-450.

In some instances, the practical impact of these interactions is simple to assess. While not directly relevant to the human health risk assessment, piperonyl butoxide was shown to enhance the toxicity of carbaryl to snails (Singh and Agarwal 1983). Piperonyl butoxide is a well-known competitive inhibitor of cytochrome P-450. Thus, co-exposure to piperonyl butoxide and carbaryl will decrease the rate of carbaryl hydrolysis, thereby increasing the apparent toxicity of

carbaryl. Generally, compounds that compete with carbaryl for cytochrome P-450 are likely to enhance the toxicity carbaryl. The nature of carbaryl's impact on other toxic agents metabolized by cytochrome P-450 will depend on whether the other agent is activated – i.e., made more toxic – or detoxified by cytochrome P-450.

As discussed by the U.S. EPA/OPP (2007a,c), there are numerous other pesticides that act by inhibiting AChE – i.e., the organophosphates and other carbamates. In general, compounds with the same mechanism of action are likely to display additive or less than additive toxicity (e.g., Mumtaz and Durkin 1992). Consistent with this general principle, Gordon et al. (2006) report that carbaryl and chlorpyrifos display additive or less than additive toxicity in rats after acute exposures.

Another form of toxicological interaction involves effects on absorption. The dermal absorption of carbaryl can be enhanced by agents such as DEET and dimethyl sulfoxide (Baynes et al 1997; Baynes and Riviere 1998).

3.2. EXPOSURE ASSESSMENT

3.2.1. Overview

All exposure assessments for carbaryl are summarized in the EXCEL workbooks that accompany this risk assessment: Attachment 1 for applications associated with leaf beetle control and Attachment 2 for applications associated with bark beetle prevention. In these workbooks, Worksheet E01 summarizes exposures for workers and Worksheet E03 summarizes exposures for the general public.

For workers applying carbaryl for leaf beetle control, three types of application methods are modeled: directed ground spray, broadcast ground spray, and aerial spray. In non-accidental scenarios involving the normal application of carbaryl, central estimates of exposure for workers are approximately 0.001 mg/kg/day for aerial and backpack workers and about 0.002 mg/kg/day for broadcast ground spray workers. Upper bounds of exposures are approximately 0.011 mg/kg/day for broadcast ground spray workers and 0.006 mg/kg/day for backpack and aerial workers.

For workers involved in applying carbaryl to tree bark for bark beetle prevention, the estimates of exposure are somewhat less: 0.0025 (0.000042 to 0.026) mg/kg bw/day. These exposure estimates, as well as corresponding exposure estimates for the general public, are unit estimates based on the treatment of a single tree with a 35 foot high treated area and an average diameter of 4 feet. In any actual application the exposures may be higher or lower depending on the number of trees that are treated and the size of the trees being treated.

All of the accidental exposure scenarios for workers involve dermal exposure. The accidental exposure scenarios lead to dose estimates that are substantially greater than the general exposure levels estimated for workers. The greatest exposure is estimated as 5.6 (3.8-8.2) mg/kg bw and is associated with wearing contaminated gloves for 1 hour.

For the general public (Worksheet E03), acute levels of exposures range from minuscule (e.g., $5x10^{-5}$ mg/kg/day) to about 67 mg/kg bw at the typical broadcast application rate of 0.75 lb a.i./acre. The upper bound of exposure, 67 mg/kg bw, is associated with the accidental direct spray of a child. This exposure scenario is extreme. The next higher estimated dose is 10.5 mg/kg bw, which is associated with the consumption of contaminated fish after an accidental spill. This exposure scenario is both extreme and also implausible in that an accidental spill would likely lead to signs of toxicity in fish and possible fish mortality. Thus, the probability that humans would consume the fish is low. The highest dose associated with a plausible exposure scenario is about 0.1 (0.03 – 1.0) mg/kg bw, which is associated with the consumption of contaminated vegetation after a broadcast application for leaf beetle control. The exposure estimates in the workbook for bark beetle prevention are lower than those in the corresponding scenario for leaf beetle control. This discrepancy, however, is an artifact of the unit exposure approach taken for applications associated with bark beetle prevention – i.e., the treatment of a single tree.

The chronic or longer-term exposure levels are much lower than the estimates of corresponding acute exposure levels. For leaf beetle control, the highest longer-term exposure levels are associated with the consumption of contaminated vegetation, and the upper bound for this scenario is about 0.06 mg/kg/day. That scenario is followed by the scenario for the longer-term consumption of contaminated fruit with an upper bound of 0.008 mg/kg/day. As with the acute exposures, longer-term exposures associated with the consumption of surface water or contaminated fish are much lower than those associated with the consumption of contaminated vegetation.

3.2.2. Workers

The exposure assessments for workers involved in the application of carbaryl for leaf beetle control are based on a standard set of exposure scenarios used for other pesticides with similar uses and application methods. While these exposure assessments vary depending on the characteristics as well as the relevant data on the specific chemical, the organization and assumptions used in the exposure assessments are standard and consistent. For leaf beetle control, all of the exposure assessments involving workers as well as members of the general public are detailed in an EXCEL workbook that accompany this risk assessment (Attachment 1: SERA EXWS 052-01-01a). This workbook contains a set of worksheets on carbaryl that detail each exposure scenario discussed in this risk assessment. The workbook also contains summary worksheets for both workers and members of the general public, which cover the range of application rates considered in this risk assessment. A separate EXCEL workbook is provided for applications associated with bark-beetle prevention (Attachment 2: SERA EXWS 052-01-02a), which is similar in structure to the workbook for leaf beetle control, except that Worksheet A01 is customized for the direct applications to tree bark.

Most the customization for Worksheet A01 of Attachment 2 relates to exposure estimates for members of the general public, as discussed further in Section 3.2.3.1. For workers, the major difference between the workbooks for bark beetle prevention and leaf beetle control involves the application methods. For bark beetle prevention, only a single application method is considered – i.e., direct spray to the tree bark. For leaf beetle prevention, all standard broadcast application methods, including aerial application, are considered.

Documentation for these worksheets is presented in SERA (2005). This section on workers and the following section on the general public provide a plain verbal description of the worksheets and discuss the carbaryl specific data used in the worksheets.

Exposure assessments for workers are summarized in Worksheet E01 of the EXCEL workbook. Two types of exposure assessments are considered: general and accidental/incidental. The term *general* exposure assessment is used to designate exposures involving absorbed dose estimates based on handling a specified amount of chemical during specific types of applications. The accidental/incidental exposure scenarios involve specific events that may 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 (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), and these risks are detailed in Worksheets E02a (central application rate), E02b (lower bound of application rate), and E02c (upper bound of application rate).

3.2.2.1. General Exposures

As described in SERA (2007a), 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.

Leaf Beetle Applications: For leaf beetle applications, the specific assumptions used for each application method are detailed in worksheets C01a (directed foliar), C01b (broadcast foliar), and C01c (aerial). The typical application rate is taken directly from the program description (Section 2.4). The central estimate of the amount handled per day is calculated as the product of the central estimate of the acres treated per day and the application rate. As detailed in SERA (2007a), three sets of worker exposure rates – i.e., absorbed dose in mg/kg bw per lb a.i. handled – are used for each type of application:

Application Method	Exposure Rate (mg/kg bw per lb a.i.
Directed foliar	0.003 (0.0003 to 0.01)
Broadcast foliar	0.0002 (0.00001 to 0.0009)
Aerial	0.00003 (0.000001 to 0.0001)

Bark Beetle Applications: While the above general exposure rates are used directly in leaf beetle applications, no studies are available that monitor absorbed dose rates for bark applications. Bark applications are clearly directed – i.e., directed at the bark – and in this respect worker exposure rates for directed foliar applications would appear to be most appropriate. On the other hand, bark applications involve higher pressures than typical directed foliar applications with a backpack.

Haverty et al. (1983) conducted a study on worker exposure to carbaryl using high-pressure hydraulic sprayers in tree bark applications. These investigators, however, measured only deposition and not absorption. Nonetheless, the study by Haverty et al. (1983) is the best available study for assessing the use of worker exposure rates based directed foliar applications for the exposure of workers involved in bark applications. The computational details of the analysis of the Haverty et al. (1983) study are given in Worksheet C01a-Sup of the workbook for bark beetle applications (Supplement 2) and the approach used in this analysis is discussed below.

In the study by Haverty et al. (1983), five workers applied carbaryl to ponderosa pines using two application methods: high-pressure sprayers and low pressure sprayers with telescoping poles. Only the high-pressure sprayer applications are relevant to the proposed applications on Forest Service lands. Thus, the low pressure sprayer data is not further considered.

Using the high pressure sprayers, each worker treated two trees with a 1% carbaryl solution. While Haverty et al. (1983) do not detail the mixing methods used in preparing the solutions, the "1% carbaryl" clearly refers to a 1% w/w solution. As discussed in Section 2.4.2, this corresponds to a solution containing 0.078 lb a.i./gallon. The Haverty publication indicates that each tree was treated with about 8 liters of the field solution. Thus, as detailed in Worksheet C01a-Sup, each worker handled about 0.33 lb a.i.

Haverty et al. (1983) monitored total body exposure based on the amount of carbaryl on deposited on chromatography paper placed with masking tape on the sides of face, sides of neck, chest, back, forearms, thighs, and lower legs. The publication does not specify whether the paper was placed inside or outside of the clothing. One of the authors of the Haverty publication was contacted and confirmed that the patches were on the outside of the protective clothing (Shea 2007). Based on the measurements of external deposition as well as standard estimates of surface areas of different parts of the body, Haverty et al. (1983) estimated total deposited doses on the workers from 0.03 mg to 10.3 mg. This level of variability – i.e., a factor of about 340 – is greater than the variability in worker exposure rates for backpack applications –i.e., a factor of about 33 [0.01 / 0.0003] and this greater variability may reflect the incidental nature (i.e., accidental splashing) of worker exposure during bark treatment.

The average worker exposure reported by Haverty et al. (1983) is 1.5 mg/worker with a standard deviation of 3.2 mg. Reanalysis of the data in Table 2 of the Haverty publication using EXCEL (C01a-Sup in Attachment 2) yields an arithmetic mean of 1.47 and a standard deviation of 3.14. These slight differences from the values reported by Haverty probably reflect rounding errors. In any event, this mean and standard deviation are arithmetic – i.e., assuming a normal distribution. For calculating confidence intervals, the deposition data from Haverty were imported into StatGraphics (Manugistics 1995) and the mean and two-tailed 95% confidence intervals were calculated assuming a lognormal distribution as 1.67 (0.0115 to 11.21) mg. To estimate the gross absorbed dose, the dermal absorption rates of 0.08962 (0.0312 to 0.2319) $hour^{-1}$ was used assuming a body weight of 70 kg and an exposure period of 8 hours. As detailed in Worksheet C01a-Sup, this resulted in gross absorbed dose rates of about 0.07 (0.03 to 0.12) mg/kg bw per lb a.i. handled. These estimates are referred to a gross absorbed doses because they do not consider the impact of protective clothing and a correction for the protective effect of clothing is needed in the comparison of the Haverty study to the standard exposure rates used for workers.

All product labels for carbaryl require that the worker wear a long-sleeved shirt, long pants, chemical resistant gloves, shoes plus socks, and chemical-resistant headgear for overhead applications. The efficiency of protective clothing – i.e., the extent to which the clothing retards deposition onto the skin of the worker – will vary with the nature of the application and the type of protective clothing. Studies involving ground applications of carbaryl indicate that protective clothing may provided efficiencies of about 89% to 93% (Gold et al. 1982; Leavitt et al. 1982) and a protection efficiency of about 90% is typical for many pesticides (Nigg 1998). Additional data on protection efficiencies are available in the U.S. EPA's Pesticide Handler's Exposure Database (PHED Task Force 1995) for various types of ground and aerial applications.

PHED does not contain specific information on high-pressure bark applications but does contain information on high and low pressure hand wand applications (protection factors of 0.95 and 0.996 respectively) as well as ground boom applications (a protection factor of 0.935). Details of the calculations of these protection factors are given at the bottom of Worksheet C01a-Sup (Attachment 2).

As detailed at the bottom of Worksheet C01a-Sup, these types of applications are associated with protections efficiencies of about 93% to over 99% based on the types of protective clothing required on the carbaryl product labels. For estimating absorbed doses from the Haverty et al. (1983) study, the protection efficiencies for protective clothing is taken as 0.95 with a range of 0.9 to 0.99. Based on the range of protection factors, the absorbed dose rate from the Haverty study is estimated as 0.0037 (0.0000022 – 0.0818) mg/kg bw per lb a.i. handled.

The central estimate of the exposure rate (0.0037 mg/kg bw per lb a.i. handled) from the Haverty study is very close to the centrl value for the standard rate (0.003 mg/kg bw per lb a.i. handled) used for directed foliar applications.

The upper and lower bounds of the absorbed dose rates from the Haverty study (0.0000022 – 0.0818 mg/kg bw per lb a.i. handled) are much broader than the standard exposure rates used in Forest Service risk assessments for directed foliar/backpack applications (0.0003 to 0.01 mg/kg bw per lb a.i. handled). This broader range is associated with the conservative nature of the calculations. Specifically, the upper range of the calculated exposure rate is based on the upper range of the deposited dose, the upper range of the first-order dermal absorption rate, and the lower range of the factor for protective clothing. While this is a conservative calculation, the use of multiple conservative assumptions can magnify and distort exposure estimates. For example, using the upper bound of the protection factor (0.99) rather than the lower bound but maintaining the upper bound of the dermal absorption rate and the upper bound of the depostion, the estimate of the upper bound of the exposure rate for workers in the Haverty study would be about 0.0082 mg/kg bw per lb a.i. handled. This estimate of the absorbed dose rate is somewhat below the upper bound of 0.01 mg/kg bw per lb a.i. handled used in Forest Service risk assessments for directed foliar applications.

For the current risk assessment, exposures to workers involved in bark applications are based on the standard exposure rate for directed foliar/backpack applications. As discussed in SERA (2007a), these rates are based on a large number of studies involving estimates of absorbed dose rates for a large number of pesticides. In addition, newer worker studies (e.g., the worker exposure study by Krieger et al. 2005 a detailed in SERA 2006b) support the use of the standard worker exposure rates used in Forest Service assessments.

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 pesticide 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 the pesticide into the eyes or contaminating the surface of the skin.

There are various methods for estimating absorbed doses associated with accidental dermal exposure (SERA 2007a). Two general types of exposures are modeled in this risk assessment: those involving direct contact with a solution of the pesticide and those associated with accidental spills of the pesticide 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 summarized 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 in a field solution of carbaryl 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 chemical for any period of time. Nevertheless, contamination of gloves or other clothing is quite plausible. For these exposure scenarios, the key assumption is that wearing gloves grossly contaminated with a chemical solution is equivalent to immersing the hands in a chemical solution. In both cases, the concentration of the chemical solution in contact with the skin and the resulting dermal absorption rate are basically constant.

For both scenarios (hand immersion and contaminated gloves), the assumption of zero-order absorption kinetics is appropriate. Following the general recommendations of U.S. EPA/ORD (1992), Fick's first law is used to estimate dermal exposure. As discussed in Section 3.1.3.2, an experimental dermal permeability coefficient (k_p) for carbaryl is not available. In the absence of experimental data, the k_p for a pesticide is typically estimated using the algorithm from U.S. EPA/ORD (1992), which is detailed in Worksheet B05. As also discussed in 3.1.3.2, however, standard algorithms for estimating the first-order dermal absorption rate appear to grossly underestimate the dermal absorption for carbaryl. This underestimate diminishes confidence in the direct use of the EPA/ORD (1992) algorithm for the dermal permeability coefficient (k_p). Consequently, the dermal permeability coefficients estimated from Worksheet B05 are multiplied by a factor of 10 and these adjusted values are entered into Worksheet B03 and these adjusted values are used in all dermal exposure scenarios based on zero-order dermal absorption kinetics.

Exposure scenarios involving chemical spills onto the skin are characterized by a spill on to the lower legs as well as a spill on to the hands. In these scenarios, it is assumed that a chemical solution is spilled on to a given surface area of skin and that a certain amount of the chemical adheres to the skin. The absorbed dose is then calculated as the product of the amount of the

chemical on the surface of the skin (i.e., the amount of liquid per unit surface area multiplied by the surface area of the skin over which the spill occurs and the concentration of the chemical in the liquid), the first-order absorption rate, and the duration of exposure. For both scenarios, it is assumed that the contaminated skin is effectively cleaned after 1 hour. As detailed in Section 3.1.3.2, the dermal absorption rates used in these scenarios is based on experimental dermal absorption rates taken from U.S. EPA/OPP (2007a) rather than the estimated dermal absorption rates given in Worksheet B06.

3.2.3. General Public

3.2.3.1. General Considerations

3.2.3.1.1. Applications for Bark Beetle Prevention

As noted in Section 3.2.2.1, pesticide applications to tree bark are somewhat atypical, and the EXCEL workbook for these applications involves the use of a custom worksheet, Worksheet A01 in Attachment 2. As discussed in Section 2.4, most Forest Service risk assessments involve broadcast applications of pesticides that are relatively uniform over the treatment area. For bark beetle prevention, carbaryl is applied directly to tree bark in a concerted effort to prevent as much pesticide loss as possible to the area surrounding the treated tree. Another atypical characteristic of pesticide applications for bark beetle prevention is that applications generally are not made to all trees in a given area. Only high value trees will be treated.

Because of these atypical application characteristics, three application areas are considered in Worksheets A01 of the workbook for bark beetle prevention: the target tree bark, the ground in the vicinity of the treated trees, and the total area over which the applications are made.

The application rate to the target trees is calculated as a function of the treated surface area of the tree, the volume of the applied field solution, and application efficiency. In Worksheet A01, application efficiency (designated as *AppEff*) refers to the proportion of the pesticide actually applied to the tree relative to the amount of the pesticide directed at the tree. Ideally, these two values would be identical. In practice, it is inevitable that some of the applied pesticide will splash off the tree during application or applied to the area surrounding the treated tree due to misdirection. Consequently, in tree bark applications, the nominal application rate (designated as *AppTree* in this worksheet) will be less than the actual amount applied to the tree (designated as *LbsTree* in this worksheet).

The application to the area surrounding the treated tree or trees is referred to as *StAcres* (area of the treated stand) in Worksheet A01. This application rate to the treated stand area (designated as *ApRt*) is calculated as the amount of the pesticide that is not applied to the bark of the treated tree or trees divided by the area of the treated stand (*StAcres*). It is recognized that this area may be noncontiguous. Within the context of this risk assessment, this circumstance has no impact. *ApRt* is used only to calculated exposure scenarios that involve deposition on nontarget vegetation – i.e., the consumption of contaminated vegetation and the scenarios involving dermal contact with contaminated vegetation. In other words, it is mostly likely that exposure to

contaminated vegetation will occur only in the areas immediately adjacent to the treated tree or trees.

The total area over which the applications are made is intended to reflect the total area of concern for the consideration of contaminated water. In this risk assessment, concentrations in surface water are estimated for both a standard pond and a standard stream. In both cases, the assumption is made that these water bodies are contained within a 10-ha (24.71-acre) area. This value (designated as *TotAcres* in this worksheet) is not used directly in Worksheet A01. Instead, *TotAcres* and *StAcres* are linked to Worksheet B04 and are used to adjust the water contaminations rates.

3.2.3.1.2. Likelihood and Magnitude of Exposure

The likelihood that members of the general public will be exposed to carbaryl in Forest Service applications is highly variable. In some Forest Service programs, carbaryl will be applied in recreational areas like campgrounds, picnic areas, and trails. In these instances, exposures to members of the general public to carbaryl residues are plausible.

It should be noted, however, that all carbaryl labels indicate that members of the general public should be excluded from treated areas during application and after application until the sprays have dried. Several of the standard acute exposure scenarios included in this risk assessment as well as other Forest Service risk assessments entail exposures to members of the general public during application: direct spray of members of the general public (Section 3.2.3.2), the consumption of contaminated vegetation immediately after application (Section 3.2.3.3), consumption of contaminated water after an accidental spill (Section 3.2.3.4.1), and consumption of contaminated fish after an accidental spill (Section 3.2.3.5). For carbaryl, these exposure scenarios are not only extreme. These exposure scenarios will not occur provided that the directions on the label to exclude members of the public from treated areas are followed. Thus, these accidental exposure scenarios are accidents that would only occur during misapplications.

In addition to excluding members of the general public from treated areas during application, the Forest Service will mark treated areas with cautionary notices indicating that a hazardous pesticide has been applied. This impacts the assessments of not only acute exposure scenarios but also of the longer-term exposure scenarios for the consumption of contaminated vegetation and fruit (Section 3.2.3.7). Both of these longer-term exposure scenarios involve the assumption that an individual will harvest the contaminated vegetation or fruit from a treated area shortly after application and will store and consume the vegetation or fruit over a prolonged period of time. Because the Forest Service will designate treated areas with warning messages, the probability that a member of the general public would consume contaminated vegetation or fruit over a prolonged period of time is remote. This is considered further in the risk characterization.

Because of the conservative exposure assumptions used in the current risk assessment, neither the probability of exposure nor the number of individuals who might be exposed has a substantial impact on the characterization of risk presented in Section 3.4. As noted in Section 1 (Introduction) and detailed in SERA (2007a, Section 1.2.2.2), the exposure assessments

developed in this risk assessment are based on ***Extreme Values*** rather than a single value. Extreme value exposure assessments, as the name implies, bracket the most plausible estimate of exposure (referred to statistically as the central or maximum likelihood estimate) with extreme lower and upper bounds of plausible exposures.

This Extreme Value approach is essentially an elaboration on the concept of the *Most Exposed Individual* (MEI), sometime referred to as the *Maximum Exposed Individual* (MEI). As this name also implies, exposure assessments that use the MEI approach are based on an attempt to characterize the extreme but still plausible upper limit on exposure. This is a common approach to exposure assessment used by the U. S. EPA, other governmental agencies, as well as the International Commission on Radiological Protection (e.g., ATSDR 2002; ICRP 2005; Payne-Sturges et al. 2004). In the current risk assessment, the upper bounds on exposure are all based on the MEI.

In addition to this upper bound MEI value, the Extreme Value approach used in this risk assessment also provides a central estimate of exposure as well as a lower bound on exposure. While not germane to the assessment of upper bound risk, it is worth noting that the use of the central estimate and especially the lower bound estimate is not intended to lessen concern. To the contrary, the central and lower estimates of exposure are used to assess the feasibility of mitigation – e.g., protective measures to limit exposure. If lower bound exposure estimates exceed a level of concern (which is not the case in the current risk assessment), this is strong indication that the pesticide cannot be used in a manner that will lead to acceptable risk.

Thus, the Extreme Value approach in the exposure assessment is part of an integrated approach that is designed to encompass plausible upper limits of risk for the most exposed and most sensitive individuals, regardless of the specific probabilities or number of exposures.

3.2.3.1.1. Summary of Assessments

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 D01–D11). 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. Two direct spray scenarios are given, one for a young child (D01a) and the other for a young woman (D01b).

For the young child, it is assumed that a naked child is sprayed directly during a ground broadcast application and that the child is completely covered (that is, 100% of the surface area of the body is exposed). This scenario is, and is intended to be, extreme. As discussed in Section 3.2.3.1.1, the upper limits of this exposure scenario are intended to represent the *Extreme Value* upper limits of exposure for the *Most Exposed Individual* (MEI).

The exposure scenario involving the young woman (Worksheet D01b) is somewhat less extreme but more plausible. In this scenario, it is assumed that the woman is accidentally sprayed over the feet and lower legs. A young woman rather than an adult male is used in many of the exposure assessments. By reason of allometric relationships between body size and dose-scaling, a young woman will typically be subject to a somewhat higher dose than the standard 70 kg man.

For the direct spray scenarios, assumptions are made regarding the surface area of the skin and the body weight of the individual, as detailed in Worksheet A03. The rationale for and sources of the specific values used in these and other exposure scenarios are provided in the documentation for the worksheets (SERA 2005) and in the methods document for preparing Forest Service risk assessments (SERA 2007a).

3.2.3.3. Dermal Exposure from Contaminated Vegetation

As detailed in SERA (2007a), this exposure scenario assumes that the pesticide is sprayed at a given application rate and that a young woman comes in contact with sprayed vegetation or other contaminated surfaces at some period after the spray operation (D02). For these exposure scenarios, some estimates of dislodgeable residue (a measure of the amount of the chemical that could be released from the vegetation) and the rate of transfer of the chemical from the contaminated vegetation to the surface of the skin must be available. As detailed in Durkin et al. (1995), dermal transfer rates are reasonably consistent for a number of different pesticides and the methods and rates derived in Durkin et al. (1995) are used as defined in Worksheet D02. The exposure scenario assumes a contact period of 1 hour and further 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, from unintentional direct spray from aerial applications, or drift from either ground or aerial applications. This component of the exposure assessment derives the three types of

estimates of carbaryl concentrations in ambient water: an accidental spill (Section 3.2.3.4.1), unintended direct spray or drift (Section 3.2.3.4.2), as well as both acute and longer-term exposures in ponds and streams that might be associated with the carbaryl applications (Section 3.2.3.4.3).

3.2.3.4.1. Accidental Spill

The accidental spill scenario assumes that a young child consumes contaminated water from a small pond (0.25 acres in surface area and 1 meter deep) shortly after an accidental spill of 200 gallons of a field solution into a small pond. The specifics of this scenario are given in Worksheet D05. Because this scenario is based on the assumption that exposure occurs shortly after the spill, no dissipation or degradation is considered. This scenario is dominated by arbitrary variability, and the specific assumptions used generally overestimate exposure. The actual concentration 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 carbaryl in a small pond is estimated to range from about 0.6 to 1.5 mg/L with a central estimate of about 1 mg/L (Worksheet D05).

3.2.3.4.2. Accidental Direct Spray/drift for a Pond or Stream

Leaf Beetle Control (Attachment 1)**:** These scenarios are less severe but more plausible than the accidental spill scenario described above. The U.S. EPA typically uses a 2 meter deep pond to develop exposure assessments (SERA 2004). If such a pond is directly sprayed with carbaryl at the central estimate of the application rate (0.75 lb a.i./acre), the peak concentration in the pond would be about 0.042 mg/L, equivalent to 42 µg/L or 42 ppb (Worksheet D10a). This concentration is a factor of about 35 below the upper bound of the peak concentration of 1.5 mg/L after the accidental spill of a liquid formulation (Section 3.2.3.4.1, Worksheet D05). Worksheet D10a also models concentrations at distances of 25-900 feet downwind based on standard values adapted from AgDrift (SERA 2007a). Based on these estimates, carbaryl concentrations in a small pond contaminated by drift would range from about 0.000038 to 0.006 mg/L.

Similar calculations can be made for the direct spray of or drift into a stream. For this scenario, the resulting water concentrations depend on the surface area of the stream and the rate of water flow in the stream. The stream modeled using GLEAMS (see below) is about 6 feet wide (1.82 meters), and it is assumed that the pesticide is applied along a 1038 foot (316.38 meters) length of the stream with a flow rate of 710,000 L/day. Using these values, the concentration in stream water after a direct spray is estimated at about 0.068 mg/L. Much lower concentrations, ranging from about 0.000062 to 0.01 mg/L are estimated based on drift at distances of 25-900 feet (Worksheet D10b).

Bark Beetle Prevention (Attachment 2)**:** Because of the differences in the functional application rate – i.e., the amount applied that misses the tree bark – the corresponding scenarios for bark beetle prevention lead to somewhat lower concentrations than those for leaf beetle control. For

the direct spray of a pond, the peak concentration in the pond would be about 0.01 mg/L (Worksheet D10a). At distances of 25-900 feet down wind, carbaryl concentrations in a small pond contaminated by drift would range from about 0.0000095 to 0.0015 mg/L. The concentration in stream water after a direct spray is estimated at about 0.017 mg/L. Based on drift at distances of 25-900 feet, the estimated concentrations range from about 0.000015 to 0.0025 mg/L (Worksheet D10b).

3.2.3.4.3. Standard GLEAMS Modeling

For compounds that may be applied over a large proportion of a watershed, drift and even direct spray are not the only and may not be the greatest source of contamination of surface water. Water contamination may also occur from soil runoff (the pesticide dissolved in runoff water), sediment (pesticide adsorbed to organic carbon with sediment in runoff water), or percolation (pesticides leaching into subsurface water). Depending on local conditions, these losses can lead to substantial contamination of ponds or streams. This section describes a relatively standardized and generic modeling approach used in Forest Service risk assessments. This description is followed by subsections on GLEAMS modeling at specific locations (Section 3.2.3.4.5), other modeling efforts (Section 3.2.3.4.6), and monitoring data (Section 3.2.3.4.7).

The standard application of the GLEAMS model and the use of the output from this model to estimate concentrations in ambient water are detailed in SERA (2004d). The application site was assumed to consist of a 10-hectare square area that drained directly into a small pond or stream. As detailed in SERA (2004), the standard GLEAMS modeling encompasses rainfall rates of 5-250 inches per year, assuming that the rainfall occurs uniformly on every 10th day, with the first rainfall event occurring on the day after pesticide application. This approach to the use of GLEAMS is referred to as *standard GLEAMS modeling*. More realistic rainfall patterns are in the location-specific modeling in Section 3.2.3.4.5.

Modeling of carbaryl concentrations in stream water conducted for this risk assessment are based 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).

Both the standard GLEAMS modeling discussed in this section as well as the location-specific modeling in Section 3.2.3.4.5 are based on a common set of assumptions that are intended to be generally conservative. As detailed in SERA (2004), all model runs are conducted at an application rate of 1 lb a.i./acre. This approach is taken simply because GLEAMS outputs information in a fixed decimal format, which can result in the loss of information if the model is run at low application rates. Because pesticide losses in runoff, sediment, and percolation are all linearly related to application rate, the expected concentrations in water and soil, based on the application rates used in Forest Service programs, can be calculated simply as the value from the GLEAMS modeling at 1 lb/acre multiplied by the application rate that actually will be used.

The standard GLEAMS modeling as well as the location-specific modeling (Section 3.2.3.4.5) are conducted for three types of soils: clay, loam, and sand. For clay, site conditions are

assumed to favor runoff. For sand, site conditions are assumed to favor percolation. For loam, moderate assumptions are used in the modeling in terms of surface conditions. For all model runs, buffers are not considered – i.e., the applications are assumed to occur up to the edge of the water. The generic approach to GLEAMS modeling is described in SERA (2004).

The chemical specific values as well as the details of the pond and stream scenarios used in the GLEAMS modeling are summarized in Table 6. For the most part, the chemical specific input values used in the GLEAMS modeling are similar to those used by the U.S. EPA (U.S. EPA/OPP 2003d). The EPA modeling efforts are discussed below (Section 3.2.3.4.4). The modeling input values are based on the environmental fate studies submitted to the U.S. EPA as well as standard values from the USDA Pesticides Properties Database (USDA/ARS 1995). The specific sources of information used in the GLEAMS modeling are given in the notes to Table 6.

Estimates of runoff, sediment, and percolation concentrations in a stream adjacent to a treated plot were determined by running the GLEAMS model, as discussed in Section 6.4 of SERA (2004). The results of the GLEAMS modeling for the small stream are summarized in Table 7, and the corresponding values for the small pond are summarized in Table 8. These estimates are expressed both as average and peak concentrations in water. All of these GLEAMS runs were conducted at an application rate of 1 lb a.i./acre, the values given in Tables 7 and 8 are expressed as water contamination rates (WCR) – i.e., the concentration of the compound in water in units of ppb (µg/L) normalized for an application rate of 1 lb a.i./acre. In the worksheets that accompany this risk assessment, the WCR values are multiplied by the application rate to estimate concentrations in surface water.

Surface water contamination is not estimated for very arid regions – i.e., annual rainfall of 10 inches or less. It should be noted, however, that this result may be an artifact of the way the GLEAMS modeling is conducted. As described above, the generic GLEAMS modeling is based on a rainfall pattern in which rainfall occurs every 10^{th} day and the amount of rainfall is uniform each day. Thus, for an annual rainfall of 10 inches per year, the amount of rainfall in each event is about 0.25 inches – i.e., 10 inches per year divided by 37 rainfall events per year.

At higher rainfall rates and the application rate of 1 lb a.i./acre, the modeled peak concentrations in streams range from about 44 ppb (clay at an annual rainfall rate of 15 inches) to about 361 ppb (clay at an annual rainfall rate of 250 inches) (Table 7). Modeled peak concentrations in a small pond (Table 8) are somewhat lower than those modeled in the stream. As with the stream modeling, no surface water contamination is expected in very arid regions. For regions with annual rainfall rates of 15 inches or more, the modeled peak concentrations in ponds at an application rate of 1 lb a.i./acre range from 2.4 ppb (clay at an annual rainfall rate of 15 inches) to 173 ppb (clay at an annual rainfall rate of 250 inches). Average concentrations in the pond range from negligible (less than 0.000003 mg/L for sand at 50 inches per year) to1.57 ppb (clay at 250 inches per year), very similar to the modeled average concentrations for the stream.

3.2.3.4.4. GLEAMS Modeling At Specific Sites

The standard GLEAMS modeling discussed in the previous section is used in many past pesticide risk assessments and incorporates a number of conservative assumptions (SERA 2004). Nonetheless, a limitation in the standard approach to using GLEAMS to model concentrations in ambient water involves the assumption that rainfall is evenly distributed over an every 10th day interval. To address this limitation and to more generally facilitate site-specific assessments of pesticide applications, the Forest Service developed Gleams-Driver, a computer program that serves as a preprocessor and postprocessor for GLEAMS (SERA 2007b). One feature of Gleams-Driver involves a utility for importing weather files from Cligen, a climate generator program developed and maintained by the USDA Agricultural Research Service (http://horizon.nserl.purdue.edu/Cligen).

Gleams-Driver offers the option of conducting general exposure assessments identical to those described in the previous section but using site-specific weather files from Cligen rather than the every 10th rainfall files. To explore the potential impact of more realistic rainfall patterns on the estimated concentrations of carbaryl in surface water, Gleams-Driver was used to model concentrations in a small stream and small pond using the same parameters specified in Table 6 as well as the characteristics of a small stream and a small pond that are used in the standard GLEAMS modeling (SERA 2004d).

The locations selected for modeling included a total of nine sites, as illustrated in Figure 4. As detailed in SERA (2007b), these sites are standard test sites for Gleams-Driver intended to represent combinations of precipitation (dry, average, and wet) and temperature (hot, temperate, and cool). For each site, Gleams-Driver was used to simulate 100 applications of carbaryl at a unit application rate of 1 lb/acre to clay, loam, and sand soils, and each of the simulations was followed over a 1½ year period after application.

The results of the Gleams-Driver simulations are given in Table 9 (peak concentrations) and Table 10 (one-year average concentrations) for a small stream and Table 11 (peak concentrations) and Table 12 (one-year average concentrations) for a small pond. As discussed in SERA (2007b), all values are expressed as the midpoint (median) with 95% empirical confidence intervals.

For the small stream, the peak concentrations based on Gleams-Driver simulations (Table 9) are somewhat less than those based on standard GLEAMS modeling (Table 7). In arid regions, the lower ranges of estimated concentrations are zero and the central estimates of peak concentrations do not exceed 0.000041 ppb. In areas with average to high rainfall rates, the maximum concentration in streams is 34.9 ppb (Table 9, average rainfall, clay), about a factor of 10 lower than the 336 ppb concentration based on standard GLEAMS modeling using an every 10th day rainfall pattern (Table 7, 250 inches per year, clay). In both sets of simulations, the lowest peak concentrations are estimated in areas with predominantly sandy soil.

The differences in average concentrations of carbaryl in a small stream based on standard GLEAMS modeling (Table 7) and the Gleams-Driver simulations (Table 10) are similar to those

based on peak exposures. The highest average concentration in a small stream based on standard GLEAMS modeling is 1.47 ppb (100 inches of rainfall in clay soil). The corresponding maximum from the Gleams-Driver simulations is 0.18 ppb in a wet/warm region with clay soil, is lower than the standard GLEAMS average by a factor of about 8.

The differences between the standard GLEAMS modeling and Gleams-Driver simulations for a small pond are similar to those for the small stream, with substantially lower concentrations modeled with Gleams-Driver relative to the standard GLEAMS modeling. The peak concentrations from Gleams-Driver (Table 11) are less than those from standard GLEAMS modeling by a factor of about 7 (23.1 ppb vs 173 ppb). The differences between standard GLEAMS modeling (Table 8) and Gleams-Driver simulations based on average concentrations in a small pond (Table 12) are much smaller – i.e., about a factor of 3 based on upper bounds from Gleams-Driver (1.41 ppb vs 4.2 ppb) but more substantial based on central estimates from Gleams-Driver (0.24 ppb vs 4.2 ppb or a factor of about 17.5).

3.2.3.4.5. Other Modeling Efforts

A summary of the GLEAMS modeling discussed above as well as modeling of carbaryl presented by the U.S. EPA/OPP (U.S. EPA/OPP 2003d) is given in Table 13. Table 13 includes a summary of both the standard GLEAMS modeling (Section 3.2.3.4.3) as well as the location specific modeling conducted with Gleams-Driver (Section 3.2.3.4.4).

In the human health risk assessment of carbaryl, U.S. EPA/OPP (U.S. EPA/OPP 2003d) uses two water contamination models: PRZM/EXAMS and SCI-GROW. As discussed in SERA (2007b), PRZM/EXAMS is a model, or more accurately a system of linked models, that the U.S. EPA uses to assess plausible concentrations of pesticides in water after agricultural applications. Different types of PRZM/EXAMS scenarios can be conducted, and the modeling summarized in Table 13 involves the use of an index reservoir (i.e., a standard reservoir) commonly used by the U.S. EPA/OPP. SCI-GROW is a Tier 1 screening model developed by the U.S. EPA to estimate concentrations of a compound in groundwater based on a given application rate, number of applications, the interval between applications, and standard environmental fate parameters for a specific compound.

The U.S. EPA/OPP modeled concentrations of carbaryl in water over a range of labeled rates from 1 to 4.26 lb a.i./acre as well as varying numbers of applications per year (U.S. EPA/OPP-HED 2003d, Table 7, p. 19). In Table 13 of the current risk assessment, the reported concentrations are normalized to 1 lb a.i./acre by dividing the concentration reported by the U.S. EPA by the product of the application rate used in the modeling and the number of applications. The estimate of the peak concentration from PRZM/EXAMS is about 30 ppb at an application rate of 1 lb a.i./acre. This peak concentration is virtually identical to the peak concentrations in ponds modeled in the Gleams-Driver simulations – i.e., 33 ppb at 1 lb/acre. The lower bound of range of concentrations modeled by the U.S. EPA is 3.6 ppb which is only somewhat greater than the central estimate from the Gleams-Driver pond simulations – i.e., 2 ppb. As noted above, the standard GLEAMS simulations lead to substantially higher estimated concentrations than either PRZM/EXAMS or Gleams-Driver.

In comparisons of PRZM/EXAMS modeling conducted by the U.S. EPA to GLEAMS modeling conducted in this series of risk assessments, higher estimates are typically found using the standard GLEAMS modeling because of the conservative assumptions built into the standard GLEAMS modeling (SERA 2004) – i.e., rainfall rates up to 250 inches/year with rainfall occurring on every 10^{th} day.

As with the peak concentrations, the results of the PRZM/EXAMS modeling are comparable to the results of the Gleams-Driver modeling at the upper bound of the estimated concentrations – i.e., 1.07 ppb from PRZM/EXAMS and 1.6 ppb from Gleams-Driver. In addition, the standard GLEAMS simulations for a small pond yielded an upper bound concentration of 1.6 ppb, identical to that of Gleams-Driver. While this exact concordance is coincidental, the average concentrations among models will tend to be less divergent than peak concentrations because averaging, by definition, will reduce the impact of extreme 1-day events.

3.2.3.4.6. Monitoring Data

There is a large body of monitoring data available on carbaryl, much of which is reviewed by the U.S. EPA/OPP (2003d) and summarized in Table 13 along with the data on modeling. With the exception of a reported concentration of 610 ppb in well water, both the PRZM/EXAM modeling conducted by the U.S. EPA (Section 3.2.3.4.5) and the GLEAMS and Gleams-Driver modeling conducted for the current Forest Service risk assessment encompass the available monitoring data. As discussed in U.S. EPA /OPP (2003d, p. 11), the reported carbaryl concentration of 610 ppb in well water came from one well in New York, and this value is atypical: *The maximum concentration detected was 610 µg L^{-1} in NY, though typically the measured concentrations were orders of magnitude lower.*

3.2.3.4.7. Concentrations in Water Used for Risk Assessment

Table 12 summarizes the carbaryl concentrations in water used for the current risk assessment. The upper part of this table gives the concentrations expected at the nominal application rate of 0.75 lb a.i./acre, in units of micrograms per liter or ppb. The lower part of this table gives the water contamination rates, the concentrations in water expected at a normalized application rate of 1 lb a.i./acre, converted to units of ppm or mg/L per lb a.i./acre. The conversion from ppb to ppm is made because these latter units – i.e., ppm or mg/L – are used in the EXCEL workbook in the various exposure scenarios involving contaminated water in both the human health and ecological risk assessments. The water contamination rates are entered in Worksheet B04, and links to these values are used in scenario specific worksheets in the EXCEL workbook.

The upper range of the expected peak WCR of carbaryl in surface water is taken as 0.033 ppm per lb a.i./acre. This estimate is based on rounding to one significant place the peak carbaryl concentration in streams modeled using Gleams-Driver simulations as summarized in Table 13 and detailed in Table 9 (an upper bound of 33.5 ppb for clay at 250 inches per year). As discussed in Section 3.2.3.4.5, this WRC is very close to the upper bound estimate of 0.030 ppm from the PRZM/EXAMS modeling conducted by the U.S. EPA. The standard GLEAMS simulations (Section 3.2.3.4.3) yield estimates that are about an order of magnitude higher.

Based on the concordance of the Gleams-Driver and PRZM/EXAMS modeling, both of which are based on natural patterns of rainfall rates, the upper bound from the standard GLEAMS simulations appears to be impacted primarily by the assumption of rainfall on every 10^{th} day. As also noted in Table 13, this upper bound of the peak water contamination rate is likely to encompass accidental or incidental exposures due to spray drift but not direct spray. In other words, while inadvertent contamination due to drift might be considered an extreme or at least atypical exposure, higher concentrations in water could be associated with normal use of carbaryl in some areas. Accidental direct spray of a pond or stream, however, is likely to result in higher concentrations of carbaryl in water than would be associated with expected contamination due to runoff or percolation.

For the lower bound of the peak WCR, an argument may be made that carbaryl concentrations are likely to be essentially zero – i.e., applications at sites that are distant from open bodies of water and in areas in which runoff or percolation are not likely to occur. For this risk assessment, the lower range of the peak water contamination rate is set at 0.002 ppm per lb/acre. This is about the concentration modeled in Gleams-Driver simulations of streams and ponds in areas with average rainfall and average to warm temperatures.

The central estimate for the peak WCR is set at 0.02 ppm per lb/acre. This central estimate is based on an average of the central estimates for ponds (27 ppb) and streams (13 ppb) modeled using standard and probably very conservative GLEAMS simulations. This concentration is also approximately equal to the median concentration of carbaryl in a small stream modeled using Gleams-Driver for wet and cool regions with predominantly clay soil.

The water contamination rates for longer-term exposures are derived in a similar manner. At an application rate of 1 lb/acre, the highest longer-term concentration is taken as 2 ppb or 0.002 ppm per lb a.i./acre. As summarized in Table 13, the value of 2 ppb is based on the upper bound of the average concentrations modeled in Gleams-Driver and standard GLEAMS simulations for ponds (i.e., 1.6 ppb) rounded upward to one significant place (i.e., 2 ppb).

As with the lower bound estimates of peak concentrations, the lower bound of the longer-term concentration could be taken as zero. For the current risk assessment, the lower bound is taken as 0.1 ppb or 0.0001 ppm per lb a.i./acre, which coincides approximately with the longer-term concentrations of carbaryl in streams modeled using Gleams-Driver in areas of average rainfall, normal to high temperatures, and predominantly clay or loam soil (Table 10).

The judgmental and to some degree arbitrary nature of the selected water contamination rates and the assumptions used to derive these rates should be apparent and appreciated. GLEAMS as well as PRZM/EXAMS are highly parameterized models intended for use in site-specific exposure assessments. The generic applications of GLEAMS and Gleams-Driver in this current risk assessment are intended only to provide general estimates of plausible exposures in order to identify which exposure scenarios might present the greatest risk under a wide-ranging set of conditions and some very conservative assumptions. In the assessment of any site-specific application of carbaryl, site specific data should be used to refine these estimates.

3.2.3.5. Oral Exposure from Contaminated Fish

Three sets of exposure scenarios – one for the general population and the other for subsistence populations – are presented for the consumption of contaminated fish: one set for acute exposures following an accidental spill (Worksheets D08a and D08b), another set for acute exposures based on expected peak concentrations (Worksheets D08c and D08d), and the third set for chronic exposures based estimates of longer-term concentrations in water (Worksheets D09a and D09b). The two worksheets in each of these three sets are intended to account for different rates of wild-caught fish consumption in both general and subsistence populations. Details of exposure scenarios involving the consumption of contaminated fish are provided in Section 3.2.3.5 of SERA (2007a).

As summarized in the worksheets for an accidental spill (Worksheets D08a and D08b), the estimated water concentrations range from about 3.4 to 68 ppm. As noted in Section 4.1.3.1, however, the LC_{50} values for fish range from less than 1 to around 20 ppm. Thus, it is not clear that the exposure scenarios associated with the consumption of contaminated fish after an accidental spill are plausible or even reasonable. In other words, after the accidental spill modeled in Worksheets D08a and D08b, it is likely that fish would be obviously in distress or quite possibly dead, as discussed further in the risk characterization (Section 3.4).

In addition to estimates of peak and longer-term term carbaryl concentrations in water, this exposure scenario requires information on the bioconcentration factor (BCF). As summarized in Table 1, the U.S. EPA/OPP (2003d) uses the study by Chib (1986) – an unpublished study submitted to the Agency in support of the reregistration of carbaryl – in which the BCF in edible tissue of sunfish was determined to be 14. This value is used in all exposure assessments involving the consumption of contaminated fish by humans. In the ecological risk assessment, the BCF in whole fish, 45, is used for the consumption of fish by wildlife.

3.2.3.6. Dermal Exposure from Swimming in Contaminated Water

Some sites maintained by the Forest Service contain surface water in which members of the general public might swim. To assess the potential risks associated with swimming in contaminated water, an exposure assessment is developed for a young woman swimming in surface water for 1 hour (Worksheet D11).

Conceptually and computationally, this exposure scenario is virtually identical to the contaminated gloves scenario used for workers (Section 3.2.2.2) – i.e., a portion of the body is immersed in an aqueous solution of the compound at a fixed concentration for a fixed period of time. The major differences in the two scenarios involve the concentration in water and the surface area of the body that is exposed. For the worker wearing contaminated gloves, the assumption is made that both hands are exposed to the field solution – i.e., the concentration of the compound in the solution that is being applied. For the swimmer, the assumption is made that the entire body surface area is exposed to the expected peak concentrations in ambient water (Table 14). While the swimmer will not be immersed for 1 hour, the entire body surface is used both as a conservative approximation (i.e., the MEI) and to consider intermittent episodes during which the whole body might be immersed or at least wet.

As with the corresponding worker exposure scenario, the 1-hour period of exposure is somewhat arbitrary, and longer periods of exposure are plausible. The 1-hour period, however, is not completely arbitrary but is intended as a unit exposure estimate. In other words, the exposure and consequently the risk will increase linearly with the duration of exposure as indicated in Worksheet D11. Thus, a 2-hour exposure would lead to a hazard quotient that is twice as high as that associated with an exposure period of 1 hour. In cases in which this or other similar exposures approach a level of concern, further consideration is given to the duration of exposure in the risk characterization (Section 3.4).

3.2.3.7. Oral Exposure from Contaminated Vegetation

Although none of the Forest Service applications of carbaryl will involve crop treatment, Forest Service risk assessments typically include standard exposure scenarios for the acute and longer-term consumption of contaminated vegetation. Two sets of exposure scenarios are provided: one for the consumption of contaminated fruit and the other for the consumption of contaminated vegetation. These scenarios are detailed in Worksheets D03a and D03b for acute exposure and in Worksheets D04a and D04b for chronic exposure.

The concentration of the pesticide on contaminated fruit and vegetation is estimated using the empirical relationships between application rate and concentration on different types of vegetation (Fletcher et al. 1994). While the human health risk assessment conducted by the U.S. EPA/OPP (2007a,c) does not consider this exposure scenario, the use of the residue rates recommended by Fletcher et al. (1994) both here and in the ecological risk assessment (Section 4.2) is identical to the approach used by U.S. EPA/OPP in their ecological risk assessment of carbaryl (U.S. EPA/OPP-EFED 2003d).

For chronic exposures, both initial concentrations and a half-life on vegetation are required to estimate the time-weighted average exposure (Worksheet D04a and D04b). As in the GLEAMS modeling, a foliar half-time of 3.71 days is used. As noted in Table 6, this value is an upper 90% confidence bound on the mean from 30 studies from which a foliar half-life could be estimated (U.S. EPA/OPP 2003d, p. 64).

3.3. DOSE-RESPONSE ASSESSMENT

3.3.1. Overview

While the hazard identification for carbaryl is somewhat complex, the dose-response assessment for systemic toxicity is relatively simple. The recent U.S. EPA risk assessment derives an acute RfD of 0.01 mg/kg bw/day based on neurotoxicity. Because of the rapid reversibility of AChE inhibition, the EPA does not derive a chronic RfD. For the current Forest Service risk assessments, the acute RfD of 0.01 mg/kg bw is used to characterize risks associated with both acute and chronic exposure. The primary reservation with this approach concerns the effects of carbaryl on immune function. While there is little doubt that carbaryl can cause changes, including inhibition, in immune function, most studies suggest that neurotoxicity is the critical effect and that changes in immune function are most likely to occur at doses above the threshold for neurotoxicity.

The U.S. EPA has determined that carbaryl is a likely human carcinogen and derived a cancer potency factor for carbaryl. This cancer potency factor is used in the current risk assessment to derive a dose of 0.02774 mg/kg bw/day which is associated with a risk level of one in one-million.

Because many of the hazard quotients discussed in the risk characterization exceed a value of one by a substantial margin, dose-severity relationships for carbaryl are considered. Hazard quotients of up to 10 might not be associated with detectable or clinically significant adverse effects. It is likely that hazard quotients between 10 and 20 would be associated with adverse effects on the kidneys althought it does not appear that overt signs of toxicity would be apparent. The poentail effects associated with hazard quotients between 20 and about 250 cannot be well-characterized. Single oral doses corresponding to hazard quotients of 50, 100, and 200 have not been associated with signs or symptions of toxicity in humans. Hazard quotients in the range of about 250 to 500 could be associated with overt signs and symptoms of cholinesterase inhibition – i.e., salivation, lacrimation, sweating, contraction of the pupil, increased peristalsis with abdominal pain, and muscular fasciculation (twitching). Without medical attention, it is possible that these exposures could also involve effects such as decreased heart rate, decreased blood pressure, increased respiratory rate, and involuntary urination and defecation, and convulsions. As hazard quotients increase above 500, concern for lethality would increase. Death due to the suicidal ingestion of carbaryl has been demonstrated at a dose of about 5,700 mg/kg bw. This death occurred despite emergency medical treatment. It is plausible that much lower doses, perhaps as low as 100 mg/kg bw (corresponding to a hazard quotient of 10,000), could present a risk of death in the absence of medical intervention.

3.3.2. Acute RfD

Forest Service risk assessments generally adopt oral RfDs derived by the U.S. EPA unless there is a compelling basis for doing otherwise. The toxicity values recommended by the U.S. EPA in their most recent risk assessment of carbaryl (U.S. EPA/OPP 2007a) are summarized in Table 15. As indicated in Table 15 the U.S. EPA specifies several types of risk values for different

routes and durations of exposure. For some compounds, different values may be used in each of these classifications. This, however, is not the case with carbaryl, and only two risk values are derived: an oral RfD of 0.01 mg/kg/day and a dermal dose of 86 mg/kg/day with a margin of exposure of 100 for adults and 180 for children.

Many RfD values derived by the U.S. EPA are based on an experimental NOAEL divided by an uncertainty factor. In Forest Service pesticide risk assessments, the same approach is taken for most toxicity values adopted from the U.S. EPA. For carbaryl, the U.S. EPA used a different approach involving benchmark dose analysis (U.S. EPA/ORD 2000). As discussed in SERA (2007a, Section 3.3.4), benchmark dose analysis involves fitting dose-response data to a mathematical model and estimating the lower limit of a dose associated with a fixed response rate (most often an ED_{10}). In Table 15, this value is abbreviated as the $BMDL_{10}$ and this value is used as a replacement for the NOAEL. In the nomenclature of the benchmark dose method, this surrogate NOAEL is called a *point of departure*.

The acute RfD for carbaryl is also somewhat atypical in that the toxicity value is not based on a registrant submitted study. Instead, the U.S. EPA/OPP collaborated with the National Health and Environmental Effects Research Laboratory (NHEERL) of the U.S. EPA and conducted a study on AChE inhibition in rats in which the animals were dosed by gavage at 3, 7.5, 15, or 30 mg/kg bw/day (U.S. EPA/OPP 2007f). In order to assess the sensitivity of young animals to carbaryl relative to adults, the study involved three groups of rats: adults, 11-day old rats, and 17-day old rats. The toxicity value of 1.1 mg/kg/day is based on the benchmark dose analysis of brain AChE inhibition in 11-day-old rats (U.S. EPA/OPP 2007f, p. 6).

As indicated in Table 15, the U.S. EPA derives an explicit RfD only for acute dietary exposures. For incidental oral exposures, the EPA uses the $BMDL_{10}$ with a margin of exposure (MOE) of 100. As discussed in SERA (2007a, Section 3.3.3), this is again an issue of nomenclature concerning the way that the EPA presents risk characterization. In terms of the current Forest Service risk assessment, using a $BMDL_{10}$ of 1.1 mg/kg/day with a MOE of 100 is equivalent to using an acute RfD of 0.01 – i.e., 1.1 mg/kg/day divided by the MOE and rounded to one significant place.

For dermal exposures, the U.S. EPA uses a $BMDL_{10}$ of 86 mg/kg/day with a MOE of100 for adults and a MOE of 180 for children. This approach reflects the different methods used by the U.S. EPA and Forest Service. The U.S. EPA sometimes uses dermal toxicity studies to derive dermal toxicity values. Then, in the risk characterization, the U.S. EPA calculates hazard quotients by dividing dermal exposure levels by the dermal toxicity value. Generally, Forest Service risk assessments use only the oral RfD. Then, to derive hazard quotients, the dermal exposure level is multiplied by a dermal absorption rate to derive an equivalent oral dose. This approach is taken in Forest Service risk assessments because it typically leads to more conservative and protective risk quotients, as is the case for carbaryl. Taking the dermal $BMDL_{10}$ of 86 mg/kg/day and dividing by the highest MOE (180) leads to a dose of 0.4777 mg/kg/day. Taking this number and multiplying by the dermal absorption rate of 0.127 day^{-1} (the value used in both this Forest Service risk assessment and the value recommended by EPA) leads to a dose of about 0.06 mg/kg bw/day, a factor of 6 greater than the acute oral RfD. Thus,

for the current Forest Service risk assessment, only the acute oral RfD of 0.01 mg/kg bw/day is used.

While most studies indicate that the prevention of neurotoxic effects will be protective of the many other effects that carbaryl can induce (Section 3.1), the $BMDL_{10}$/NOAEL of 1.1 mg/kg/day is very close to the dose of 2 mg/kg bw/day for 2 weeks that caused a decrease in splenocytes in rats (Dong et al. 1998). The U.S. EPA risk assessments (U.S. EPA/OPP 2007a,d) do not address the issue of potential effects of carbaryl on immune function. This omission is particularly regrettable because the Dong et al. (1998) study was a collaborative effort between the Immunotoxicology Branch of the U.S. EPA and investigators at University of North Carolina. By definition of the benchmark dose approach, a dose of 2 mg/kg/day would be associated with greater than 10% inhibition of brain cholinesterase – i.e., 2 mg/kg/day is about twice the $BMDL_{10}$. In this respect, a case can be made for asserting that the immune effect is documented only at doses above the $BMDL_{10}$. On the other hand, the dose-response relationship for splenocyte proliferation noted by Dong et al. (1998, Figure 3, p. 66) does not evidence a threshold, and a NOEL for this endpoint is not identified in the study.

While the study by Dong et al. (1998) does provide an indication that carbaryl has the ability to impact immune function, the study does not provide a quantitative basis for asserting that carbaryl is likely to cause adverse effects – e.g., increase susceptibility to infections – at sub-neurotoxic doses. Consequently, this Forest Service risk assessment does not consider immunosuppression quantitatively.

3.3.3. Chronic RfD

As indicated in Table 15, the U.S. EPA/OPP (2007a) does not quantitatively consider longer-term exposures to carbaryl: *Due to the rapid recovery of ChE activity, the acute exposure from carbaryl is the main duration of concern and therefore a chronic assessment is not appropriate for carbaryl*.

As discussed in Section 3.1, the rapid recovery AChE activity is well-documented (Section 3.1.2) and carbaryl will not accumulate substantially in the body as the duration of exposure increases (Section 3.1.3.3). Thus, the approach taken by the U.S. EPA is reasonable. Nonetheless, as detailed in Section 3.2 (Exposure Assessment), longer-term exposures will occur, and the potential risks associated with these exposures are considered quantitatively in this risk assessment. In assessing longer-term exposures, however, there is no basis for developing a chronic RfD. The rationale for this argument is identical to EPA's rationale in considering longer-term exposures.

While the U.S. EPA/OPP has not derived a chronic RfD for carbaryl, the U.S. EPA's Integrated Risk Information System (IRIS) does list a chronic RfD for carbaryl of 0.1 mg/kg bw/day. IRIS RfDs are derived by the U.S. EPA's National Center for Environmental Assessment (NCEA), which is part of the Agency's Offices of Research and Development. These RfDs are intended to represent Agency-wide values but it is not uncommon for the Office of Pesticide Programs (OPP) to derived alternative RfDs. The IRIS RfD is based on a two year feeding study in rats

(Carpenter et al. 1961) in which no adverse effects were noted at a dietary concentration 200 ppm. At 400 ppm, cloudy swelling of the hepatic cords and renal tubules were noted. Based on measured food consumption and body weights, the 200 ppm NOAEL corresponded to a dose of 9.6 mg/kg bw/day and the 400 ppm LOAEL corresponded to a dose of 15.6 mg/kg bw/day. The IRIS RfD was derived and last reviewed in 1987 and last updated in 2002.

It is the general practice of Forest Service risk assessments to defer to the U.S. EPA in the derivation of RfDs. When different parts of the Agency have different RfDs, Forest Service risk assessments will generally adopt the lowest RfD. It is not sensible to adopt the chronic RfD of 0.1 mg/kg bw/day from ORD and use the ten-fold lower RfD of 0.01 mg/kg bw/day from OPP. Consequently, the acute RfD of 0.01 mg/kg bw/day derived by the U.S. EPA/OPP (2007a) is adopted directly for the assessment of risks associated with longer-term exposures. Nonetheless, the higher RfD of 0.1 mg/kg bw/day from U.S. EPA/ORD is considered further in the assessment of dose-severity relathionships (Section 3.3.5).

3.3.4. Carcinogenicity

As discussed in Section 3.1.10, the U.S. EPA has determined that carbaryl is a likely human carcinogen based an increase in malignant tumors in mice and rats. Based a 2-year feeding study in mice in which an increase was noted in hemangiosarcomas, the U.S. EPA (1997) derived a cancer slope factor, referred to as a Q_1^* of 8.75×10^{-4} $(mg/kg/day)^{-1}$ for lifetime exposures.

Cancer risk over a lifetime (P) is calculated as the product of the daily dose (d) over a lifetime and the potency parameter (Q_1^*):

$$P = d\, Q_1^*$$

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

$$d = P \div Q_1^*$$

Thus, the lifetime daily dose of carbaryl associated with a risk of one in one-million (1÷1,000,000 or 0.000001) is 0.00114 mg/kg/day:

$$d_{(mg/kg/day)} = 0.000001 \div (8.75 \times 10^{-4}\ (mg/kg/day)^{-1}).$$

Using the nomenclature of the U.S. EPA (U.S. EPA/OPP 2007c), the dose of 0.00114 mg/kg/day would be the average daily dose (ADD) that would be associated with a risk level of 1 in one-million. As summarized in Section 3.2, many of the exposure assessments used in this risk assessment involve much shorter periods of time. For these shorter-term exposures, cancer risk is not quantified.

For the longer-terms exposures, the ADD is further adjusted to reflect the fact that none of the longer-term exposures are anticipated to occur over the full lifespan of the individual. Thus, the

dose is adjusted upward to account for the fraction of the individuals lifespan over which the exposures will occur. Again using the nomenclature of the U.S. EPA, this adjusted dose will be referred to as the Lifetime Average Daily Dose (LADD). U.S. EPA/OPP (2007c, p. 56) makes two sets of adjustments: 10 use events per year for private growers and 30 events per year for commercial growers. For the current risk assessment, only the more conservative 30 events per approach is used. Thus, the dose of 0.00114 mg/kg/day is adjusted to 0.01387 mg/kg bw/day [0.00114 mg/kg/day x 365 day per year / 30 day of exposure per year]. In other words, for an individual to receive a dose equal to an average of 0.00114 mg/kg/day from 30 exposures over the course of a year, the dose per event would have to be equal to 0.01387 mg/kg bw.

Finally, U.S. EPA/OPP (2007c, p. 56) assumes that occupational exposures will occur only over a period of a 35 year career over a 70 year lifespan and the dose of 0.01387 mg/kg bw is adjusted further to 0.02774 mg/kg bw/day [0.01387 mg/kg bw/day x 70 years / 35 year]. Thus, the dose of 0.02774 mg/kg bw/day is used in the worksheets to characterize cancer risks of 1 in one-million.

While the dose of 0.02774 mg/kg bw/day is derived from the assumptions made by the U.S. EPA for workers, the value is applied to both workers and members of the general public. As discussed in Section 3.2.3.1.2, the Forest Service will designate treated areas with warning messages. Consequently, the probability that a member of the general public would consume contaminated vegetation or fruit over a prolonged period of time is remote. As detailed further in Section 3.4.2, the consumption of contaminated vegetation is the only longer-term exposure scenario that approaches or exceeds a level of concern for members of the general public. The more plausible longer-term exposures that are associated with the longer-term consumption of contaminated water or fish are below the level of concern for carcinogenicity by factors of 500 to about 150,000. Consequently, the adjusted dose of 0.02774 mg/kg bw/day has no impact on the interpretation of risk for these scenarios.

3.3.5. Dose-Severity Relationships

As summarized in the exposure assessment (Section 3.2), there is substantial uncertainty in the estimates of exposure doses and absorbed doses for workers and the general public. Particularly for members of the general public, there is also substantial uncertainty concerning the likelihood that many of the exposure scenarios will or could occur. Nonetheless, and as detailed further in Section 3.4 (Risk Characterization for human health effects), many of the standard exposure scenarios used in Forest Service risk assessments for both workers and members of the general public exceed the RfD of 0.01 mg/kg bw/day by substantial margins. Thus, some effort must be made to characterize the health consequences of such exposures.

There is particular concern in the derivation and interpretation of dose-severity relationships for carbaryl because the RfD for carbaryl is based on the inhibition of AChE activity in the brain. The inhibition of brain AChE as well as the inhibition of AChE in the peripheral nervous system may lead to subtle effects on behavior or responsiveness that are difficult to assess or detect in humans but which could have serious consequences in terms of the capability of the individual to react to events. Consequently, the consideration of dose-severity relationships for carbaryl

should be used primarily to assess the likelihood that particular exposures might be associated with overt signs of toxicity. The dose-severity relationships themselves, however, should not be viewed as suggesting that exposure levels above the RfD are acceptable or should be tolerated.

Conversely, RfD values are intended to be conservative estimates of acceptable doses that incorporate a large number of conservative assumptions. The RfD does not represent a clear demarcation between doses that are safe and doses that will cause adverse effects. For many compounds, it is clear that exposure levels above and sometimes substantially above the RfD might not be associated with any signs of overt or clinically significant toxicity.

Numerous toxicity studies are available in experimental mammals, and these studies could be used in developing dose-severity relationships for carbaryl. This approach is avoided in the current risk assessment because of uncertainties in using dose-severity relationships from animal toxicity studies to assess responses in humans and difficulties in comparing studies conducted over a wide period of time with different experimental protocols.

As an alternative to the reliance on experimental studies in mammals, the available information on dose-severity relationships in humans is used as the primary basis for assessing the consequences of exposure levels that exceed the RfD. The information considered includes an occupational exposure study (Best and Murray 1962), a suicidal ingestion of carbaryl (Farago 1969), and two toxicity studies involving controlled human exposures to carbaryl (Hayes 1982; Wills et al. 1968. Summaries of the studies by Best and Murray (1962), Hayes (1982) and Farago (1969) are taken from the review by Cranmer (1986), and the study by Wills et al. (1968) was provided by the U.S. EPA via FOIA.

These studies in humans are limited in that they involve small numbers of individuals and noninvasive observations, except for the determination of plasma cholinesterase inhibition. Nonetheless, these studies are useful in characterizing the consequences of human exposures to doses above the RfD of 0.01 mg/kg bw/day. This information on dose-severity relationships in humans is supplemented by the RfD values proposed by U.S. EPA/OPP (2007a) and U.S. EPA/ORD (2002). Lastly, reported LD_{50} values in two species of mammals are taken from WHO (1994). These studies are used only to elaborate on the approximate lethal dose in humans.

The dose-severity relationships proposed for the current risk assessment are summarized in Table 16. This tables gives the human dose in the first column, the corresponding hazard quotient in the second column, a verbal description of the effect in the third column, and the reference in the fourth column. All hazard quotients are based on the RfD of 0.01 mg/kg bw/day derived by the U.S. EPA's Office of Pesticide Programs (OPP) (U.S. EPA/OPP 2007a). While this is not a human dose in the sense that it has or can be verified experimentally, the RfD is interpreted as a dose at or below which no adverse effects would be expected in humans.

As discussed in Section 3.3.3, different groups within the U.S. EPA derived two RfD values for carbaryl, the RfD of 0.01 mg/kg bw/day from the Office of Pesticide Programs (U.S. EPA/OPP

2007a) and the 10-fold higher RfD of 0.1 mg/kg bw/day from the U.S. EPA's Office of Research and Development (U.S. EPA/ORD 2002). Thus, a dose of 0.1 mg/kg bw/day could also be considered a dose at which no adverse effects would be expected. This illustrates the point made above that the RfD is a judgmental estimate of an acceptable dose but is not a clear delimiter for signs of expected toxicity.

It is regrettable that EPA/OPP (2007a) does not discuss the previous RfD or dose-severity relationships for carbaryl. Implicit in the EPA/OPP (2007a) analysis, however, is the determination the newer toxicity data available on carbaryl combined with the use of the benchmark dose method provides a superior basis for assessing an acceptable level of exposure to carbaryl. As detailed further below, the consideration of dose-severity relationships in this current Forest Service risk assessment supports the assessment of EPA/OPP (2007a).

As indicated in Table 16, the study by Wills et al. (1968) indicates that a dose of 0.06 mg/kg bw/day administered for 6 weeks was associated with a slight decrease in plasma cholinesterase in five individuals and symptoms of abdominal cramps and neck pain in one individual. The slight decrease in plasma cholinesterase in the absence of other effects should be regarded as little more than an indicator of exposure and rather than a sign of toxicity (e.g., ATSDR 1993; Wills 1972). As discussed by Wills et al. (1968), slight decreases in plasma cholinesterase were also observed in the control group; furthermore, signs of toxicity were more pronounced in the control group (2 of 5 individuals) than in the 0.06 mg/kg bw/day dose group (1 of 5 individuals). Thus, the dose of 0.06 mg/kg bw/day from the study by Wills et al. (1968) does not provide a basis for asserting that adverse effects in humans would be observed at doses corresponding to a hazard quotient of up to 6. This assessment is consistent with the RfD derived by U.S. EPA/ORD (2002) suggesting that a dose of 0.1 mg/kg bw/day, corresponding to a hazard quotient of 10, would not be associated with adverse effects in humans.

At a slightly higher dose of 0.12 mg/kg bw/day for 6 weeks, however, Wills et al. (1968) noted an increase in the ratio of the concentration of amino acid nitrogen to that of creatinine in urine (see Wills et al. 1968, p. 269, Figure 2). This effect was not observed at the dose of 0.06 mg/kg bw/day. The increase in this ratio is an indication of the impairment of the proximal tubules of the kidney to reabsorb amino acids. This is the only effect that Wills et al. (1968) unequivocally associate with carbaryl exposures. Wills et al. (1968) also report that epigastric cramps were observed in 2 of 6 individuals and difficulty sleeping was reported in 1 of 6 individuals. Wills et al. (1968) note that both of these symptoms … *would be recognized as more or less typical effects of cholinesterase inhibitors* (Wills et al., 1968, p. 267) but state that these effects could not be directly attributed to carbaryl. The dose of 0.12 mg/kg bw/day, corresponding to a hazard quotient of 12, is very close to the RfD of 0.1 mg/kg bw/day from U.S. EPA/ORD (2002). Based on the Wills et al. (1968) study, effects on kidney function are plausible and the possibility of mild signs of toxicity cannot ruled out at a hazard quotient of 12.

Concern for the observations by Wills et al. (1968) at the dose of 0.12 mg/kg bw/day is supported by the study used by U.S. EPA/ORD (2002) to derive the RfD of 0.1 mg/kg bw/day. As summarized in Section 3.1.5, this higher RfD is based on the study by Carpenter et al. (1961)

in which the NOAEL in rats was 9.6 mg/kg bw/day and the LOAEL based on liver and kidney pathology was 15.6 mg/kg bw/day. These two doses are very closely spaced, differing by only a factor of about 1.6. This very small difference in dose is a concern in terms of the protection afforded by the ORD RfD of 0.1 mg/kg bw/day. Dividing the LOAEL in rats by the uncertainty factor of 100, the resulting estimated human LOAEL is 0.156 mg/kg bw/day, which is very close to the observed LOAEL in humans of 0.12 mg/kg bw/day from the study by Wills et al. (1968). The association between the animal and human LOAEL is strengthened by the fact that both the Wills et al. (1968) study in humans as well as the Carpenter et al. (1961) study in rats note adverse effects on the kidney.

In a preliminary phase of study by Wills et al. (1968), two individuals each had been given single oral doses of 0.5, 1.0, or 2.0 mg/kg bw. No effects were noted based on plasma cholinesterase inhibition as well as signs or symptoms of toxicity. These doses would correspond to hazard quotients of 50, 100, and 200.

The study by Best and Murray (1962), which is also summarized in Table 16, involves a worker exposure study in which the estimated dose of 0.55 mg/kg bw/day is based on estimates of 1-naphthol excretion in the urine. This study might be interpreted as suggesting that a dose of 0.55 mg/kg bw/day, corresponding to an HQ of 55, might not be associated with adverse effects. While this possibility cannot be unequivocally excluded, the occupational study by Best and Murray (1962) was conducted under far less controlled conditions than the study by Wills et al. (1968), and the dose-estimate of 0.55 mg/kg bw/day is questionable. Further considering the LOAEL from the study by Carpenter et al. (1961), the summary of the Best and Murray (1962) study given by Cranmer (1986) is included in Table 16 only for the sake of completeness. The reported human NOAEL of 0.55 mg/kg bw/day, however, is not used in the current Forest Service risk assessment as part of the dose-severity assessment for carbaryl.

The study reported by Hayes (1982) involves only two individuals but can be used to define single-dose oral exposures that would be regarded as clearly hazardous. As summarized in Table 16, single oral doses of 2.8 and 5.45 mg/kg bw resulted in overt signs of toxicity – i.e., nausea, abdominal pain, sweating, lightheadedness, and weakness. Each of the two individuals in the study reported by Hayes (1982) received medical treatments (atropine injections). In other words, the severity of the effects were sufficient to warrant medical attention. As indicated in Table 16, the doses in the study by Hayes (1982) are associated with hazard quotients of 280 and 545.

As discussed in Section 3.4 (Risk Characterization), some hazard quotients for accidental exposure scenarios exceed 1000 and approach 10,000. In some respects, there is little need to elaborate on dose-severity relationships of this magnitude. These exposures are clearly unacceptable. In addition, there is very little data in humans that can be used to assess the consequences of such exposures. The report by Farago (1969) involves an intentional and suicidal ingestion of carbaryl. The dose is characterized as the ingestion of 500 ml of an 80% solution of carbaryl. As indicated in Table 2, none of the liquid formulations considered in this risk assessment consist of 80% w/w solutions and the specific formulation ingested by the

individual in the Farago (1969) report is not further characterized. Assuming a body weight of 70 kg, the dose ingested by the individual is estimated at about 5700 mg/kg bw [500 ml x 0.8 x 1000 mg/ml / 70 kg = 5714 mg/kg bw]. This dose would correspond to an HQ of 570,000. Death occurred in this individual despite emergency medical treatment.

The lethal dose of 5700 mg/kg bw is based on only one individual who received medical attention, and it would not be prudent to view this dose as the approximate lethal dose for humans. The approximate lethal dose for humans could be and probably is lower and perhaps much lower. No additional human data have been identified that can be used to further refine the estimate of a human dose that might be associated with a significant risk of lethality. As summarized in Table 16, the lowest reported LD_{50} value in mammals is the value of 90 mg/kg bw for sheep (WHO 1994). The LD_{50} value for monkeys is substantially higher, 1000 mg/kg bw (WHO 1994). It is plausible that the LD_{50} value for monkeys would be a better indicator of toxic potency in humans than an LD_{50} value for sheep. However, an LD_{50} value is of limited use in characterizing risk because of the severity of the endpoint (mortality) and the incidence of the endpoint (half of the population). For the current Forest Service risk assessment, 100 mg/kg bw, corresponding to a hazard quotient of 10,000 is used as an estimate of a dose that might be lethal to humans – i.e., an exposure that would raise significant concern that death could occur in the absence of prompt medical treatment.

3.4. RISK CHARACTERIZATION

3.4.1. Overview

Although carbaryl is more toxic to insects than to mammals, including humans, carbaryl effectively inhibits enzyme activity essential to the regulation of the human nervous system – i.e., AChE activity. Consequently exposure to carbaryl is potentially hazardous to workers as well as members of the general public.

Virtually all accidental exposure scenarios for workers and members of the general public lead to hazard quotients that are clearly unacceptable. Hazard quotients for accidental exposures exceed 7000 for workers and 9000 for members of the general public. By definition, all of the accidental exposure scenarios should be regarded as extreme. In addition, all of the accidental exposure scenarios are highly implausible because members of the general public are excluded from treated areas during and immediately after application. Nonetheless, these implausible scenarios are used consistently in Forest Service risk assessments to identify which types of accidental exposures may present a risk that exceeds the level of concern. For carbaryl, all of the accidental exposures fall into this category and the exclusion of members of the general public from the treated area during application is a prudent and necessary practice.

Because of the different methods used to assess exposures associated with carbaryl applications for leaf beetle control and bark beetle prevention, the risk characterizations of non-accidental exposures for the two uses are interpreted differently. Broadcast applications for leaf beetle control are relatively standard, and interpreting the resulting hazard quotients is relatively simple. Applications for bark beetle prevention, however, are based on unit exposure assumptions – i.e., the application to a single high-value tree of a fixed size. Consequently, the hazard quotients for bark beetle applications are relative, and the risk characterization for bark beetle applications has to be assessed at the program level, once the details of the application can be specified – i.e., the number and size of the trees to be treated and the area over which the treatments will be applied.

Under general conditions of exposure anticipated in Forest Service programs, workers can apply carbaryl in a manner that will not lead to any significant toxic effect, so long as care is exercised to minimize exposure. If, however, care is not exercised, the level of exposure is likely to exceed the level of concern at all but the lowest application rate. At the typical application rate for leaf beetle control, hazard quotients for systemic toxicity range from 6 to 11 at the upper bound of exposures. At the highest anticipated application rates, the corresponding hazard quotients range from 8 to 15.

For members of the general public, many of the hazard quotients associated with acute non-accidental exposures are greater in magnitude than those for workers. The greatest hazards are associated with the consumption of contaminated vegetation (HQ values up to 135) and swimming in contaminated surface water (HQ values up to 62). For longer-term exposures, the hazard quotients are lower, and the level of concern – i.e., an HQ greater than 1 – is exceeded only for those exposures associated with the consumption of contaminated vegetation.

3.4.2. Workers

Quantitative summaries of the risk characterization for workers associated with exposure to carbaryl is presented in Attachment 1 for leaf beetle control and Attachment 2 for bark beetle prevention. For leaf beetle control (Attachment 1), risk characterization summary worksheets are provided for the range of application rates considered in this risk assessment – i.e., 0.1 to 1 lb a.i./acre with a typical application rate of 0.75 lb a.i./acre. Risk characterization worksheets for systemic toxicity are given in the E02a Series of worksheets: E02a1 (typical rate), E02a2 (lowest anticipated application rate) and E02a3 (highest aniticipated application rate). Risk characterization worksheets for carcinogenicity are given in the E02b Series of worksheets: E02b1 (typical rate), E02b2 (lowest anticipated application rate) and E02b3 (highest aniticipated application rate). As discussed in Section 2.4.2, applications for bark beetle prevention are based on a standard unit application to a single high value tree. Thus, Attachment 2 contains only a single risk characterization worksheet for systemic toxicity (Worksheet E02a) and a single risk characterization worksheet for carcinogenicity (Worksheet E02b). In both Attachment 1 and Attachment 2, all hazard quotients for systemic toxicity are based on the RfD of 0.01 mg/kg bw/day (Section 3.3.2) and all hazard quotients for carcinogenicity are based on a dose of 0.02774 mg/kg bw/day which is associated with a cancer risk of 1 in ono-million.

As detailed in the exposure assessment (Section 3.2), the exposures and consequent risk characterization for workers exposed to carbaryl applications associated with leaf beetle control (Attachment 1) are relatively standard – i.e., the exposures and consequent risks are based on estimates of exposure, given the application rates likely to be used in Forest Service programs. This is not the case for workers involved in bark beetle prevention programs where the estimates of exposure and consequent risk are based on a unit application to a single tree. Consequently, carbaryl exposures associated with leaf beetle control are the focus of the risk characterization. Assessments for bark beetle prevention are best made at the project level, once the extent of the application is defined in Worksheet A01 (Attachment 2).

The risk quotients associated with accidental exposures – i.e., wearing contaminated gloves or spilling a carbaryl solution on the hands or lower legs – lead to hazard quotients that are much higher than those associated with the general levels of exposure anticipated for routine applications of carbaryl. Even at the lowest application rate, 0.1 lb a.i./acre, all of the accidental exposure scenarios reach or exceed an HQ of 1.0, the level of concern in Forest Service risk assessments, based on the central estimates of exposure (Worksheet C02a2). Of the two types of exposures – i.e., wearing contaminated gloves and spills on to the hands or legs – wearing contaminated gloves results in much higher HQ values ranging from an HQ of 3 (the lower bound for wearing contaminated gloves for 1 minute) to 7700 (the upper bound for wearing contaminated gloves for 1 hour).

Some of the accidental exposure scenarios lead to hazard quotients that approach a level of concern for effects that would require prompt medical attention and for which there would be plausible concern for potentially lethal effects (Section 3.3.5). This assessment is consistent with warning statements on the product labels concerning the effects of over-exposure:

IN SEVERE CASES [of over-exposure] *CONVULSION, UNCONSCIOUSNESS AND RESPIRATORY FAILURE MAY OCCUR. SIGNS AND SYMPTOMS OCCUR RAPIDLY FOLLOWING OVEREXPOSURE TO THIS PRODUCT.*

All of the accidental exposure scenarios for workers are impacted by uncertainties in the rates of dermal absorption. As noted in Section 3.1.3.2 (Dermal Absorption), the first-order dermal absorption rate is taken from U.S. EPA/OPP (2003e). This rate is about a factor of higher than the rate that would be estimated from the chemical properties of carbaryl (Worksheet B06 in Attachments 1 and 2). Because of this, the estimate of the zero-order absorption used in the accidental scenarios is also increased by a factor of 10 from the estimate based on chemical properties (Worksheet B05 in Attachments 1 and 2). Nonetheless, the hazard quotients for accidental worker exposures would still be substantially above the RfD if the lower estimates of the dermal absorption rate were used.

The hazard quotients for general exposures are much lower. As discussed in Section 3.2.2.1, the term *general exposures* refers to the levels of exposure during the normal application of carbaryl for the three general types of application methods that are considered – i.e., backpack, ground spray, and aerial spray. All three types of applications are considered in the workbook for leaf beetle control (Attachment 1).

None of the general application methods correspond directly to the direct spray of carbaryl onto tree bark. Nonetheless, as detailed in Section 3.2.2.1, exposure rates for backpack applications are used as surrogates for tree bark applications based on the study of worker exposure in bark applications by Haverty et al. (1983). There is uncertainty in the use of the standard backpack applications in terms of the efficiency of protective clothing. If proper protective clothing and proper care in application methods are not used, worker exposures could be higher than those estimated in this risk assessment. In addition, all of the hazard quotients for bark beetle applications are based on a unit application – i.e., a single tree. The hazard quotients presented in Attachment II will need to be adjusted at the program level based on the number and size of the trees that a worker would treat.

The risk characterization for systemic toxicity in general exposures is highly dependant on the variability in the underlying exposure rates. At the lower bound of the exposure rates, none of the HQ values for systemic toxic effects exceed the level of concern even at the highest proposed application rate – i.e., the highest HQ is 0.07 (Worksheet E02a3). At the upper bound of the exposure rates, the HQ values approach or exceed the level of concern, even at the lowest application rate (HQ values range from 0.8 to 1.5) (Worksheet E02a2). At the highest application rate (Worksheet E02a3), the exceedances are substantial at the upper bound of the exposure rates (HQ values range from 8 to15) but marginal at the central estimate of exposure (HQ values range from 1.3 to 2).

The hazard quotients for carcinogenicity are lower than the hazard quotients for systemic toxicity by a factor of about 2.8. This relationship follows from the RfD of 0.01 mg/kg bw/day, relative

to the dose associated with a 1 in one-million risk of cancer, 0.02774 mg/kg bw/day. Qualitatively, this leads to a similar risk characterization. At the lower bound and central estimates of exposure, the HQ values for carcinogenicity are below the level of concern over the range of application rates that might be used in Forest Service programs. At the upper bound of exposure, the HQ values are below the level of concern only at the lowest application rate. At application rates of 0.75 and 1 lb a.i./acre, the upper bound of the HQ values range from 2 to 5.

The quantitative risk characterization for workers in this risk assessment is generally consistent with the risk characterization for workers in U.S. EPA/OPP (2007c). The U.S. EPA uses a very different method for estimating worker exposure as well as for expressing risk (see SERA 2007a for details). In terms of quantifying risk, the U.S. EPA uses a margin of exposure (MOE) of 100. This corresponds to an HQ of 1 in the current Forest Service risk assessment. As the MOE decreases, the corresponding HQ increases. Thus, an MOE of 50 would correspond to an HQ of 2. The lowest MOE given in the EPA risk assessment is 36 and is associated with an application rate of 0.5 lb a.i./acre. Adjusting to an application rate of 1 lb a.i./acre, the EPA MOE corresponds to an HQ of about 5.5, which is only about a factor of 3 below the maximum HQ of 15 derived in the current risk assessment. It is not uncommon for Forest Service risk assessments to yield quantitative risk estimates that are somewhat higher risk than those in corresponding EPA assessments. The reason for the difference is the wide range of exposure rates incorporated into Forest Service risk assessments.

The basic explication of this quantitative risk characterization is that it is possible for workers to apply carbaryl in a manner that will not lead to significant toxic effects, so long as they exercise care to minimize exposure. If care is not exercised, however, the level of exposure is likely to exceed the level of concern at all but the lowest application rate. This explication is similar to the one provided in U.S. EPA/OPP (2003e, p. 104): *For the most part, current label requirements for personal protection (single layer clothing, gloves, and no respirator) appear to be generally inadequate for most scenarios except for operations where exposures are low and the amount of chemical used is also low.*

3.4.3. General Public

Quantitative summaries of the risk characterization for members of the general public associated with exposures to carbaryl are presented in EXCEL workbooks for leaf beetle control (Attachment 1) and bark beetle prevention (Attachment 2). As with the risk characterization for workers, the risk characterization for members of the general public exposed to carbaryl after applications for leaf beetle control (Attachment 1) is relatively standard; whereas, the risk characterization associated with exposure to carbaryl after applications for bark beetle prevention are based on a unit application to a single tree. Consequently, risk characterizations associated with bark beetle prevention should be made at the project level.

As with workers involved in applications for leaf beetle control, two sets of three worksheets per set are included in Attachment 1, one for systemic toxicity (Worksheets E04a1, E04a2, and E04a3) and the other for carcinogenicity (Worksheets E04b1, E04b2, and E04b3c). For leaf beetle control (Attachment 1), the three worksheets in each set are based on the typical

application rate of 0.75 lb a.i./acre (Worksheets E04a1, E04b1), the lowest anticipated application rate of 0.1 lb a.i./acre (Worksheets E04a2, E04b2), and the highest anticipated application rate of 1 lb a.i./acre (Worksheets E04a3, E04b3). For bark beetle prevention, the corresponding worksheets are based on the unit application as in the worker exposure estimates but also incorporate assumptions of the variable application efficiencies (Section 2.4.2): a central estimate of 80% with a range of 75-90%.

Also, as with workers, the risk quotients for systemic toxicity are based on the RfD of 0.01 mg/kg bw/day, and this toxicity value is applied to both acute and chronic exposure scenarios (Sections 3.3.2 and 3.3.3). The risk quotients for carcinogenicity are based on the dose of 0.02774 mg/kg bw/day. As discussed in Section 3.3.4, this is the adjusted dose associated with a cancer risk of 1 in one-million.

As discussed in Section 3.2.3.1.1. (Likelihood and Magnitude of Exposure), all exposure assessments used for members of the general public are based on the Most Exposed Individual (MEI). The consideration of the extreme value approach to characterizing risk is extremely important in interpreting the HQ values for members of the general public. The other important distinction involves the differences between accidental exposures – i.e., direct spray of a child or woman and the spill of carbaryl into a small pond – and the exposure levels anticipated in the normal course of carbaryl applications in Forest Service programs.

3.4.3.1. Accidental Exposures

In terms of accidental scenarios, the risk characterization for the general public is relatively simple. Across the range of application rates used in leaf beetle control and across the range of assumptions used in defining the extreme value exposures, almost all accidental exposure scenarios result in HQ values that exceed the level of concern by a substantial margin. At the lowest anticipated application rate (Attachment 1, Worksheet E04a2, the lower bound of the lowest HQ value associated with an accidental exposure scenario is 0.7. This HQ is associated with the direct spray of a young woman on the lower legs. The highest HQ value is greater than 9000 – i.e., the HQ associated with the upper bound exposure of a young child accidentally sprayed with a field solution of carbaryl. As discussed in Section 3.3.5, HQ values on the order of 9000 approach a level of concern for potentially lethal efeects and such exposures would require medical attention.

As with the risk characterization for accidental exposures in workers (Section 3.4.2), these hazard quotients are influenced by conservative assumptions in estimating dermal absorption rates. Nonetheless, many of the hazard quotients associated with accidental dermal exposures would remain substantially above a level of concern even if less conservative assumptions were used to estimate dermal absorption rates.

As detailed in Section 3.2.3.1.1, many of these accidental exposure scenarios can be viewed not only as extreme but also highly improbable. As required by the product labels, members of the general public will be excluded from the treated area. Unless the labeled directions are not

followed – i.e., a gross misapplication – all of the accidental exposure scenarios are not relevant to the interpretation of risks in well-conducted Forest Service programs.

These standard accidental exposure scenarios include in this risk assessment to illustrate the consequences of ignoring label restrictions on carbaryl applications and Forest Service practice after carbaryl applications – i.e., designating treated areas with cautionary notices. The inclusion of these scenarios is appropriate in order to distinguish the risks of carbaryl misapplications from risks associated with many herbicides that are used in Forest Service programs. For many of these herbicides, very extreme exposures result in no or very minor exceedances in the level of concern.

Carbaryl, however, is much more toxic than most herbicides to mammals. For carbaryl, accidental exposures should be regarded with a substantial level of concern, and aggressive efforts should be made to limit and/or mitigate any accidental exposure to members of the general public.

3.4.3.2. Acute Non-accidental Exposures

For leaf beetle control, acute non-accidental exposures are also a concern; however, the level of concern varies with the application rate. At the lowest application rate, 0.1 lb a.i./acre, exposure levels associated with the consumption of contaminated fruit and contaminated vegetation exceed the level of concern at the upper bound of exposure assumptions with HQ values of 1.9 and 14, respectively. At the upper bound of exposures, dermal contact with contaminated vegetation reaches, but does not exceed, the level of concern.

Hazard quotients are linearly related to the application rate. Thus, the HQ values for the highest anticipated application rate (1 lb a.i./acre) are a factor of 10 greater than the corresponding HQ values associated with the lowest anticipated application rate. At the highest application rate, exposures associated with the consumption of contaminated fruit (HQ values ranging from 1.2 to 19), the consumption of leafy vegetation (HQ values ranging from 3 to 135), dermal contact with contaminated vegetation (HQ values ranging from 5 to 10), and swimming in contaminated water (HQ values from ranging 1.8 to 62) exceed the level of concern across the range of exposure assumptions.

For broadcast applications involving leaf beetle control, the basic explication of the risk characterization is relatively simple. Based on the exposure assessment methods used in Forest Service risk assessments, broadcast applications for leaf beetle control are likely to result in exposures that would be considered unacceptable or imprudent if these applications are made in areas where members of the general public are likely to be exposed. If such applications are made, measures to limit exposures to members of the general public should be considered.

While the HQ values for applications associated with bark beetle prevention are not directly comparable to those for leaf beetle control, the patterns in the HQ values are similar based on the upper bound of exposure assumptions. The interpretation of these risk values, however, is not as straightforward. Leaf beetle applications are broadcast, and, if broadcast applications are made

over a large area, the effectiveness of mitigation measures may be limited. Bark beetle applications, however, are directed and most often limited to a much smaller area, making mitigation measures easier to implement.

As discussed in Section 3.2.3.1.1, exposures associated with the consumption of contaminated vegetation or fruit are implausible because the Forest Service will post cautionary notices in treated areas indicating that the area has been treated with a hazardous pesticide. Based on the current risk assessment, this cautionary practice to limit exposure is prudent and justified.

3.4.3.3. Longer-term Exposures

The longer-term exposure scenarios for carbaryl lead to HQ values that are substantially lower those associated with acute exposures. At the lower bound of the anticipated application rates for leaf beetle control, 0.1 lb a.i./acre, none of the longer-term risk quotients exceed a level of concern based on systemic toxicity (Worksheet C04a2) or carcinogenicity (Worksheet C04b2). At the typical application rate of 0.75 lb a.i./acre, the exposure scenario associated with the consumption of contaminated vegetation exceeds the level of concern at the upper bound of the exposure estimate for both systemic toxicity (an HQ of 6 in Worksheet C04a1) and carcinogenicity (an HQ of 2 in Worksheet C04b1). At the highest anticipated application rate of 1 lb a.i./acre, the exposure scenario associated with the consumption of contaminated vegetation approaches the level of concern (HQ of 0.96 in Worksheet C04a3) at the central estimate of exposure and exceeds the level of concern at the upper bound of the exposure estimate for both systemic toxicity (an HQ of 8 in Worksheet C04a3) and carcinogenicity (an HQ of 3 in Worksheet C04b3). In addition, the scenario for the consumption of contaminated fruit modestly exceeds the level of concern at the upper bound of the exposure estimate for systemic toxicity (HQ of 1.1 in Worksheet C04a3). None of the longer-term exposures associated with the contamination of surface water – i.e., the consumption of contaminated water or fish – exceed the level of concern.

The basic explication of the risk characterization for longer-term exposure scenarios is relatively simple. If broadcast applications of carbaryl are made in areas where members of the general public might consume contaminated vegetation over a prolonged period of time, the upper bound estimates of exposure would be considered unacceptable or imprudent. The contamination of ambient water is not a concern in longer-term exposures.

As with the risk characterization for acute exposures, the longer-term consumption of contaminated vegetation may be considered implausible because of the Forest Service will restrict access of the general public during and immediately after carbaryl applications. In addition, the Forest Service will place cautionary notices in treated areas indicating that a hazardous pesticide has been applied. Given these practices, it is very unlikely that individuals would consume contaminated vegetation.

3.4.4. Sensitive Subgroups

Under the Food Quality Protection Act (FQPA), the U.S. EPA is explicitly required to consider sensitive subgroups. As discussed in Section 3.3.2, the current Forest Service risk assessment

adopts the acute RfD from the U.S. EPA's most recent risk assessments (U.S. EPA/OPP 2007c), and the RfD is based on an explicit consideration of sensitive populations. Thus, at least in terms of neurotoxicity, sensitive subgroups are encompassed by the dose-response assessment.

As discussed in Section 3.1.7, however, there is a concern that carbaryl may have an adverse impact on immune function. Most studies on immune function suggest that the immune system is affected at doses above those associated with neurotoxicity. Nonetheless, the study by Dong et al. (1998) does demonstrate immune suppression in rodents at doses that are very close to the NOAEL for neurotoxicity. Consequently, there is a residual concern that individuals with immune disorders or otherwise compromised immune systems might belong to a group that is more sensitive than members of the general population to carbaryl exposures. This concern is increased particularly for exposure scenarios in which exposure levels substantially exceed the RfD.

3.4.5. Connected Actions

The U.S. EPA does not specifically address connected actions in their human health risk assessment of carbaryl (U.S. EPA/OPP 2007a,c). This is a very typical situation because pesticides are registered by the U.S. EPA under FIFRA (Federal Insecticide, Fungicide and Rodenticide Act) and considerations of connected actions are required under NEPA (National Environmental Policy Act).

The Council on Environmental Quality (CEQ), which provides the framework for implementing NEPA, defines connected actions (40 CFR 1508.25) as actions which occur in close association with the action of concern; in this case, the use of carbaryl as proposed in Section 2. Actions are considered to be connected if they: (i) automatically trigger other actions which may require environmental impact statements; (ii) cannot or will not proceed unless other actions are taken previously or simultaneously, and (iii) are interdependent parts of a larger action and depend on the larger action for their justification. Within the context of this assessment of carbaryl, "connected actions" include actions or the use of other chemicals which are necessary and occur *in close association* with use of carbaryl.

As discussed in Section 2 and summarized in Table 1, the carbaryl formulations used in Forest Service programs do not contain other pesticides. The use of inerts and adjuvants as well as the occurrence of impurities and metabolites would be classified as connected actions under the CEQ definition. As discussed in detail in Section 3.1.14 (Inerts and Adjuvants), the carbaryl formulations covered in this risk assessment do not contain inerts that are classified as hazardous. As discussed in Section 3.1.15, there is no basis for contending that carbaryl impurities or metabolites are likely to cause adverse effects of exposure that are not encompassed by the hazard quotients for humans discussed in Section 3.4.2 (workers) and Section 3.4.3 (general public).

3.4.6. Cumulative Effects

Cumulative effects may involve either repeated exposures to an individual agent or simultaneous exposures to the agent of concern (in this case carbaryl) and other agents that may cause the same effect or effects by the same or a similar mode of action.

Cumulative effects, within the context of the Food Quality Protection Act (FQPA), are addressed by the U.S. EPA (U.S. EPA/OPP 2007c):

> *Carbaryl is a member of the N-methyl carbamate class of pesticides. This class also includes carbofuran, aldicarb, methomyl and oxamyl among others. The N-methyl carbamates, as a group, have been determined to share a common mechanism of toxicity... The revised CRA* [Cumulative Risk Assessment] *is currently being developed and will be released during 2007. The results of this NMC cumulative assessment as well as the single chemical carbaryl assessment presented here will be considered during the carbaryl reregistration process in which decisions regarding establishing, modifying, or revoking carbaryl tolerances will be made.* (U.S. EPA/OPP 2007c, p. 49)

Within the context of Forest Service programs, the consideration of cumulative effects due to exposures to multiple chemicals should be assessed in the context of co-exposures to other carbamate insecticides and, more generally, to other insecticides that inhibit cholinesterase activity. These considerations will need to be made on a program specific and perhaps region specific basis. The general approach taken by the U.S. EPA is to assume that chemicals with common mechanisms of action will involve additive risks – i.e., the HQ values should be added for each chemical (Section 3.1.16).

In terms of repeated exposures, the current risk assessment does specifically consider the effect of repeated and longer-term exposures to carbaryl for both workers and members of the general public. Consequently, the risk characterizations presented in this risk assessment for longer-term exposures specifically address and encompass the potential impact of the cumulative effects of carbaryl due to repeated use.

4. ECOLOGICAL RISK ASSESSMENT

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

The endpoints of concern in the ecological risk assessment are similar to those discussed in the human health risk assessment – i.e., AChE inhibition. Vertebrates including mammals, birds, reptiles, amphibians, and fish may be adversely affected by exposure to carbaryl because of its well-characterized neurotoxicity. Although standard toxicity studies may demonstrate other toxicological endpoints, neurotoxicity is the critical effect on which the ecological risk assessment is based. For mammals, there is no apparent systematic relationship between toxicity and body size. For birds, however, there is a weak relationship between sensitivity and body size, suggesting that smaller birds may be more sensitive than larger birds. As with mammals, studies in fish indicate that neurotoxicity, although rapidly reversible, is the most sensitive endpoint. Thus, this risk assessment differs from most Forest Service risk assessments, in that sublethal neurotoxic effects, rather than longer-term reproductive effects, dominate the hazard identification for fish. Although the available studies on amphibians are far fewer than those on fish, they provide adequate evidence that certain amphibians (i.e., some species of salamanders) may be even more sensitive than some sensitive fish to the effects of carbaryl. The very limited amount of information on reptiles qualitatively suggests that their response to carbaryl exposure is like that of other vertebrates and that neurotoxicity is the endpoint of primary concern.

Terrestrial arthropods appear to be much more sensitive than vertebrates to carbaryl exposure. Based on the arthropod species tested in standard laboratory toxicity studies, the honey bee appears to be the most sensitive terrestrial arthropod. Nevertheless, some field studies suggest that carbaryl may have a substantial impact on ground spiders. It is unclear, however, whether the impact can be attributed to greater exposure levels, greater inherent susceptibility, or both. Standard toxicity studies on other terrestrial invertebrates are restricted to earthworms. These studies as well as more general field studies suggest that non-arthropod terrestrial invertebrates – i.e., worms and snails – are much less sensitive than arthropods to the effects of carbaryl exposure.

Like terrestrial arthropods, aquatic arthropods tend to be more sensitive than non-arthropod invertebrates and most aquatic vertebrates to the effects of carbaryl exposure. Sensitive amphibians are the exception. The open literature regarding the effects of carbaryl on the numerous species of aquatic invertebrates is diverse and in some instances very old. While most of the open literature is reasonably consistent with the data used by the U.S. EPA, one study suggests that dragonfly nymphs (*Brachythermis contaminata*) may be much more sensitive than other species to the effects of carbaryl exposure. Given, however that the study on dragonflies involves exposure to a poorly characterized formulation, the study on dragonflies is classified as an outlier and not otherwise used in the current risk assessment.

The direct effects of carbaryl on plants are not well or clearly documented. The available standard laboratory toxicity studies suggest that terrestrial plants are relatively tolerant. Nonetheless, incident reports cited by the U.S. EPA suggest that carbaryl may damage certain crops, particularly citrus. The available toxicity studies on aquatic plants suggest that algae are not highly sensitive to carbaryl. In fact, the major impact of carbaryl applications on aquatic plants might be the algal blooms secondary to adverse effects on the aquatic invertebrates that graze on the plants.

4.1.2. Toxicity to Terrestrial Organisms

4.1.2.1. Mammals

As summarized in the human health risk assessment (see Section 3.1), the data base on carbaryl toxicity to experimental mammals is extensive. These data are useful for assessing effects in nontarget terrestrial mammals covered in the ecological risk assessment. Moreover, these data support the assumption that carbaryl will inhibit AChE and induce neurological effects in all exposed nontarget mammalian species (see Section 3.1.6).

A major difference between the human health and ecological risk assessment, however, concerns the way in which these data are used. In the human health risk assessment, data on several mammalian species are used to assess risk in a single species (humans) with an emphasis on protecting the most sensitive individuals through the use of conservative methods and uncertainty factors. In the ecological risk assessment, the data on several mammalian species must be used to assess risk in numerous nontarget mammalian species. For this reason, patterns in species sensitivity can be useful in assessing how species-to-species extrapolations should be made.

For many chemicals, systematic or allometric relationships are apparent between body weight and toxicity (e.g., Boxenbaum and D'Souza 1990). For some chemicals, larger mammals are more sensitive than smaller mammals, and the opposite relationship is true for other chemicals. Several reviews, (CCME 1999a; Cranmer 1986; Mount and Oehme 1981; WHO 1994) on carbaryl demonstrate a weak allometric relationship among mammalian species, which suggests that larger mammals may be somewhat less sensitive than smaller mammals, based on acute LD_{50} values. The acute oral LD_{50} for cats is 150 mg/kg, which is marginally lower than the reported LD_{50} values for rats – i.e., about 180-850 mg/kg bw as discussed in Section 3.1.4. Larger mammals – i.e., pigs and monkeys – tend to have somewhat higher LD50 values – i.e., >1000 mg/kg bw. No marked or systematic species differences are apparent in long-term feeding studies (WHO 1994, Table 44).

Field studies in the published literature do not provide a clear association between carbaryl applications and effects on mammalian wildlife. Similarly, U.S. EPA/OPP (2003d) includes only two incident reports purportedly involving adverse effects in mammals exposed to carbaryl. Neither of the reported incidents provides enough information to determine what role, if any, carbaryl played in causing adverse effects in field exposures.

The lack of clear interspecies relationships regarding carbaryl sensitivity among mammals, suggests that subgroups are not at special risk of exposure. Consequently, as discussed in Section 4.3.2, only one dose-response assessment is made for mammals. This approach is similar to the one taken by the Environmental Fate and Effects Division (EFED) in the recent ecological risk assessment for carbaryl (U.S. EPA/OPP 2003d).

4.1.2.2. Birds

For birds as well as other nontarget organisms covered in this ecological risk assessment, data regarding the effects of carbaryl exposure are ample. The unpublished avian study submitted to the U.S. EPA in support of the reregistration of carbaryl is summarized in the ecological risk assessment conducted by EFED (U.S. EPA/OPP 2003d); some of the earlier unpublished studies are summarized in the review by Cranmer (1986). Much of the published literature is summarized in the reviews by Mount and Oehme (1981) and WHO (1994).

Based on an acute gavage LD_{50} greater than 2000 mg/kg bw in mallard ducks (MRID 45820601) and an acute dietary LC_{50} greater than 5000 ppm (MRID 00022923), the U.S. EPA/OPP (2003d) classifies carbaryl as practically nontoxic to birds (U.S. EPA/OPP 2003d, Table 12, p. 25). In Appendix F of the EFED ecological risk assessment (U.S. EPA/OPP 2003d, Table 2, p. 145), the U.S. EPA indicates that no acute toxicity value is used for birds because of the *practically nontoxic* classification.

An issue with the approach taken by the U.S. EPA to hazard identification for acute level exposures to birds involves information in the compendia by Schafer et al. (1983) indicating that some birds, specifically small passerines, may be more sensitive than the standard test species used by the U.S. EPA (i.e., mallards and quail) to the effects of carbaryl exposure. The information from the Schafer compendia along with other acute toxicity data on birds are summarized in the Table 17.

As indicated in Table 17, the results of acute gavage studies reveal that smaller birds, like red-winged blackbirds and starlings (Schafer et al. 1983), are remarkably more sensitive (i.e, by a factor of 100) than larger birds. In the ecological risk assessment of carbaryl by the U.S. EPA, the data from Schafer et al. (1983) and does recommend that ...*that acute toxicity testing be conducted with passerine species to address this uncertainty* (U.S. EPA/OPP 2003d, p. 26). While not providing a detailed discussion, the Agency seems to be referring to the uncertainty in determining whether or not the data reported by Schafer et al. (1983) accurately reflect an high sensitivity in passerines. This cannot be directly determined from the Schafer et al. (1983) report. Schafer et al. (1983) as well as Hudson et al. (1984) are compendia listing the results of a very large number of studies. These compendia do provide information on the test organisms or experimental methodologies that is sufficiently detailed to assertain whether results reported by Schafer et al. (1983) reflect a greater sensitivity in passerines or are simply spurious outliers. As suggested by U.S. EPA/OPP (2003d, p. 26), additional studies would be needed on passerine species in order to make this determination. As with the U.S. EPA/OPP (2003d), the sensitivity of passerines reported by Schafer et al. (1983) is acknowledged but is in used quantitatively in the current Forest Service risk assessment.

U.S. EPA/OPP (2003d) considers the hazard to birds based on longer-term exposure to carbaryl. The assessment, which is based on a dietary reproduction study in mallard ducks, is referred to by the U.S. EPA/OPP (2003d) as ACC263701 and is not otherwise identified. The *ACC* designation typically refers to an accession number; furthermore, the designation suggests that the study is an older one submitted to the U.S. EPA prior to the adoption of the MRID designation system. In the study, adverse effects observed at 600 ppm included decreased egg production and an increased number of cracked eggs. No adverse effects were observed at 300 ppm. Based on typical food consumption values for mallards in reproduction studies, mallards consume food at a proportion of approximately 0.07 of their body weight (SERA 2007c). Thus, the NOAEC of 300 ppm corresponds to a daily dose of approximately 21 mg/kg bw/day; the LOAEC of 600 ppm corresponds to a daily dose of approximately 42 mg/kg bw/day. There is no information in the open literature suggesting a more sensitive NOAEC. Bursian and Edens (1977) report a 600 ppm dietary NOAEC in quail corresponding to a somewhat higher dose of about 90 mg/kg bw/day. Other more recent studies from the open literature (Appendix 4) report a broad spectrum of adverse effects, all of which are associated with doses substantially greater than 21 mg/kg bw/day. For example, Wojcik and Swiecicka-Grabowska (2004) report the suppression of immune function in turkeys after carbaryl exposures but only at doses of 200 mg/kg bw.

There are numerous field studies concerning the impact of carbaryl applications in free-ranging bird populations (WHO 1994). WHO (1994) concluded that: … *There was no evidence of field effects on birds in forest areas sprayed with 1.1 kg carbaryl/ha*. This application rate corresponds to about 1 lb a.i./acre. In addition, WHO (1994) indicates that some field studies found no detectable adverse effects in bird populations exposed to application rates of up to 6.6 kg/ha or about 6 lbs a.i./acre.

4.1.2.3. Reptiles

The U.S. EPA does not require testing of reptiles as part of the pesticide registration process. As indicated in their ecological risk assessment for carbaryl, the EPA assumes that toxicity to reptiles will be similar to toxicity in birds (U.S. EPA/OPP 2003d).

As summarized in Appendix 9, the published literature regarding the toxicity of carbaryl to reptiles is not substantial. In an effort to evaluate several insecticides for their effectiveness in controlling tick infestations in the African tortoise, the investigators applied a dust formulation of carbaryl to the skin of tortoises once per week for 3 weeks. Although several signs of toxicity were observed (i.e., decreased food consumption, diarrhea and reduced defecation, skin irritation, and eye irritation), the effects are not reported in detail, and it is not clear which if any of these effects can be attributed to carbaryl toxicity versus the stress induced by treatment with a dust formulation.

The only other studies concerning the effects of carbaryl exposure on reptiles involve the impaired swimming ability of water snakes exposed to concentrations of 2.5 or 5.0 mg/L (Hopkins and Winne 2006; Hopkins et al. 2005). These effects are consistent with AChE

inhibition. As discussed in Section 4.1.3.1, similar effects were observed at lower concentrations in more detailed studies on fish (i.e., Beauvais et al. 2001).

The reptile studies suggest that carbaryl exposure probably causes adverse effects in reptiles that are similar to those observed reported in more extensively studied groups of terrestrial and aquatic organisms. Nevertheless, the available information on reptiles does not provide sufficient detail for a separate quantitative assessment.

4.1.2.4. Terrestrial Invertebrates

Efficacy studies regarding the use of carbaryl to control insect pests imply that carbaryl applications are likely to be toxic to a host of terrestrial insects. Consistent with the approach taken by U.S. EPA/OPP (2003d), the risk assessment for terrestrial invertebrates is based primarily on toxicity to the honey bee. Additional information on toxicity to earthworms and more general observations from field studies are also considered.

4.1.2.4.1. Honey bees and Other Arthropods

The honey bee is the standard test species used by the U.S. EPA to assess toxicity to nontarget terrestrial invertebrates. As summarized in U.S. EPA/OPP (2003d, Table 5, p. 101), technical grade carbaryl is highly toxic to the honey bee: oral LC_{50} values range from 0.11 to 0.231 µg/bee. Using a body weight of 0.093 g (0.000093 kg) for the honey bee (USDA/APHIS 1993), this range of doses per bee corresponds to a mg/kg bw dose of ranging from approximately 1.2 to 2.5 mg/kg bw [0.00011 to 0.000231 mg/0.000093 kg]. These toxicity values indicate that carbaryl is about 70-700 times more toxic to the honey bee than to mammals – i.e., mammalian oral LD_{50} values range from approximately 180 to 850 mg/kg bw, as discussed in Section 3.1.4.

Consistent with the relative toxicity of oral and dermal exposure levels in mammals, the contact toxicity of carbaryl in honey bees is less than the exposure level for oral toxicity. As summarized in U.S. EPA/OPP (2003d, Table 5, p. 101), the contact LD_{50} values for the honey bee range from 1.1 to 1.3 µg/bee, corresponding to approximately 11.8-14 mg/kg bw [0.0011 to 0.0013 mg/0.000093 kg].

U.S. EPA/OPP (2003d, Table 5, p. 101) also provides honey bee toxicity data with respect to carbaryl formulations. Although the formulations are not named in the EPA risk assessment, they are identified as containing 479 mg/L carbaryl. This formulation is less toxic to honey bees by a factor ranging from about 10 to 20, in terms of both contact and oral LD_{50} values.

Carbaryl toxicity to terrestrial invertebrates is summarized in Appendix 5. The lowest published toxicity value for the honey bee is 2.72 mg/kg bw (Helson et al. 1994), and some published toxicity values are as high as 26 mg/kg bw (Deo et al. 1988). All of the published toxicity values involve topical application. Thus, the topical LD_{50} value of 2.72 mg/kg bw reported by Helson et al. (1994) is lower than the lowest topical value reported by the U.S. EPA – i.e., 11.8 mg/kg bw, which has no impact on the current risk assessment. As discussed further in Section 4.3.2.3, the lowest toxicity value reported by the U.S. EPA – i.e., 1.2 mg/kg bw – is used to characterize risks to terrestrial insects.

Helson et al. (1994) examined sensitivity among various species of bees, and found the honey bee to be the most sensitive species with an LD_{50} of 2.72 mg/kg bw. The least sensitive species was the bumble bee with an LD_{50} of 268.8 mg/kg bw. As with mammals (Section 4.1.2.1), there was no apparent systematic relationship between toxicity and body mass. Sharma and Nath (1996) speculate that differences in the bacterial populations in honey bees and the capability of the bacteria to degrade carbaryl may partially account for differences in sensitivity among bee populations exposed to carbaryl.

From a number of studies submitted in support of the reregistration of carbaryl, U.S. EPA/OPP (2003d) concludes that carbaryl is moderately to highly toxic to many predaceous arthropods, predaceous mites, and spiders. U.S. EPA does not provide details of these studies; nonetheless, this conclusion is consistent with published studies concerning carbaryl toxicity to insects (Appendix 5). While many of the published toxicity studies summarized in Appendix 5 do not express exposure levels in units that are directly comparable to those used in bioassays on honey bees, those studies that do express LD_{50} or LC_{50} values in units of mg/kg bw – i.e., Trisyono et al. 2000; Zhong et al. 1995 – indicate that the honey bee is the most sensitive species of arthropod.

As noted above, technical grade carbaryl appears to be substantially more toxic than commercial formulations are to honey bees. Consequently, field studies may be preferable to standard toxicity bioassays as a source of information for assessing risks to bees and other arthropods. Citing an unpublished study (MRID 457854-07), the U.S. EPA/OPP (2003d, p. 102) indicates that an application of a carbaryl formulation at a rate of 0.8 lb a.i./acre had no significant impact on bee behavior or bee mortality; however a much lower application rate of 0.062 lb a.i./acre caused adverse effects in ground spiders (Boetel et al. 2005). The study by Boetel et al. (2005), however, involved the application of carbaryl in a bait formulation containing an attractant. The role that the attractant played in increasing the exposure of ground dwelling spiders cannot be assessed quantitatively and it is not clear that this type of an effect would be noted in Forest Service applications because these applications do not involve the use of attactants. Moreover, an application rate of 1.12 lb a.i./acre, comparable to application rates that may be used in Forest Service programs, caused adverse effects in parasitic wasps (Rehman et al. 1999). Most of the other field studies in Appendix 6 were conducted at very high application rates (e.g., Gels et al. 2002; Hoy and Shea 1981), and adverse effects were observed among several groups of terrestrial invertebrates.

4.1.2.4.2. Earthworms

Earthworms are not a standard test species; furthermore, earthworm toxicity studies are not required for pesticide registration. Accordingly, a variety of non-standardized toxicity studies are conducted on earthworms, which are often used to assess the consequences of exposure to fossorial invertebrates. Contact LD_{50} values – i.e., carbaryl on moistened filter paper—are available for several earthworm species and range from about 0.5 $\mu g/cm^2$ (Neuhauser et al. 1986) to about 8.3 $\mu g/cm^2$ (Edwards and Bater 1992). Other types of assays include direct exposure to

contaminated water in which the reported LC_{50} values range from 3.1 to 800 mg/L (Stenersen 1979).

In terms of Forest Service terrestrial applications of carbaryl, the most relevant bioassay of earthworm toxicity involves exposures to contaminated soil containing a known concentration of carbaryl. As summarized in Appendix 4, most soil bioassays with carbaryl indicate soil LC_{50} values that range from about 9 mg/kg soil (Mostert et al. 2002) to about 263 mg/kg soil (Neuhauser et al. 1985). A major exception, however, is the study by Callahan et al. (1994) which reports soil LC_{50} values ranging from about 0.00009 to 0.001 mg/kg soil. This study is atypical, and the basis for the discrepancy in reported toxicity values is not apparent.

In the only field study with specific information concerning the toxicity of carbaryl to earthworms (Potter et al. 1990), earthworm populations decreased over a 20-week period after carbaryl was applied at a rate of 8 lbs. a.i./acre.

4.1.2.5. Terrestrial Plants (Macrophytes)

It is not unusual for combinations of insecticides and herbicides to enhance damage to terrestrial plants relative to the damage caused by the herbicide alone. The mechanism for this effect is most often associated with an inhibition of the detoxification of the herbicide by the insecticide (Baerg et al. 1996). Nonetheless, insecticides alone are not typically considered hazardous to terrestrial plants.

According to U.S. EPA/OPP (2003d), a preliminary assay indicates that carbaryl is not highly phytotoxic. The assay involved Sevin XLR Plus at an application rate of 0.803 lbs a.i./acre to cabbage, cucumber, onion, ryegrass, soybean, and tomato (MRID 457848-07). Standard endpoints for plant toxicity did not indicate any reductions greater than 25%. Consequently, the EPA risk assessment does not quantify risks to terrestrial plants. Nonetheless, the EPA risk assessment also notes several incident reports in which carbaryl applications were associated with phytotoxicity. In discussing the weight-of-evidence concerning the incident reports, the EPA comments:

> *The large scale damage inflicted to orchard crops is a greater concern. The limited terrestrial plant data available on carbaryl does not indicate the likelihood of phytotoxic effects; however, the incident data imply that phytotoxic effects are possible.* U.S. EPA/OPP 2003d, p. 115.

The open literature contains very little information concerning the toxicity of carbaryl to terrestrial plants. The metabolic pathways of carbaryl in terrestrial plants are similar to those in mammals and involve cytochrome P450 monooxygenases. As indicated in the WHO (1994) review, numerous studies were conducted on the uptake, distribution, metabolism, and retention of carbaryl in terrestrial plants. These studies indicate that carbaryl is rapidly absorbed by terrestrial plants and may bioconcentrate to a greater extent in plants than in animals. None of the studies cited in WHO (1994), however, suggest that carbaryl is likely to damage plants. Bakke (2004) cites a summary of a study conducted by Eid et al. (1971) indicating that carbaryl

solutions may slightly enhance seed germination at low concentrations and inhibit seed germination at higher concentrations. This biphasic pattern is not unusual and, in itself, is not a strong indication of phytotoxicity.

The current Forest Service risk assessment adopts the approach taken in recent EPA risk assessment (U.S. EPA/OPP 2003d) with respect to the phytotoxicity of carbaryl: the potential hazard to some plants exposed to carbaryl is acknowledged qualitatively; however, the information on phytotoxicity is not sufficiently detailed or specific to propose a quantitative assessment.

4.1.2.6. Terrestrial Microorganisms

There is abundant and detailed literature concerning the metabolism of carbaryl by soil microorganisms (e.g., Mount and Oehme 1981); however, the literature concerning adverse effects of exposure on soil microorganisms is sparse. As reviewed by WHO (1994), very high concentrations of carbaryl – i.e., 5000 ppm – altered the species composition of soil fungi. In laboratory cultures, 1 ppm carbaryl caused decreases in protozoan populations, while 10 ppm resulted in virtually complete mortality. Somewhat higher concentrations of about 50 ppm were associated with inhibition of rumen microorganisms, particularly microorganisms involved in the breakdown of cellulose (Mount and Oehme 1981).

4.1.3. Aquatic Organisms

4.1.3.1. Fish

The database regarding carbaryl toxicity to fish and other aquatic organisms is extensive. The U.S. EPA considered numerous studies submitted in support of the reregistration of carbaryl (U.S. EPA/OPP 2003d). Also, there is an abundance of studies in the published literature regarding the effects of carbaryl on fish. A broad selection of this literature is summarized in Appendix 6. In addition, the earlier literature concerning the toxicity of carbaryl to fish and other aquatic species is reviewed in some detail by Mount and Oehme (1981) and WHO (1994).

As with the other major groups of nontarget species covered in EPA's recent ecological risk assessment for the reregistration of carbaryl (U.S. EPA/OPP 2003d), the focus of this hazard identification for fish is to evaluate the extent to which the EPA risk assessment safeguards this group of organisms. As illustrated in Figure 2 of U.S. EPA/OPP (2003d, p. 28), reported LC_{50} values in fish are highly variable, ranging from less than 1 to 20 ppm. The lowest acute toxicity value reported by the U.S. EPA is a 96-hour LC_{50} of 0.25 ppm in salmon (Mayer and Ellersieck 1986). The chronic toxicity value used by the U.S. EPA is based on a full life-cycle study with fathead minnows in which the NOAEC is 0.21 ppm, and the LOAEC, based on survival and reproduction, is 0.68 ppm (Carlson 1972).

Many of the toxicity studies in fish summarized in Appendix 7 are consistent with the toxicity values selected by the U.S. EPA. There are, however, several important exceptions indicating adverse effects at lower concentrations. In some cases, the difference is not substantial. For example, growth inhibition in the bonytail chub was observed at a concentration of 0.25 ppm

(Dwyer et al. 2005a), which is only somewhat greater than 0.21 ppm chronic NOAEC used by the U.S. EPA. Similarly, Beauvais et al. (2001) reported significantly decreased ChE activity in rainbow trout at concentrations as low as 0.188 ppm. The ChE inhibition was significantly (p = 0.0006) correlated with a reduction in swimming speed; however, the correlation coefficient was low ($r^2 = 0.7057$) and it is not clear that the concentration of 0.188 ppm was associated with a significant reduction in swimming speed. Nonetheless, Beauvais et al. (2001) offer the following conclusion:

> *Correlation of ChE activity with changes in swimming behavior resulting from carbaryl exposure provides evidence that when ChE inhibition is detected the organism is affected in a manner that may ultimately decrease its survival.* – Beauvais et al. 2001, p. 89.

Within the context of the Beauvais et al. (2001) publication, this comment clearly refers to an inhibition of brain AChE activity. Thus, this conclusion is essentially the same approach taken by the U.S. EPA to the human health risk assessment (U.S. EPA/OPP 2007c).

Relatively few studies provide estimates of NOEC values for brain AChE activity in fish. In Colorado Squawfish (*Ptychocheilus lucius*), the NOEC for brain AChE after a 24-hour *in vivo* exposure is reported as approximately 0.03 ppm (Beyers and Sikoski 1994). Based on the study by Ferrari et al. (2004a), juvenile rainbow trout (*Oncorhynchus mykiss*) appear to be a much more sensitive species. The 96-hour static exposure EC_{50} for brain cholinesterase inhibition is 0.019 ppm, which is lower than the LD_{50} of 5.4 ppm by a factor of about 284. As observed in mammals, AChE recovery to normal activity was rapid, once the fish were transferred to uncontaminated media. Ferrari et al. (2004a) do not explicitly identify or discuss an NOEC. Based on Figure 1 in the publication (Ferrari et al. 2004a, p. 241), it appears that the lowest concentration of carbaryl tested was about 0.006 ppm and that brain AChE activity was inhibited by about 40%.

While much of the published literature supports the toxicity values derived by the U.S. EPA/OPP (2003d), the suggestion by Beauvais et al. (2001) that brain AChE is the most relevant endpoint for identifying potential hazards to fish seems reasonable and is consistent with the position adopted by the U.S. EPA/OPP (2007c) for the assessment of human health effects. As discussed further in the dose-response assessment (Section 4.3.3.1), the inhibition of brain AChE activity is the basis for quantitatively assessing the risk of adverse effects in fish exposed to carbaryl.

4.1.3.2. Amphibians

As with reptiles (Section 4.1.2.3), the U.S. EPA does not require testing of amphibians as part of the pesticide registration process. U.S. EPA assumes that carbaryl toxicity is similar for fish and amphibians (U.S. EPA/OPP 2003d).

U.S. EPA/OPP (2003d) cites an LD_{50} of >4000 mg/kg bw for bullfrogs, and classifies carbaryl as practically nontoxic to bullfrogs. This $LD_{50,}$ however, is not from a registrant submitted study but is taken from the compendia of older toxicity studies by Hudson et al. (1984). Hudson et al.

(1984, p. 18) reports that only three male bull frogs were used in the study and does not identify the test material as either technical grade carbaryl or a carbaryl formulation. While the reported results suggest that adult bullfrogs may be tolerant of carbaryl exposure, the study would typically be considered a crude screening tool or preliminary range-finding study and is not an appropriate basis for concluding that carbaryl presents a low hazard to adult amphibians. Nonetheless, the presumption that carbaryl has a low order of toxicity to adult frogs is supported by Sampath et al. (1995) who report that the intraperitoneal LD_{50} of a 50% carbaryl formulation to adult tiger frogs is 640 mg formulation/kg bw or 320 mg a.i./kg bw.

U.S. EPA/OPP (2003d) includes a number of published studies concerning the toxicity of carbaryl to amphibians. These and other published studies are summarized in Appendix 8. The studies reviewed by the U.S. EPA consist of a series of studies conducted jointly by the USGS and the University of Missouri (i.e., Boone and Bridges 1999, 2003; Bridges and Boone 2003; Bridges and Semlitsch 1999, 2001, 2002, 2003; Boone et al. 2001, 2005). Most of these studies involve the exposure of tadpoles from several frog species. In terms of acute LC_{50} values, these studies indicate that frogs are similar in sensitivity to fish with 96-hour LC_{50} values ranging from 8.4 mg/L (Bridges and Semlitsch 2001) to 22 mg/L (Boone and Bridges 1999). Other investigators report LC_{50} values as low as 1.73 mg/L (Zaga et al. 1998) and as high as 150 mg/L (Khangarot et al. 1985). This somewhat broader range of LC_{50} values is still within the range of acute LC_{50} values reported for fish.

As discussed in Section 4.1.3.1, brain AChE inhibition appears to be the most sensitive endpoint for carbaryl toxicity in fish. AChE inhibition in amphibians is reported only in the Ferrari et al. (2004a) study which compares carbaryl toxicity in a sensitive fish species (rainbow trout) and in a South American toad, *Bufo arenarum*. As discussed in Section 4.1.3.2, the IC_{50} for brain cholinesterase inhibition in rainbow trout is reported as 0.019 ppm, a factor of 284 below the trout 96-hour LC_{50} of 5.4 ppm. In the toad, the IC_{50} for brain cholinesterase inhibition is much higher, 7.58 ppm. Unlike the relationship between the IC_{50} and LC_{50} in trout, however, the 96-hour LC_{50} is 24.64 ppm, only a factor of 3 greater than the IC_{50}.

The 96-hour LC_{50} of 24.64 ppm in the toad is very close to the upper bound of the range of reported LC_{50} values in fish – i.e., from about 1 to 20 ppm (Section 4.1.31) – and the LC_{50} for the toad is among the higher LC_{50} values reported for amphibians. Thus, the study by Ferrari et al. (2004a) does not suggest that amphibians are generally more tolerant than fish to carbaryl exposure. The more reasonable interpretation is that Ferrari et al. (2004a) happened to select a sensitive species of fish and a relatively tolerant species of amphibian.

Only one study (Rohr et al. 2003) is available regarding carbaryl toxicity in salamanders. As summarized in Appendix 8, this study reports significant larval mortality at 0.005 and 0.05 ppm as well as developmental effects over a 36-day exposure period in the streamside salamander (*Ambystoma barbouri*). The only clear NOEC for all adverse effects appears to be 0.0005 ppm. Spotted salamanders (*Ambystoma maculatum*) were used in the study by Relyea and Mills (2001) as a predator stressor in assays on treefrog tadpoles. Relyea and Mills (2001) report that some salamanders died during the test but do not provide sufficient information to determine if the

mortality was attributable to carbaryl exposure – i.e., carbaryl concentrations of up to 0.09 ppm over a 16-day period.

4.1.3.3. Aquatic Invertebrates

For aquatic invertebrates, like fish (Section 4.1.3.2), there are numerous studies concerning carbaryl toxicity. The studies submitted to the EPA in support of the reregistration of carbaryl are reviewed in the EPA risk assessment (U.S. EPA/OPP 2003d), and the studies from the earlier open literature are summarized in Mount and Oehme (1981) and WHO (1994). More recent studies in the open literature are summarized in Appendix 10 of this Forest Service risk assessment. Appendix 10 also includes a selection of some of the earlier studies on carbaryl.

Given the many studies available concerning carbaryl toxicity to aquatic invertebrates, the approach to the hazard identification is similar to the one taken for fish, which is to determine whether the toxicity values covered in the EPA's recent ecological risk assessment (U.S. EPA/OPP 2003d) adequately encompasses the range of toxicity values and focuses on the most sensitive endpoints.

U.S. EPA/OPP (2003d, Table 2, p. 145) notes a broad range of sensitivity among aquatic invertebrates. The lowest acute toxicity value cited by the U.S. EPA is 5.1 ppb (0.0051 ppm), an acute LC_{50} in stonefly larvae (*Chloroperla grammatica*, MRID 458206-02). The highest acute toxicity value cited by the EPA is 23.6 ppm, an acute LC_{50} in oysters (MRID 425973-01). Both the stonefly study and the oyster study are unpublished submissions to the U.S. EPA in support of the reregistration of carbaryl.

For longer-term exposures, the most sensitive endpoint identified by the U.S. EPA is a NOAEC of 0.0015 mg/L with a LOAEC of 0.0033 mg/L from a study in *Daphnia magna* (MRID 00150901). The least sensitive endpoint is from an emergence study in midge (*Chironomous riparius*) with a NOEC of 0.5 mg/L and a LOEC of 1.0 mg/L. Both of these studies are also unpublished submissions to the U.S. EPA in support of the reregistration of carbaryl.

Some LC_{50} values reported in the open literature are lower than the 0.0051 ppm value used by the U.S. EPA. The lowest reported 96-hour LC_{50} value is 0.0000007 ppm [$7x10^{-7}$ ppm] for dragonfly nymphs (*Brachythermis contaminata*) (Shukla and Mishra 1980). This study used wild caught organisms and a formulation of carbaryl that is characterized only as *10% WDP*. Gaaboub et al. (1975) report an LC_{50} value of 0.0011 ppm for *Daphnia magna*. This LC_{50} value, however, is reported for an unspecified Sevin formulation. Patil et al. (1992) report a 96-hour LC_{50} of 0.0042 mg/L for a formulation of carbaryl identified as Sevimol. This formulation is not otherwise identified and may be a formulation that is or was used in India. The publication indicates that explanatory footnotes should be included to describe the formulation but the footnotes are missing from the publication. A more recent study, Sakamoto et al. (2005), reports very low 24-hour LC_{50} values in two species of cladocerans: 0.0041 mg/L in *Bosmina fatalis* and 0.0035 in *Leptodora kindtii*. While these are not common test species, the study by Sakamoto et al. (2005) used technical grade carbaryl, and the study appears to have been well-conducted but

used OECD guidelines rather than EPA guidelines. The only other toxicity value similar to the value selected by the U.S. EPA is the LC_{50} of 0.0065 in an amphipod (Pantani et al. 1997).

There are relatively few reproduction studies summarized in the open literature. Hanazato (1991b) conducted a reproduction study in *Daphnia ambigua*, and Oris et al (1991) conducted a reproduction study in *Ceriodaphnia dubia*. In both of these cladoceran reproduction studies, an NOEC of 0.001 mg/L is reported and this value is only modestly below the NOEC of 0.0015 mg/L identified by the EPA. While the two species in the study by Hanazato (1991b) and Oris et al. (1991) appear to be similar in sensitivity to *Daphnia magna*, the most sensitive species identified in the EPA ecological risk assessment (U.S. EPA/OPP 2003d), the study by Barry (1999) suggests that another cladoceran species, *Daphnia longicephala*, may be much more sensitive. At a concentration of 0.00032 mg/L, Barry (1999) noted a decrease in reproduction rate and decrease in brood size in *Daphnia longicephala*. This effect was noted in the presence and absence of kairomones released by *Anisops gratus*, a daphnid predator, but the effect was greater with the presence of kairomones. The decrease in the reproduction rate was associated with an increase in time to maturity, including an increase in the number of pre-reproductive instars. The NOEC for this effect was 0.0001 mg/L. This is a factor of 15 below the NOAEC of 0.0015 mg/L identified by the EPA.

The least sensitive reproductive endpoint in the open literature comes from the report by Dwyer et al. (2005b) which indicates that 0.33 mg/L resulted in an inhibition of reproduction greater than 25% in *Ceriodaphnia dubia*. This study, however, does not provide sufficient detail to identify an NOEC. This limitation has no impact on the current risk assessment because the NOEC for the least sensitive chronic endpoint – i.e., 0.5 mg/L in the emergence study in midge – is greater than the 0.33 mg/L concentration from the study by Dwyer et al. (2005b).

Field studies and mesocosm studies involving aquatic invertebrates are summarized in Appendix 12. Adverse effects on stream invertebrates were observed after field broadcast applications similar to those that may be used in Forest Service programs for leaf beetle control (Beyers et al.1995; Courtemanch and Gibbs 1980; Coutant 1964). These studies are considered further in the risk characterization (Section 4.4). Mesocosm studies provide a somewhat more controlled exposure and are more readily compared to the laboratory toxicity studies. Consistent with the results from laboratory toxicity studies, the mesocosm studies report adverse effects on aquatic invertebrates in the low ppb range. The lowest reported concentration causing adverse effects in a mesocosm study is 0.005 ppm. At this exposure concentration, Havens (1994) observed a greater than 50% decline in biomass of *Daphnia galeata*. This concentration is virtually identical to the most sensitive toxicity value identified in the EPA ecological risk assessment – i.e., an LC_{50} in stonefly larvae of 0.0051 ppm. Also consistent with the toxicity values identified by the U.S. EPA, mesocosm studies indicate that mollusks are relatively tolerant to carbaryl (Dumbauld et al 2001).

Of greatest concern in the current risk assessment is the very low 96-hour LC_{50} value of 0.0000007 ppm for dragonfly nymphs (*Brachythermis contaminata*) reported by Shukla and Mishra (1980). No species of dragonfly were assayed in mesocosm or field studies on carbaryl.

Nonetheless, *Brachythermis contaminata* is described as a sensitive species in a U.S. EPA/OPP assessment of carbofuran, another AChE inhibitor (Tarkowski 2004). Tarkowski (2004), reports an LC_{50} of 0.119 ppb carbofuran for *Brachythermis contaminata*, which is a factor of about 16 less than the lowest LC_{50} (2 ppb) in *Ceriodaphnia dubia* and a factor of 470 less than the EC_{50} of 56 ppb for emergence in midge larva. Finally, the Shukla and Mishra (1980) study is included in ECOTOX, a database of studies maintained by the U.S. EPA (http://cfpub.epa.gov/ecotox/help.cfm?sub=about). While a full discussion of ECOTOX is beyond the scope of this risk assessment, ECOTOX is designed by the U.S. EPA to contain information that may be useful in ecological risk assessment and to screen out studies that should not be used.

Another concern in the hazard identification for aquatic invertebrates involves the reversibility of AChE inhibition. As discussed in the human health risk assessment (Section 3.1.2) as well as the previous sections on mammals, birds, and fish, the recovery of AChE activity in vertebrates occurs rapidly after exposure to carbaryl is terminated. This is not the case with aquatic invertebrates. A prolonged recovery period has been noted both in laboratory studies (Jayaprada and Rao 1991) and field studies (Gibbs et al. 1984).

4.1.3.4. Aquatic Plants

For some pesticides, particularly the herbicides, the U.S. EPA requires a battery of bioassays in aquatic algae as well as a bioassay in at least one aquatic macrophyte, typically a species of *Lemna*. For insecticides like carbaryl, however, the testing requirements are minimal. As summarized in U.S. EPA/OPP (2004d), two studies on *Pseudokirchneriella subcaptitata*, a filamentous green algae, were submitted to the Agency in support of the reregistration of carbaryl. One study assayed technical grade carbaryl and reports an EC_{50} value for growth of 1.27 ppm with an NOAEC of 0.29 ppm (MRID 42372802). The other study assayed the Sevin XLR Plus formulation and reports an EC_{50} of 3.2 ppm with an NOAEC of 1.8 ppm (MRID 45784808).

No studies are available concerning carbaryl toxicity to aquatic macrophytes, although the U.S. EPA recommended that a study should be conducted on *Lemma gibba* as well as additional studies on other species of algae.

U.S. EPA/OPP (2004d, p. 116) cites a paper by Bridges and Boone (2003) indicating that at a concentration of 2.5 ppm, an increase in chlorophyll concentrations was observed during a mesocosm study. Bridges and Boone (2003) suggest that the increase might be attributed to the decreased grazing by zooplankton secondary to the increased mortality in zooplankton caused by carbaryl. Given the toxicity of carbaryl to aquatic invertebrates (Section 4.1.3.3), this supposition seems plausible.

Very little data are available on the toxicity of carbaryl to other aquatic microorganisms. Edmiston et al. (1985) conducted plate assays as well as assays of oxygen uptake in *Paramecium multimicronucleatum* exposed to technical grade carbaryl. The 24-hour LC_{50} was 28 ppm in the plate assay. Oxygen consumption was inhibited by 50% at a concentration of 120 ppm. [Note:

This paper is cited in the WHO (1994) review and the LC_{50} is reported as "28 μg/litre". The Edmiston et al. 1985 paper indicates that the units are ppm or mg/L.]

4.2. EXPOSURE ASSESSMENT

4.2.1. Overview

Terrestrial animals might be exposed to any applied pesticide from direct spray, the ingestion of contaminated media (vegetation, prey species, or water), grooming activities, or indirect contact with contaminated vegetation. The exposure scenarios for terrestrial species are summarized in Worksheet G01 of the EXCEL workbooks that accompany this risk assessment for the typical application rate used in leaf beetle control (Attachment 1) and the unit application rate used in bark beetle prevention (Attachment 2).

In acute exposure scenarios, the highest exposure for terrestrial vertebrates involves the consumption of contaminated fish by a predatory bird after an accidental spill which could amount to approximately 460 mg/kg. There is a wide range of exposure levels anticipated from the consumption of contaminated vegetation by terrestrial animals: central estimates range from 1 mg/kg for a small mammal consuming fruit to 20 mg/kg for a large bird consuming grasses. Upper bound estimates for the consumption of contaminated vegetation range from about 2 mg/kg for a small mammal consuming fruit and 57 mg/kg for a large bird consuming grasses. The consumption of contaminated water based on expected environmental concentrations will generally lead to much lower levels of acute exposure – i.e., in the range of about 0.002-0.004 mg/kg. The accidental spill scenario leads to much higher estimates of exposure – i.e., about 0.5-10 mg/kg. A similar pattern is seen for chronic exposures.

The central estimate for daily doses for a small mammal from the longer-term consumption of contaminated vegetation at the application site is about 0.003 mg/kg/day, with an upper estimate of about 0.024 mg/kg/day. Dose estimates associated with the consumption of contaminated water are in the range from 0.00001 to 0.0002 mg/kg bw/day for a small mammal. Based on general relationships of body size to body volume, larger vertebrates, relative to small vertebrates, will be exposed to lower doses, under comparable exposure conditions.

Estimates of the exposures of aquatic organisms to carbaryl are based on essentially the same information used to assess the exposure of terrestrial species to contaminated water. The peak estimated rate of contamination of ambient water associated with the application of carbaryl for leaf beetle control is 0.02 (0.002 to 0.033) mg a.i./L at a normalized application rate of 1 lb a.i./acre. For longer-term exposures, the estimated rate of contamination of ambient water is 0.0003 (0.0001 to 0.002) mg a.i./L at a normalized application rate of 1 lb a.i./acre. For the assessment of potential hazards to aquatic species, these water contamination rates are adjusted based on the application rates considered in this risk assessment.

As in the exposure assessment for human health, the unit application rate used in bark beetle prevention (Attachment 2) generally leads to lower estimates of exposure than the corresponding exposure estimates based on broadcast applications for leaf beetle control. Actual exposures associated with applications for bark beetle prevention will depend on the number and size of the treated trees as well as the acreage that is treated.

4.2.2. Terrestrial Animals

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

In the exposure assessments for the ecological risk 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 terrestrial animals. For dermal exposures to terrestrial animals, the units of exposure are expressed in mg of agent per cm^2 of surface area of the organism and abbreviated as mg/cm^2. In estimating dermal dose, 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. As in the human health risk assessment, all exposure scenarios for mammals are detailed in the EXCEL workbooks for carbaryl (Attachment 1 for leaf beetle control and Attachment 2 for bark beetle prevention). In each of these attachments, the exposure assessments for terrestrial animals are summarized in Worksheet G01. The computational details for each exposure assessment presented in this section are provided as scenario-specific worksheets (Worksheets F01 through F16b).

Because of the relationship of body weight to surface area as well as to the consumption of food and water, small animals will generally receive a higher dose, in terms of mg/kg body weight, relative to large animals, for a given type of exposure. Consequently, most general exposure scenarios for mammals and birds are based on a small mammal or a small bird. For small mammals, exposure assessments are conducted for direct spray (F01 and F02a), consumption of contaminated fruit (F03a, F04a, F04b), and consumption of contaminated water (F05, F06, F07). Generally, pesticide concentrations will be higher on grasses than on fruits and other types of vegetation (Fletcher et al. 1994). Although most small mammals do not typically consume large amounts of grass over prolonged periods of time, some small mammals, like the meadow vole (*Microtus pennsylvanicus*), may consume grasses as a substantial proportion of their diet at certain times of the year. Consequently, the acute consumption of contaminated grass by a small mammal is considered in this risk assessment (F03b). Large mammals may consume grasses over a long period of time, and these scenarios are included both for acute exposures (Worksheet F10) and longer-term exposures (Worksheets 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 by a predatory bird of small mammals contaminated by direct spray (F16b), and the consumption of contaminated grasses by a large bird (F12, F13a, and F13b).

Clearly, numerous other exposure assessments could be generated. The specific exposure scenarios outlined in this section are designed to identify the groups of organisms and routes of exposure of greatest concern and to serve as guides to more detailed site-specific assessments.

4.2.2.1. Direct Spray

The unintentional direct spray of wildlife during broadcast applications of pesticides is a plausible exposure scenario 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 or broadcast exposure assessments are conducted (Worksheets F01, F02a, and F02b). The first spray scenario, 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. This exposure assessment assumes first-order dermal absorption. The second exposure assessment (detailed in Worksheet F02a) assumes complete absorption over one day of exposure. This assessment is included in an effort to encompass the increased exposure due to grooming. The third exposure assessment is developed using the typical body weight of a honey bee, again assuming complete absorption of the compound. There are no exposure assessments for the direct spray of large mammals, principally because allometric relationships dictate that the amounts of a compound to which a large mammal will be exposed on the basis of body weight as a result of direct spray is proportionately less than the amount to which smaller mammals will be exposed on a body weight basis.

4.2.2.2. Contact with Contaminated Vegetation

As in the human health risk assessment (Section 3.2.3.3), the only approach for estimating the potential significance of dermal contact with contaminated vegetation is to assume a relationship between the application rate and dislodgeable foliar residue. Unlike the human health risk assessment in which transfer rates for humans are available, there are no transfer rates available for wildlife species. Wildlife species, 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 equilibrium may be reached regarding levels on the skin, rates of absorption, and levels on contaminated vegetation. Nonetheless, there are no data regarding the kinetics of any such process. In the absence of such data, no quantitative assessments are made for this scenario in the ecological risk assessment.

4.2.2.3. Ingestion of Contaminated Vegetation or Prey

Since carbaryl will be applied to vegetation, the consumption of contaminated vegetation is an obvious concern. Separate exposure assessments are developed for acute and chronic exposure scenarios involving a small mammal (Worksheets F03a, F03b, F04a and F04b), a large mammal (Worksheets F10, F11a, and F11b), and large birds (Worksheets F12, F13a, and F13b). Similarly, the consumption of contaminated insects is modeled for a small bird (Worksheet 14a) and a small mammal (Worksheet 14b). As with residues on vegetation and consistent with the approach taken in the recent U.S. EPA ecological risk assessment of carbaryl (U.S. EPA/OPP

2003d), the empirical relationships recommended by Fletcher et al. (1994) are used to estimate residues in contaminated insects (Worksheets F14a and F14b).

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). In addition to the risks of exposure associated with the consumption of contaminated vegetation, insects, and other terrestrial prey, carbaryl may reach ambient water and aquatic organisms. 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. Details of each scenario are given in the cited worksheets.

Since multi-route exposures (e.g., the consumption of contaminated vegetation and contaminated water) are likely, numerous exposure assessments could be developed to account for the various combinations. In the current risk assessment, such assessments are not included because, as illustrated in Worksheet G01, the predominant route of plausible exposure is the consumption of contaminated vegetation by herbivores or the consumption of prey by predators; therefore, explicit considerations of multiple routes of exposure would have no impact on the characterization of risk.

In applications for the prevention of bark beetle infestations, a substantial amount of carbaryl is applied directly to tree bark. This method of application may impact exposures to organisms that inhabit tree bark, organisms, like some birds, that consume organisms from tree bark, or some mammals, like deer, that may eat tree bark. Methods for estimating exposures for these organisms are not available, and the risks of these exposures are considered qualitatively in the risk characterization (Section 4.4).

4.2.2.4. Ingestion of Contaminated Water

The methods for estimating carbaryl concentrations in water are identical to those used in the human health risk assessment (Section 3.2.3.4). The only major differences in the estimates of exposure involve the weight of the animal and the amount of water consumed. These differences are detailed and documented in the worksheets regarding the consumption of contaminated water (F05, F06, F07).

Unlike the human health risk assessment, estimates concerning the variability of water consumption are not available. Thus, for the acute scenario, the only factors affecting the estimate of the ingested dose include the field dilution rates (i.e., the concentration of the chemical in the spilled solution) and the amount of solution 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 ponds or streams contaminated by runoff or percolation, the factors that affect the variability in exposure estimates are the water contamination rates (Section 3.2.3.4.2) and the application rates.

4.2.3. Terrestrial Plants

In general, the primary hazard to nontarget terrestrial plants associated with the application of herbicides is unintended direct spray or deposition of spray drift. In addition, herbicides may be transported off-site by percolation or runoff or by wind erosion of soil. Consequently, a relatively standard set of exposure scenarios is typically employed in Forest Service risk assessments for herbicides.

These exposure scenarios are not used with carbaryl. As detailed in Section 4.1.2.5, standard laboratory studies concerning the toxicity of carbaryl applications to plants suggest that risks are likely to be low. Consistent with the approach taken by the U.S. EPA/OPP (2003d), these studies are not used to derive quantitative values for risk characterization – i.e., RQ values in the EPA assessment and HQ values in this Forest Service risk assessment.

4.2.4. Soil Organisms

As discussed in Section 3.2.3.4.3, estimates of carbaryl concentrations in soil as well as estimates from off-site movement (runoff, sediment, and percolation) are output from GLEAMS. Based on the GLEAMS modeling, concentrations in clay, loam, and sand over a wide range of rainfall rates are summarized in Table 18 for the top 60 inches of soil and in Table 19 for the top 1 foot of soil.

Peak modeled soil concentrations in the top 1 foot of soil at an application rate of 1 lb a.i./acre range from 131 to 217 ppb. At the nominal application rate of 0.75 lb a.i./acre, the corresponding concentrations would range from about 100 to 160 ppb. The average modeled soil concentrations in the top 12 inches of soil at an application rate of 1 lb/acre range from about 0.00456 ppb (clay at 250 inches of rainfall per year) to 0.0169 ppb (clay at 10 inches of rainfall per year). At the nominal application rate of 0.75 lb a.i./acre, these concentration correspond to a range of about 0.003 ppb (3 parts per trillion) to 0.013 ppb (13 parts per trillion).

4.2.5. Aquatic Organisms

For the application of carbaryl, the plausibility of effects on aquatic species is based on estimated concentrations of carbaryl in water that are identical to those used in the human health risk assessment. These values are summarized in Table 14 and discussed in Section 3.2.3.4.7.

4.3. DOSE-RESPONSE ASSESSMENT

4.3.1. Overview

The specific toxicity values used in this risk assessment are summarized in Table 20, and the derivation of each of these values is discussed in the various subsections of this dose-response assessment. The first column in Table 20 specifies the organism to which the toxicity value applies. The available toxicity data support separate dose-response assessments in seven groups of organisms: terrestrial mammals, birds, nontarget terrestrial invertebrates, fish, amphibians, aquatic invertebrates, and aquatic algae. Different units of exposure are used for different groups of organisms depending on how exposures are likely to occur and how the available toxicity data are expressed.

For mammals, birds, and fish, separate toxicity values are not derived for acute and chronic exposures. As with the dose-response assessment for human health, the rationale for this approach is the rapid reversibility of AChE inhibition. For mammals, an NOEC of 4 mg/kg bw/day is used from a reproduction study. The same approach is used for birds with an NOEC of 21 mg/kg bw/day from a reproduction study. A somewhat different approach is used for fish. While the U.S. EPA uses a reproductive NOEC of 0.21 ppm, the current risk assessment identifies the inhibition of brain AChE as a more sensitive sublethal effect and uses an NOEC 0.03 ppm for tolerant fish species and a LOEC of 0.006 ppm for sensitive fish species.

The U.S. EPA uses toxicity values from fish studies to assess risks to amphibians. This approach appears to be justified with the exception of longer-term risks to sensitive species of amphibians. Based on a recent toxicity study in salamanders from the open literature that is not cited in the U.S. EPA, the longer-term risks to sensitive amphibian species is based on a NOEC of 0.0005 ppm.

Arthropods are much more sensitive than vertebrates to carbaryl exposure. For terrestrial arthropods, the LD_{50} value of 1.2 mg/kg bw is adopted from the recent EPA risk assessment. For aquatic arthropods, a NOEC of 0.0035 ppm is used for acute exposures and a reproductive NOEC of 0.0015 is used for longer-term exposures. Other groups of aquatic invertebrates – e.g., mollusks and aquatic worms – are much more tolerant of exposure to carbaryl. For characterizing risks in these groups, an acute EC_{50} of 2.7 mg/L is used for acute exposures and a NOEC of 0.5 mg/L is used for longer-term exposures.

Risks to terrestrial plants are not considered quantitatively but are addressed qualitatively in the risk characterization. No data are available on aquatic macrophytes. For aquatic algae, an NOEC of 0.29 ppm is used to characterize risks after both acute and longer-term exposures.

4.3.2. Toxicity to Terrestrial Organisms

4.3.2.1. Mammals

Most Forest Service risk assessments use the same toxicity values for mammals that are used in the human health risk assessment. This is not done in the current risk assessment because of the atypical use of the Benchmark Dose method in the dose-response assessment for human health effects (Section 3.3). This method is appropriate for the human health risk assessment because of the focus on the individual. The ecological risk assessment, however, is focused on the population.

The EFED (U.S. EPA/OPP 2003d) assessment for carbaryl toxicity to mammals focuses on lethality (LD_{50}) for acute exposures and reproductive effects for longer-term exposures. As indicated in the EFED ecological risk assessment (U.S. EPA/OPP 2003d, Table 4, p. 100), acute exposures are assessed using the LD_{50} value of 301 mg/kg bw (MRID 00148500) and longer-term exposures are based on a reproductive NOAEC of 4 mg/kg bw/day (MRID 44732901). EFED refers to the reproductive NOAEC in terms of dietary concentrations – i.e., 75 ppm NOAEC and 300 ppm LOAEL. This appears to be a dose-conversion that is not explained by EFED. As indicated in the risk assessment by the U.S. EPA/OPP Health Effects Division (U.S. EPA/OPP 2007c, Table A.2.2, p. 80), the reproductive study used by EFED involves gavage, not dietary, administration.

As discussed in the hazard identification for human health (Section 3.1.5), a distinction between acute and chronic toxicity is not warranted for carbaryl. Thus, only a single toxicity value is used in the current Forest Service risk assessment (Section 4.3.2). The reproductive NOAEC of 4 mg/kg bw/day is used for both acute and chronic exposures. The oral LD_{50} is not used for deriving HQ values because the Forest Service elects not to base risk assessments on LD_{50} values if NOAEC values are available (SERA 2007a).

4.3.2.2. Birds

As discussed in Section 4.1.2.2, the U.S. EPA/OPP (2003d) elected not to consider acute risks to birds quantitatively because carbaryl is classified as practically nontoxic to birds after acute gavage exposures. While this classification is justified within the system used by the U.S. EPA – i.e., registrant submitted studies on quail and mallards – other studies are available with acute gavage LD_{50} values as low as 18 mg/kg bw indicating that carbaryl may be toxic to smaller birds. Based on the general classification scheme used by the U.S. EPA (SERA 2007a, Table 4-1), these lower toxicity values could be used to classify carbaryl as *highly toxic* to birds.

For the current risk assessment, the approach taken with birds is similar to that used for mammals – i.e., the same toxicity value is used for both acute and chronic exposures. The lowest chronic toxicity value for birds is from a dietary reproduction study in mallard ducks in which no effects were noted at 300 ppm (21 mg/kg bw/day) and decreased egg production was noted at 600 ppm (42 mg/kg bw/day) (U.S. EPA/OPP 2003d, ACC263701, p. 25). The NOEC of 21 mg/kg bw/day is used to assess risks to birds from both acute and chronic exposures.

A reservation with this approach involves the LD_{50} values of 56 mg/kg bw in red-winged blackbirds and 16 mg/kg bw in starlings (Table 15). These LD_{50} values are from gavage exposures – i.e., the direct placement of the chemical into the stomach of the bird, which are not representative of exposures through food consumption, the relevant route of exposure in this risk assessment. In addition, the available field studies in birds do not report adverse effects after exposure to carbaryl involving application rates of up to about 6 lbs a.i./acre (Section 4.1.2.2). Thus, the use of the chronic dietary NOEC of 21 mg/kg bw/day used by the U.S. EPA/OPP (2003d) should be protective for both acute and longer-term exposures.

4.3.2.3. Reptiles

Very little information is available concerning the toxicity of carbaryl to reptiles (Section 4.1.2.3) and this information does not support the derivation of separate toxicity values for this group of organisms. The limited quantitative information that is available on reptiles involves aquatic exposures to water snakes and indicates that fish are more sensitive than snakes.

4.3.2.4. Terrestrial Invertebrates

As summarized in Section 4.1.2.3.1, published studies regarding carbaryl toxicity to honey bees do not report lower toxicity values than the LD_{50} value cited by the U.S. EPA/OPP (2003d) – i.e., 0.11 μg/bee or 1.2 mg/kg bw. Furthermore, based on standard toxicity studies, the honey bee appears to be the most sensitive terrestrial arthropod. Thus, the toxicity value of 1.2 mg/kg bw is used to assess the effects of carbaryl exposures to terrestrial arthropods. As also discussed in Section 4.1.2.3.1, however, field studies suggest that other arthropods such as some spiders may be more sensitive than honeybees to carbaryl exposure. Since controlled bioassays on spiders are not available, the exposure assessment is considered qualitatively in the risk characterization (Section 4.4).

4.3.2.5. Terrestrial Plants (Macrophytes)

Consistent with the approach taken in the recent ecological risk assessment conducted by the U.S. EPA (U.S. EPA/OPP 2003d), no quantitative toxicity values are derived for terrestrial plants. As summarized in 4.1.2.5, however, incident reports are available suggesting that carbaryl may damage some terrestrial plants, particularly crops such as citrus. This assessment is considered qualitatively in the risk characterization.

4.3.2.6. Terrestrial Microorganisms

As with terrestrial plants, the limited data concerning carbaryl toxicity to terrestrial microorganisms do not support a dose-response relationship for this group of organisms.

4.3.3. Aquatic Organisms

4.3.3.1. Fish

Generally, the Forest Service tries to adopt toxicity values consistent with those of the U.S. EPA. As discussed in Section 4.1.3.1, however, the EPA's ecological risk assessment uses an acute LC_{50} of 0.25 ppm for characterizing acute risks and a reproductive NOEC of 0.21 for characterizing chronic risks to fish (U.S. EPA/OPP 2003d, Table 12, p. 161). While these are

standard endpoints for ecological risk assessments conducted by the U.S. EPA, they do not appear to be sufficiently protective for carbaryl, based on recent information from the published literature.

For the current Forest Service risk assessment, the dose-response assessment for fish is based on the inhibition of brain AChE activity. The same approach is used in this risk assessment for mammals and birds and is identical to the approach used by the U.S. EPA in their most recent human health risk assessment (U.S. EPA/OPP 2007c). As discussed in Section 4.1.3.1, this approach follows the suggestion by Beauvais et al. (2001) that a significant inhibition of brain AChE activity in fish may be associated with secondary effects such as changes in swimming behavior that may impact the survival of fish. As with mammals, this appears to be a more sensitive endpoint than reproductive toxicity for carbaryl.

While data concerning the inhibition of brain AChE activity in fish are not as extensive as the data concerning acute toxicity, substantial differences in sensitivity among species are apparent. The NOEC for brain AChE inhibition of 0.03 ppm for squawfish from the study by Beyers and Sikoski (1994) is used to characterize risks to tolerant species. Based on the study by Ferrari et al. (2004a), rainbow trout are identified as the most sensitive species. An NOEC for trout is not identified in the Ferrari et al. (2004a) study. The LOEC of 0.006 ppm is used directly in the calculation of hazard quotients. Concerns about this approach are considered in the risk characterization for fish. As with mammals, the inhibition of brain cholinesterase in fish is rapidly reversible. Thus, following the same reasoning as applied in the dose-response assessment for mammals and birds, the same toxicity values are used to characterize risks for both acute and chronic exposures.

4.3.3.2. Amphibians

The U.S. EPA's ecological risk assessment for carbaryl does not derive separate toxicity values for amphibians. Following standard EPA practice, the Agency uses the toxicity values for fish to characterize risks to amphibians – i.e., an acute LC_{50} of 0.25 ppm for characterizing acute risks and a reproductive NOEC of 0.21 for characterizing chronic risks (U.S. EPA/OPP 2003d, Table 12, p. 161).

As discussed above, the current Forest Service risk assessment adopts a different and a more conservative approach based on the inhibition of brain AChE activity and uses toxicity values of 0.03 ppm for tolerant fish species and 0.006 ppm for sensitive fish species. As discussed in Section 4.1.3.2, data on frogs and toads suggest that these groups of amphibians are no more sensitive than fish to carbaryl exposure. Based on one comparison of AChE activity between a sensitive fish species (rainbow trout) and a tolerant amphibian species (a South American toad), a case could be made for using the fish toxicity values derived in Section 4.3.3.1 for amphibians.

A limitation with this approach, however, is that it would not consider the study by Rohr et al. (2003). As summarized in Appendix 8 and discussed in Section 4.1.3.2, this study reports adverse effects in a species of salamander (*Ambystoma barbouri*) at 0.005 ppm – i.e., larval mortality – with a NOEC of 0.0005 ppm. A bioassay by Relyea and Mills (2001) involves a

salamander of the same genus – i.e., *Ambystoma maculatum* – exposed to substantially higher concentrations of up to 0.09 ppm. Relyea and Mills (2001) report salamander mortality but, in their study, salamanders were used as a predator-stressor and the investigators do not provide details about the response of the salamanders other than to note that salamanders that died were replaced.

While the study by Relyea and Mills (2001) cannot be viewed as directly supporting the study of Rohr et al. (2003) because of the lack of detail in the Relyea and Mills (2001) study concerning the effects on salamanders, the study by Rohr et al. (2003) appears to be well designed and conducted, presents detailed statistical analyses, and is peer reviewed. Thus, the study by Rohr et al. (2003) can be accepted on its own merits.

Consequently, the current risk assessment uses the NOEC of 0.0005 ppm from the study by Rohr et al. (2003) for assessing risks to sensitive species of amphibians after longer-term exposures. For acute exposures, the toxicity value for sensitive species of fish, 0.006 ppm, is used as a surrogate for sensitive species of amphibians. This approach is taken because the endpoint in the Rohr et al. (2003) study involves a 37-day period of exposure and reproductive endpoints. It is not clear that adverse effects would be seen in even sensitive species of amphibians after short-term exposures.

There is no basis for asserting that the sensitivity to carbaryl of tolerant species of amphibians differs from the sensitivity of tolerant species of fish. Thus, as with the dose-response assessment for fish, the NOEC of 0.03 ppm is used directly to calculate hazard quotients for tolerant species of amphibians.

4.3.3.3. Aquatic Invertebrates

As noted in Section 4.3.3.1 (dose-response assessment for fish), Forest Service risk assessments generally adopt toxicity values from U.S. EPA risk assessments, at least in terms of study selection. Deviations from EPA values are generally limited to endpoint selection, with the U.S. EPA typically using LC_{50} values for acute exposures while the Forest Service prefers to use NOEC values.

The acute toxicity values selected by the U.S. EPA (U.S. EPA/OPP 2003d, Table 2, p. 145) range from 0.0051 ppm (an acute LC_{50} in stonefly larvae) to 2.7 ppm (an acute EC_{50} in oysters). The chronic toxicity values cited by the EPA range from 0.0015 ppm, a reproductive NOEC in *Daphnia magna,* to 0.5 ppm, an NOEC for midge emergence (U.S. EPA/OPP 2003d, Table 12, p. 108).

As discussed in Section 4.1.3.3, the lowest acute LC_{50} in the open literature is 0.0000007 ppm, reported by Shukla and Mishra (1980) for a species of dragonfly. While this value was taken into consideration, it is not used to characterize risk. Although dragonflies may be a sensitive species and this value may be credible, the value is a factor of more than 7000 less than the corresponding toxicity value selected by the U.S. EPA and other more recent and better documented values in the open literature. Furthermore, the study by Shukla and Mishra (1980)

used a formulation of carbaryl that is not used in Forest Service program; moreover, the nature of formulation is not well defined. The more recent study by Sakamoto et al. (2005) reports somewhat similar LC_{50} values in two species of cladocerans – 0.0041 ppm in *Bosmina fatalis* and 0.0035 ppm in *Leptodora kindtii* – which are slightly lower than the 0.0051 ppm value used by EPA. The lower value of 0.0035 ppm is used in the current risk assessment to characterize risk to sensitive aquatic invertebrates. The 2.7 ppm acute EC_{50} in oysters cited by EPA is used to characterize risks in tolerant invertebrates, recognizing that some species may be more tolerant.

For longer-term effects, the EPA NOEC of 0.0015 ppm is supported by two cladoceran reproduction studies (Hanazato 1991b; Oris et al. 1991) that report a modestly lower NOEC of 0.001 ppm. The study by Barry (1999), however, reports a lower toxicity value – i.e., a reproductive LOEC of 0.00032 mg/L in a different cladoceran species, *Daphnia longicephala,* and this value is a factor of about 5 below the EPA NOEC. The formulation of carbaryl used in the study by Barry (1999) study is characterized only as *Yates Carbaryl* with 100 g a.i./L. Little information is available on this product other than that it is registered in Australia and is used as a caterpillar and grasshopper control agent. The current risk assessment uses the NOEC of 0.0015 ppm, also used by the U.S. EPA, to characterize longer-term risks to sensitive aquatic invertebrates. The uncertainty associated with the effects of carbaryl exposure on perhaps more sensitive species is considered qualitatively in the risk characterization.

For tolerant species, the NOEC of 0.5 mg/L cited by the U.S. EPA is maintained. No other more appropriate values were encountered in the literature.

4.3.3.4. Aquatic Plants

As summarized in Section 4.1.3.4, only two toxicity studies, one on technical grade carbaryl and the other on the Sevin XLR Plus formulation, are available concerning effects on aquatic plants, and both studies involve exposure to *Pseudokirchneriella subcaptitata*. Consistent with the approach used by the U.S. EPA/OPP (20043), the lowest toxicity value is used. In this case, the toxicity value is from the bioassay on technical grade carbaryl. The U.S. EPA/OPP (2003d) used the EC_{50} of 1.27 ppm for acute exposures and the NOEC of 0.29 ppm for longer-term exposures. Following standard Forest Service practice (SERA 2007a), this risk assessment uses the NOEC of 0.29 ppm for both acute and longer-term exposures.

4.4. RISK CHARACTERIZATION

4.4.1. Overview

As with the human health risk assessment, the risk characterization for nontarget species focuses primarily on broadcast applications for leaf beetle control, because the exposure assessments that underlie the development of the hazard quotients are relatively standard – i.e., they represent exposures that can be reasonably anticipated in programs for leaf beetle control. For bark beetle prevention, exposures are based on treatment unit assumptions, specifically the treatment of a single high-value tree. Because of this limitation, the hazard quotients for bark beetle applications are relative, and the risk characterization for bark beetle applications must be assessed at the program level, once the number and size of the trees to be treated as well as the area over which the treatments will be applied can be specified. Qualitatively, the general identification of the nontarget organisms at greatest risk may be similar in applications for both leaf and bark beetle.

While carbaryl is more toxic to insects and some other arthropods, terrestrial vertebrates may be at risk at all but the lowest anticipated application rate. At 0.1 lb a.i./acre, the consumption of contaminated grasses by large and small mammals leads to hazard quotients that marginally exceed the level of concern (1.1 to 1.2) and only at the upper range of plausible exposures. The only other risk quotients that exceeds the level of concern at the lowest application rate is the upper bound of the risk quotient for a predatory bird consuming contaminated fish after an accidental spill (an HQ of 3) and the upper bound of the risk upper bound of the quotient for a small mammal consuming insects (an HQ of 1.7).

The typical application rate (0.75 lb a.i./acre) and the highest application rate (1 lb a.i./acre) do not differ remarkably, and the risk characterizations for birds and mammals are similar. Hazard quotients associated with acute exposures exceed the level of concern for both accidental scenarios (i.e., direct spray and a spill into a pond) as well as expected exposures based on the consumption of contaminated vegetation and prey. No hazard quotients for the longer-term exposure scenarios exceed the level of concern.

Carbaryl is an effective insecticide. Accordingly, adverse effects, including mortality, are likely to be observed in terrestrial insects exposed to carbaryl during direct spray applications. This does not mean, however, that the consequences of broadcast or directed applications of carbaryl will lead to significant environmental harm (i.e., wide-spread mortality in all insect species). The environmental impact of carbaryl applications will vary in degree according to the timing of the applications as well as which insects and other arthropods are exposed. The available data suggest that the impact of carbaryl exposure is not likely to be substantial or significant with respect to terrestrial non-arthropods.

As with terrestrial invertebrates, the available data on aquatic invertebrates indicate that arthropods are generally more sensitive than non-arthropods to the effects of carbaryl. While the differences in sensitivity among arthropods are not substantial for acute exposures, longer-term

studies suggest that some arthropods (e.g., midges) may be more tolerant than others (e.g., daphnids) to the effects of carbaryl exposure.

Based on the standard accidental spill scenario used in this risk assessment as well as other Forest Service risk assessments, spills of field solutions of carbaryl in the range of application rates considered in this risk assessment could adversely impact most groups of aquatic organisms. The only exception involves tolerant invertebrates (e.g., mollusks) at the lowest application rate. In fact, the consequence of a serious accidental spill is likely to be substantial mortality among exposed fish, invertebrates, amphibians, and aquatic plants. Secondary effects, such as algal blooms, could be part of the recovery process and be interconnected with population shifts among invertebrate grazers and predators.

Based on expected environmental concentrations – i.e., carbaryl concentrations anticipated from the normal application of the insecticide – the risk characterization is highly dependant on the application rate. At the lowest anticipated application rate (0.1 lb a.i./acre), no adverse effects are anticipated in any group of organisms. At the typical and upper bound of the application rate (i.e., 0.75 and 1 lb a.i./acre), expected peak concentrations could have adverse effects on sensitive species of fish, invertebrates, and amphibians. Based on the acute hazard quotients, sensitive invertebrates may be the group of aquatic organisms at greatest risk. For longer-term effects at the two higher application rates, the group at greatest risk appears to be amphibians. Except for the accidental spill scenario, the adverse effects would likely be subtle rather than lethal in all aquatic vertebrates, because the risk characterization is based on toxicity values for the inhibition of brain AChE.

4.4.2. Terrestrial Organisms

4.4.2.1. Mammals

For the broadcast application of carbaryl in leaf beetle control programs, the qualitative interpretation of risks to mammals is highly dependant on the application rate. At the lowest anticipated application rate of 0.1 lb a.i./acre, none of the longer-term hazard quotients exceed or even approach a level of concern. The upper bound of two of the hazard quotients associated with the consumption of contaminated grasses slightly exceed the level of concern for a small mammal (HQ of 1.1) and a large mammal (HQ of 1.2).

The two higher application rates – a typical rate of 0.75 lb a.i./acre and an anticipated maximum rate of 1 lb a.i./acre – do not differ substantially and the hazard quotients lead to similar qualitative risk characterizations. Across the range of plausible exposures, the level of concern (an HQ of 1) is exceeded for all acute scenarios involving the consumption of contaminated grass (HQ values ranging from 3 to 12). The consumption of contaminated fruit leads to hazard quotients that approach but do not exceed a level of concern – i.e., a maximum HQ of 0.7. The consumption of contaminated water leads to hazard quotients that exceed the level of concern only after an accidental spill and only at the upper bound of exposure (HQ values ranging from 2 to 3). Based on expected peak concentrations in ambient water, the hazard quotients are substantially below the level of concern – i.e., a maximum HQ of 0.001 at the application rate of 1.0 lb a.i./acre.

The risk characterization presented in the current Forest Service risk assessment is not directly comparable to that presented by the U.S. EPA (U.S. EPA/OPP 2003d) because of methodological differences. The U.S. EPA does not assess the consequences of longer-term exposures. The RQ values derived by EPA (equivalent to HQ values in the current risk assessment) are based on peak or acute exposures. As discussed in Section 4.3.2.1, the acute RQ values derived by the U.S. EPA are based on the acute LD_{50} of 301 mg/kg bw. The "chronic RQ" derived by EPA is for acute exposure but uses the 4 mg/kg bw/day NOAEL from the reproductive study in rats. This is the same NOAEL used in the current Forest Service risk assessment for both acute and chronic exposure. Thus, the acute hazard quotients used in the current Forest Service risk assessment are most directly comparable to the "chronic RQ" values given in the EPA assessment. For an application rate of 1 lb a.i./acre, the chronic RQ values reported by EPA would range from 0.2 to 3.2 (U.S. EPA/OPP, 2003d, p. 96, adjusting for differences in the application rate of 0.5 lb a.i./acre are used by EPA). As indicated in Worksheet G03c of Attachment 1, the corresponding hazard quotients derived in this risk assessment range from 4 to 11. The somewhat greater hazard quotients in this risk assessment are due to the use of a small (20g) mammal in this Forest Service risk assessment rather than the use of a substantially larger mammal (the rat) in the EPA risk assessment.

The application of any effective insecticide, including carbaryl, is likely to alter the numbers and/or species composition of terrestrial insects and other arthropods. This alteration could lead to changes in food availability, thereby causing secondary effects of exposure on mammals. These secondary effects are likely to vary over time and among the different species of mammals.

4.4.2.2. Birds

The hazard quotients for birds exposed to carbaryl are somewhat less than those for mammals. This relationship follows from the differences in toxicity values. As detailed in Section 4.3.2.2, birds appear to be somewhat less sensitive than mammals to carbaryl. For birds, the toxicity value used to calculate hazard quotients is the reproductive NOAEL of 21 mg/kg bw/day, which is about 5 times greater than 4 mg/kg bw/day, the reproductive NOAEL for mammals.

Qualitatively, the risk characterization for birds is similar to that for mammals, with respect to broadcast applications in leaf beetle control programs. None of the longer-term hazard quotients for birds even approach a level of concern (an HQ of 1.0). For acute exposure scenarios, the qualitative risk characterization for the lowest anticipated application rate (0.1 lb a.i./acre) is much less severe than for the typical application rate (0.75 lb a.i./acre) or highest anticipated application rate (1 lb a.i./acre). At the lowest application rate, none of the lower bound or central estimates exceed the level of concern. For upper bound exposure estimates, the only hazard quotient that exceeds the level of concern is the consumption of contaminated fish by a predatory bird after an accidental spill – i.e., an HQ of 3.

At the two higher application rates, the hazard quotients exceed the level of concern for the consumption of contaminated insects (HQ values ranging from 1.3 to 4 at an application rate of

0.75 lb a.i./acre and from 1.8 to 5 at an application rate of 1 lb a.i./acre). For the consumption of contaminated fish, the level of concern is exceeded only at the central estimate of the exposure level (HQ values ranging from 1.5 to 1.8) and the upper bound of the exposure level (HQ values ranging from 22 to 29).

As discussed in the dose-response assessment for birds (Section 4.3.2.2), acute gavage LD_{50} values as low as 18 mg/kg bw are reported for some species of small passerines. The hazard quotients for the consumption of contaminated fish are based on much higher levels of exposure – i.e., 460 mg/kg bw at 0.75 lb a.i./acre and about 613 mg/kg bw at 1 lb a.i./acre. The exposure scenario for consuming contaminated fish, however, is not relevant to passerines. The exposure scenario for the consumption of contaminated insects is relevant to passerines and is associated with doses of about 85 mg/kg bw at 0.75 lb a.i./acre and about 113 mg/kg bw at 1 lb a.i./acre. As discussed in the dose-response assessment for birds, reported gavage LD_{50} values are not well-documented and involve administrations that are much more severe – i.e., the insertion of the full dose directly into the crop of the bird – than dietary exposures – i.e., more gradual intake through feeding. In addition, concern for small birds is not supported by field studies in which application rates of up to 6 lb a.i./acre reportedly had no impact on bird populations.

As with mammals, secondary effects on some species of birds could occur through changes in species composition of terrestrial invertebrates, particularly arthropods. The magnitude of any secondary effects is likely to vary over time and among the different bird species. Such effects, however, are not reported in field studies, and it is not clear that secondary effects on bird populations are of reasonable concern.

4.4.2.3. Reptiles

The available information on reptiles (Section 4.1.2.3) does not support a dose-response assessment for this species. Following the suggestion made by the U.S. EPA/OPP (2003d), potential risks to reptiles may be similar to those for birds.

4.4.2.4. Terrestrial Invertebrates

Based on acute direct spray scenarios, both central and upper estimates of hazard quotients are substantially above unity for bees at all application rates – i.e., from 13 at 0.1 lb a.i./acre to 134 at 1 lb a.i./acre. Carbaryl is an effective insecticide; therefore, the lethal effects of a direct spray of insects are intuitive.

The hazard quotients for honeybees, however, may present an incomplete and possibly misleading risk characterization. While there is little doubt that directly spraying a honey bee and any other of many insects will kill the insect, it is not necessarily so that the normal use of carbaryl in the field will have an adverse impact on bee populations. As discussed in Section 4.1.2.4.1, unpublished field studies summarized by the U.S. EPA/OPP (2003d) suggest that field applications of carbaryl formulations at up to 0.8 lb a.i./acre are not associated with substantial mortality in bees or changes in bee behavior. The reason for the lack of substantial bee mortality from field applications may be that carbaryl formulations are less toxic than technical grade carbaryl to honey bees. In addition, impacts on bees may be influenced by the timing of the

application. There is no specific information concerning the influence of application timing to the impact of carbaryl exposure on honey bees.

While standard toxicity bioassays in honey bees may exaggerate risk to bees, field studies indicate that bees may not be the most sensitive species of insects. As indicated in Section 4.1.2.4.1, Boetel et al. (2005) observed adverse effects on ground spiders exposed to application rates as low as 0.062 lb a.i./acre, and Rehman et al. (1999) observed adverse effects among parasitic wasps exposed to an application rate of 1.12 lb a.i./acre. A speculative, yet perhaps reasonable conclusion is that the impact of carbaryl applications may extend to a board range of terrestrial arthropods, however, which species may be most affected will vary substantially according to specific applications rates.

The toxicity of carbaryl to non-arthropod species of terrestrial invertebrates is less well characterized. The available data in earthworms suggests that risks to non-arthropods will be less than those to arthropods and may even be minimal. As detailed in Section 4.1.2.4.2, typical LC_{50} values for earthworms range from 9 to 263 ppm. These LC_{50} values are below the highest expected peak concentration in soil (217 ppb or 0.217 ppm) by factors of about 40 to more than 1200. Thus, risks to earthworms associated with direct toxicity appear to be minimal.

4.4.2.5. Terrestrial Plants

Consistent with the approach taken by the U.S. EPA/OPP (2003d), risks to terrestrial plants are not considered quantitatively in this risk assessment. Carbaryl is an insecticide that is widely used to protect plants from insect pests. If carbaryl presented a substantial hazard to plants, the use of this compound as an insecticide on plants would be compromised.

Not withstanding this qualification, some incident reports summarized and discussed by the U.S. EPA/OPP (2003d) suggest that damage to some plant species, particularly citrus crops, are associated with carbaryl applications. The relevance of this observation to Forest Service applications seems remote. Given the impact of carbaryl applications on other groups of terrestrial and aquatic organisms, the risk to plants seems negligible.

4.4.3. Aquatic Organisms

4.4.3.1. Fish

The risk characterization for fish depends both on the exposure scenario as well as the substantial differences between sensitive and tolerant species of fish. As detailed in the exposure assessment (Section 4.2.5), three exposure scenarios are used for fish and other aquatic organisms: the concentration after an accidental spill, the peak expected environmental concentrations, and the estimated long-term concentrations of carbaryl in water. In addition, risk is characterized for both sensitive and tolerant species of fish based on the inhibition of brain AChE (Section 4.3.3.1). The rainbow trout, a salmonid, is identified in the literature as the most sensitive species of fish, with a LOAEL of 0.006 ppm for brain AChE inhibition. The most tolerant species identified is squawfish, a predatory cyprinid, with an NOEC of 0.03 ppm for brain AChE inhibition. A reservation associated with using of this range is that brain AChE

inhibition was not studied in many fish species, and greater or lesser sensitivities may exist. On the other hand, the inhibition of brain AChE is clearly the most sensitive and relevant toxicity endpoint for carbaryl.

For the accidental spill scenario, the risk characterization is relatively simple. The hazard quotients for both sensitive and tolerant fish species substantially exceed the level of concern for the entire range of application rates and all estimated concentrations. The lowest hazard quotient is 15 and is associated with tolerant species of fish at the lower bound of the estimated concentration at an application rate of 0.1 lb a.i./acre. The highest hazard quotient is 15,140 and is associated with sensitive species of fish at the upper bound of the estimated concentration at an application rate of 1 lb a.i./acre. The corresponding concentrations in water range from about 0.1 to about 90 mg/L. As discussed in Section 4.1.3.1, the acute LC_{50} values for fish range from about 0.25 to 100 mg/L. Thus, at the range of concentrations likely to be associated with the accidental spill scenario, the expected outcome is mortality among some fish species and extensive mortality among many fish species. Fish that did not die would likely show signs of brain AChE inhibition, which might lead to a spectrum of adverse sublethal effects that compromise the ability of the fish to respond to other stressors or engage in normal activity.

Just as there is little doubt that acute effects would be seen in fish after an accidental spill, there is little basis for asserting that adverse effects in fish are plausible based on expected longer-term concentrations of carbaryl in ambient water. The highest hazard quotient is 0.3 and is associated with the upper bound of expected longer-term concentration at the highest application rate in sensitive species of fish. Because the hazard quotient for sensitive fish species is based on a LOEC rather than a NOEC, sublethal effects cannot be ruled out. Based on the central estimate of longer-term concentrations, however, the hazard quotient is 0.05, below the level of concern by a factor of 20. Thus, while sublethal effects cannot be ruled out in some sensitive species of fish, the effects would probably be uncommon and transient.

The risk characterization for peak expected environmental concentrations is heavily dependant on the application rate. At the lowest anticipated application rate of 0.1 lb a.i./acre, the upper bound of the hazard quotient in sensitive species of fish is 0.6, and the central estimate of the hazard quotient is 0.3. As with the longer-term exposures, this hazard quotient is based on an LOEC rather than an NOEC. Although sublethal effects cannot be ruled out, but the biological significance of any effects is unclear. At the typical application rate of 0.75 lb a.i./acre, the central estimate and upper bound of the hazard quotient for sensitive fish are 3 and 4, respectively. Since these hazard quotients are based on an LOEC for the inhibition of brain AChE activity, adverse sublethal effects could be expected. Tolerant species of fish, however, are not likely to be affected – i.e., the upper bound of the hazard quotient (based on an NOEC) is 0.8. At the highest application rate, 1 lb a.i./acre, the risk characterization is essentially the same as for sensitive species of fish (HQ values of up to 6). For tolerant species of fish, the upper bound of the hazard quotient is 1.1, which slightly exceeds the level of concern.

4.4.3.2. Amphibians

As discussed in Section 4.3.3.2, most of the toxicity values used for amphibians are identical to those used for fish. The only exception involves longer-term exposures in sensitive species of amphibians. Consequently, the risk characterization for amphibians is identical to that for fish, except for longer-term effects in sensitive species of amphibians.

For sensitive species of amphibians, the study by Rohr et al. (2003) is used to define an NOEC of 0.0005 mg/L for larval mortality after longer-term exposures. This value is a factor of 12 below the toxicity value of 0.006 mg/L used for sensitive species of fish. Consequently, all hazard quotients associated with longer-term exposures of sensitive amphibians are a factor of 12 higher than the corresponding hazard quotients for sensitive fish. At the lowest application rate, 0.1 lb a.i./acre, this difference has no impact on the risk characterization: The upper bound of the hazard quotient is 0.4. At the two higher application rates, the upper bounds of the hazard quotients are 3 and 4, respectively, and the central estimates of the hazard quotients are 0.5 and 0.6, respectively.

Thus, unlike the situation with fish, there is an indication that expected longer-term concentrations of carbaryl in surface water could be associated with adverse effects (i.e., larval mortality) in sensitive populations of amphibians. Because the HQ values exceed the level of concern only at the upper bounds of the estimated longer-term exposure levels, these adverse effects might not occur under all conditions. Nonetheless, the upper bounds of the hazard quotients suggest a need to refine the exposure assessments with site-specific information, if applications of carbaryl are planned near surface water inhabited by sensitive species of amphibians.

4.4.3.3. Aquatic Invertebrates

The risk characterization for aquatic invertebrates differs from that of fish and amphibians primarily in terms of tolerant species. For tolerant species, the acute toxicity value is 2.7 mg/L, an EC_{50} in oysters, and the chronic value is an NOEC of 0.5 mg/L for midge emergence (Section 4.3.3.3). These values are factors of about 770 and 300 above the corresponding values for sensitive species – i.e., an acute LC_{50} of 0.0035 mg/L in a cladoceran and a NOEC of 0.0015 mg/L from a daphnid reproduction study. Thus, sensitive species of aquatic invertebrates are only somewhat more sensitive than sensitive species of fish; however, the degree of tolerance to carbaryl exposure appears to be much greater among tolerant aquatic invertebrates, relative to tolerant fish.

Concerning an accidental spill of carbaryl, sensitive species of aquatic invertebrates will be adversely affected across the range of application rates and estimated concentrations with hazard quotients ranging from 130 to over 25,000. For tolerant species of aquatic invertebrates, however, hazard quotients in accidental spill scenarios range from 0.2 to 3 at the lowest application rate and from 1.3 to 25 at the maximum application rate. While adverse effects might be seen in tolerant aquatic invertebrates, the impact would likely be much less than that on more sensitive species.

Based on expected peak and longer term concentrations of carbaryl in ambient water, none of the hazard quotients exceeds the level of concern, even at the highest application rate. The highest hazard quotient for tolerant species is 0.01 – the upper bound of the acute HQ at the highest application rate – which is below the level of concern by a factor of 100.

For sensitive species of aquatic invertebrates, however, only the lowest application rate leads to hazard quotients that are below the level of concern. At the typical application rate of 0.75 lb a.i./acre, the upper bound of the longer-term hazard quotient reaches the level of concern (HQ of 1); the hazard quotients for peak concentrations exceed the level of concern at all but the lower bound of the estimated exposure – i.e., HQ values of 4 (0.4 to 7). At the highest application rate, the upper bound of the hazard quotient for longer-term exposures modestly exceeds the level of concern (an HQ of 1.3). For peak concentrations, the hazard quotients exceed the level of concern at all but the lower bound of the estimated exposure – i.e., HQ values of 6 (0.6 to 9).

4.4.3.4. Aquatic Plants

There is relatively little information concerning carbaryl toxicity to aquatic plants, and risks are characterized for only a single species, *Pseudokirchneriella subcaptitata*, using an NOEC of 0.29 ppm. Based on the exposure scenarios applied to other aquatic species, the anticipated peak or longer-term estimates of carbaryl concentrations in water are not expected to result in adverse effects on this algal species. In the event of an accidental spill, hazard quotients could range from 1.6 (the lower bound for the lowest application rate) to over 300, the upper bound for the highest application rate.

5. REFERENCES

NOTE: The initial entry for each reference in braces {} simply specifies how the reference is cited in the text. The final entry for each reference in brackets [] is for internal tracking of documents and will be deleted before the report is delivered.

E-Docket– These are from one of the following E-Dockets maintained by U.S. EPA: EPA-HQ-OPP-2006-0801 (most recent), EPA-HQ-OPP-2003-0376, EPA-HQ-OPP-2003-0101, EPA-HQ-OPP-2002-0138 (old). To get the complete listing of items available, go to Regulations.gov. Select Advanced Search -> Docket Number. Enter one of the above ID's in the ID field. All three screened in detail on October 16, 2006. Selected references downloaded and added to reference list.

SET01– Initial literature search via NAL (National Agricultural Library), the Internet or from BioDox. N = 194.

SET02– Secondary references added to list on Oct 10, 2006. N=14.

SET03– Supplemental searches via NAL on Oct 10, 2006. N = 36.

SET04– Papers cited by Cox 2005 that may be useful but were not flagged for SET01 in our original screen. Request to NAL on Oct 10, 2006. N=5.

SET05– Odds and ends identified after Oct 16, 2005.

SET06– Update literature search conducted on April 10, 2007. N=19.

SET07– References taken from Interim Draft, Human and Ecological Risk Assessment of Carbaryl for Bark Beetle Prevention, Dave Bakke, 2004. N=10.

SET08– References identified after August, 2007.

SET09– References identified in internal review.

SET10– References identified in peer review.

FSUse– Information received from Forest Service regions on carbaryl use.

FOIA01– These are references that from U.S. EPA under FOIA (Freedom of Information Act). Added to reference list on Oct 10, 2006. N = 110.

Internet– Documents (e.g., EPA and WHO) that from the Internet. N = 4 as of October 2, 2006.

IRED– These are references from the U.S. EPA Interim Reregistration Eligibility Decision (IRED) dated Oct 22, 2004.

RED– These are EPA documents associated with the September, 2007 release of the RED for carbaryl.

Mal05- Citations from SERA malathion risk assessment in progress.

WHO01– These are references from the WHO (1994). Not all have been added to bibliography. N=735.

EXOTOX1– These are references added on January 5, 2007. The references are taken from additional searching and a screen of EXOTOX (aquatic and terrestrial). A total of 156 references have been added. Of these, 99 have been ordered from NAL.

The second entry indicates the initial assignment of the priority for retrieving the reference and not the final status of the document – i.e., most items marked as GET1 and GET2 have been recieved. For those received from BioDox, the priority is changed to BioDox. The Forest Service will have restricted rights to these under copyright law.

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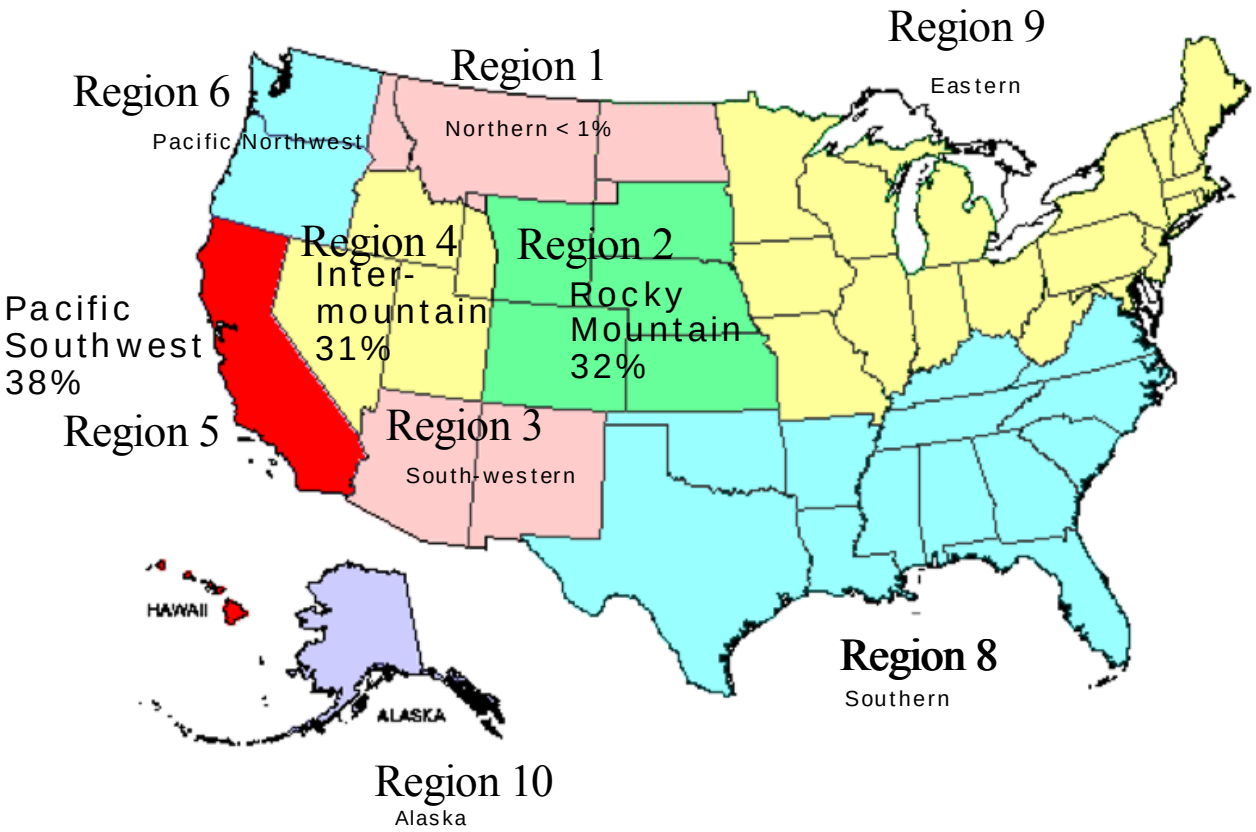
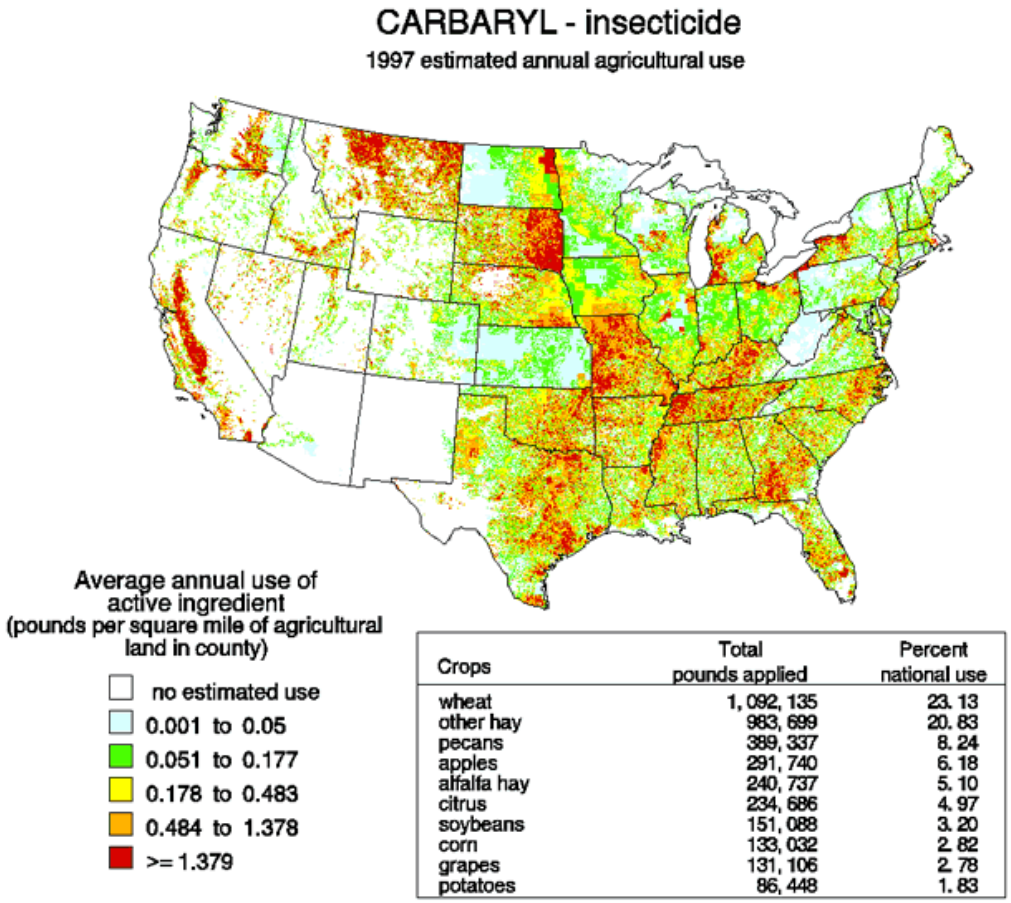


Figure 1: Uses of carbaryl by the Forest Service in 2004

Source: http://www.fs.fed.us/foresthealth/pesticide/reports.shtml



Crops	Total pounds applied	Percent national use
wheat	1,092,135	23.13
other hay	983,699	20.83
pecans	389,337	8.24
apples	291,740	6.18
alfalfa hay	240,737	5.10
citrus	234,686	4.97
soybeans	151,088	3.20
corn	133,032	2.82
grapes	131,106	2.78
potatoes	86,448	1.83

Figure 2: Agricultural uses of carbaryl in the United States.
Source: U.S. Geologic Survey (USGS 1998)

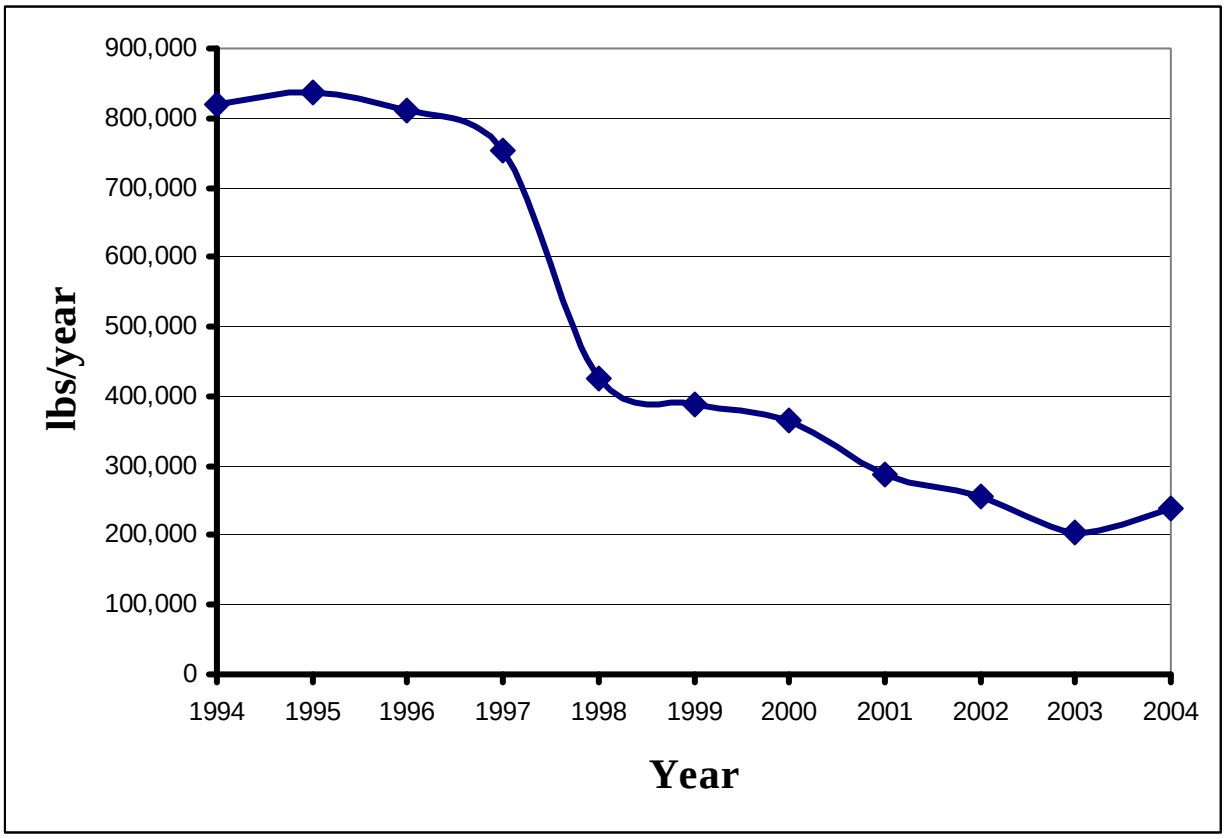


Figure 3: Use of carbaryl in California from 1994 to 2004

Source: California Department of Pesticide Regulation (CDPR 2006

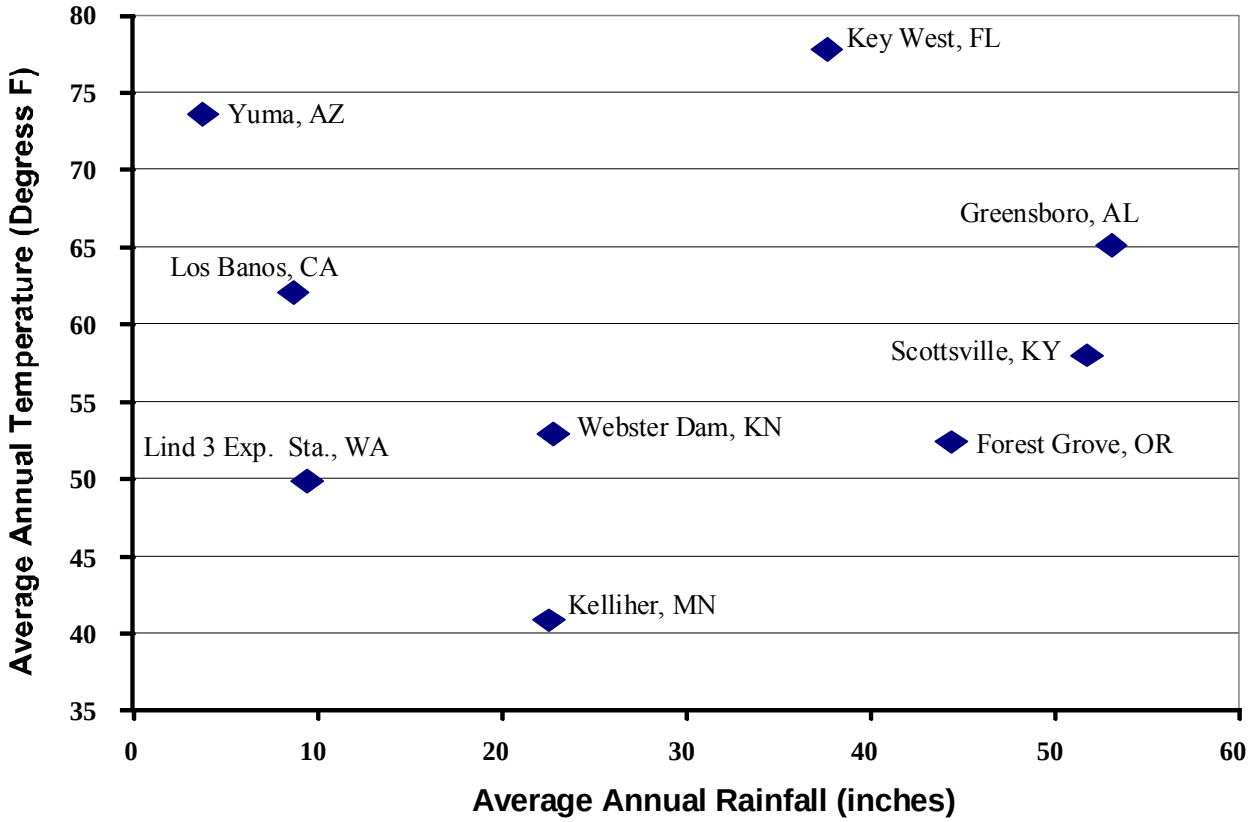


Figure 4: Specific Sites Used in Gleams-Driver Modeling

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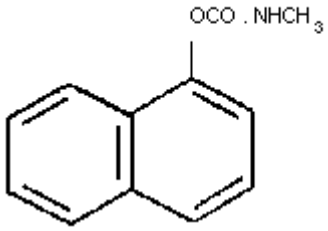
Table 1: Selected physical and chemical properties of carbaryl

Property	Value	Reference
Structure		WHO 1994
Aerobic microbial half-life	4 – 5 days (soil and water)	U.S. EPA/OPP 2004a
	4 days (sandy loam soil)	MRID 42785101 in U.S. EPA/OPP 2003d
	4.9 days (water)	MRID 43143401 in U.S. EPA/OPP 2003d
Anaerobic microbial half-life	2 – 3 months (soil/water)	U.S. EPA/OPP 2004a
	72 days (soil)	U.S. EPA/OPP 2003d
	72 days (water)	MRID 42785102 in U.S. EPA/OPP 2003d
Appearance/state, ambient	Colorless to light tan crystals	Tomlin 2004
Bioconcentration	14x: edible tissue 75x: viscera 45x: whole fish	Chib 1986 cited in U.S. EPA/OPP 2003d
	7.5x, maximum	WHO 1994 citing Kanazawa (1975)
Boiling point	315 °C	CambridgeSoft 2006
CAS number	63-25-2	Tomlin 2004
Commercial Formulations (Manufacturer)	Adios (BASF); Carbait (Micro Flo); Carbamec (PBI/Gordon); Cekubaril (Cequisa); Efaryl (Efthymiadis); Karl (Sanonda); Parasin-G (Kemio); Raid (Nagarjuna Agrichem); Sevin (Bayer CropScience, Certis Europe); SunSin (Sundat) mixtures: Sevidol (+ gamma-HCH) (Crop Health)	Tomlin 2004
Commercial Formulations (other)	Arilat, Arilate, Arylam, Atoxan, Bercema, Caprolin, Carbacine, Carbatox, Carbavur, Carbomate, Carpolin, Denapon, Dicarbam, Dyna-carbyl, Karbaryl, Karbatox, Karbosep, Menaphtam, Monsur, Mugan, Murvin, Oltitox, Panam, Pomex, Prosevor, Ravyon, Seffein, Sevimol, Vioxan	WHO 1994
Conversion factors	1 ppm in air = 8.22 mg/m^3 of air 1 mg/m^3 of air = 0.12 ppm in air	WHO 1994
Dislodgeable foliar residue	1.1 % of application rate (turf)	U.S. EPA/OPP 2003e, p. 114
	16 % of application rate average for various crops	U.S. EPA/OPP 2003e, p. 114
	1.54 – 7.12 µg/cm^2 (application rate not specified)	Walters et al. 2003

Property	Value	Reference
Field half-life	14 (4-22) [2]	USDA/ARS 1995
	Forestry Dissipation Foliar $t_{1/2}$ = 21 days Leaf Litter $t_{1/2}$ = 75 days Soil $t_{1/2}$ = 65 days	MRID 43439801 cited in U.S. EPA/OPP 2003d and Hastings et al. 2001.
Foliar half-life	3.2 days (upper 90% of **3.71 days**) **Used by EPA**	U.S. EPA/OPP 2003d
	7	Knisel and Davis 2000
Foliar washoff	0.91 **Used by EPA**	U.S. EPA/OPP 2003d
	0.55	Knisel and Davis 2000
Henry's law constant	7.39×10^{-5} Pa m^3 mol^{-1} (Calc)	Tomlin 2004
	2.74×10^{-4} Pa m^3 mol^{-1}	CDPR 2007
	2.8×10^{-4} Pa m^3 mol^{-1}	USDA/ARS 1995
	1.28×10^{-8} atm m^3 mol^{-1}	Suntio, et al., 1988 cited in U.S. EPA/OPP 2003d
	5.3×10^{-6} (unitless)	WHO 1994
Kd (Koc), soil type, ml/g	3.89 (163), sand 2.45 (1054), sand 2.93 (504), loamy sand 3.29 (157), silt loam 4.69 (152), silt loam 0.438 (26), sandy clay loam	USDA/ARS 1995
Kf (Koc), soil type, ml/g	1.74 (207), sandy loam 2.04 (249), clay loam sediment 3.00 (211), silt loam 3.52 (177), silty clay loam 1/n values ranged from 0.78-0.84	MRID 43320701 cited in U.S. EPA/OPP 2003d
Koc, ml/g	100 – 600	WHO 1994
	196 **Used by EPA**	U.S. EPA/OPP 2003d
	300	Knisel and Davis 2000
	290	CDPR 2007
Litter half-life, days		
log K_{ow}	1.85 [Kow = $10^{1.85}$ = 70]	Tomlin 2004
	2.36	CDPR 2007
	2.31 (2.29 – 3.46) [2]	USDA/ARS 1995
	2.34 (given as untransformed value of 217)	U.S. EPA/OPP 2004a
	2.36 (given as untransformed value of 229)	Windholz et al., 1976 cited in U.S. EPA/OPP 2003d
	1.59 – 2.3	WHO 1994
Melting point	142 °C	Tomlin 2004
Metabolites, animal	1-napthol	Tomlin 2004
Metabolites, environmental	1-naphthol → CO_2	U.S. EPA/OPP 2004a
Metabolites, photolysis	1-naphthol	WHO 1994
Metabolites, plant	4-hydroxycarbaryl, 5-hydroxycarbaryl and methylol-carbaryl	Tomlin 2004

Property	Value	Reference
Molecular formula	$C_{12}H_{11}NO_2$	Tomlin 2004
Molecular weight	201.2	Tomlin 2004
SMILES Notation	CNC(=O)Oc1cccc2ccccc12	Tomlin 2004
Sediment half-life, days	29.6 (aerobic) **Used by EPA**	U.S. EPA/OPP 2003d
	216.6 (anaerobic) **Used by EPA**	
	O=C(Oc(c(c(ccc1)cc2)c1)c2)NC	Meylan and Howard 2000
Soil half-life (NOS), days	7 – 4 (sandy loam)	Tomlin 2004
	14 – 28 (clay loam)	
	10	Knisel and Davis 2000
	<3 – 90 (may include dissipation)	WHO 1994
Soil half-life (aerobic), days	17 (<7 – 27)	USDA/ARS 1995
	12 **Used by EPA**	U.S. EPA/OPP 2003d
Soil half-life (anaerobic), days	46	USDA/ARS 1995
Soil photolysis	Highly variable with experimental conditions	WHO 1994
Specific gravity	1.232 (20 °C)	Tomlin 2004
Synonyms, general	1-naphthalenyl methylcarbamate (Chem Abst)	Tomlin 2004
	1-naphthyl methylcarbamate (IUPAC)	
Synonyms, commercial	Compound 7744, ENT 23,969, ENT 23969, Experimental insecticide 7744, Germain's HSDB 952, NAC, NMC 50, Union Carbide 7744	WHO 1994
U.S. EPA Dockets [3]	EPA-HQ-OPP-2003-0376	http://www.epa.gov/oppsrrd1/reregistration/carbaryl/
	EPA-HQ-OPP-2003-0101	
	EPA-HQ-OPP-2002-0138	
Vapor pressure	4.1×10^{-2} mPa (23.5 °C) [0.054 mm Hg; mPa = 0.76 mm Hg]	Tomlin 2004
	4.1×10^{-5} mm Hg (26°C)	U.S. EPA/OPP 2004a
	1.36×10^{-7} mm Hg (25°C)	Ferrira and Seiber, 1981 cited in U.S. EPA/OPP 2003d
	1.17×10^{-6} to 3.1×10^{-7} mmHg at 24-25 °C	Who 1994
Vegetation half-life	14 days	EXTOXNET 1996
	3.2 days	EFED as cited by NPIC 2003
Water half-life (NOS)	<0.1 – 100 days (low range flowing, upper range laboratory)	WHO 1994
Water hydrolysis half-life	12 days (pH 7); 3.2 hours (pH 9)	Tomlin 2004
	10.5 days ($k=0.066$ days^{-1})	USDA/ARS 1995
	Stable under acidic conditions	U.S. EPA/OPP 2004a
	12 days (pH 7); 3.2 hours (pH 9)	
	Stable (pH 5); 12 days (pH 7); 3.2 hours (pH 9)	MRID 00163847 and MRID 44759301 cited in U.S. EPA/OPP 2003d
	Stable under acidic conditions; 10 – 16 days (pH 7); 1.3 – 1.9 days (pH 8)	WHO 1994 citing Aly and El Dib, 1971a

Property	Value	Reference
Water photolysis half-life	Stable	Tomlin 2004
	45 days (k=0.0154 days^{-1})	USDA/ARS 1995
	21 days	MRID 41982603 in U.S. EPA/OPP 2003d
Water solubility (mg/L)	120 (20 °C)	Tomlin 2004
	100 (20 °C) 110 (22 °C) 120 (30 °C)	USDA/ARS 1995
	32 (20 °C) **Used by EPA**	Suntio, et al., 1988 cited in U.S. EPA/OPP 2003d
	40 (25 °C)	U.S. EPA/OPP 2004a
	120	Knisel and Davis 2000
	40 (30 °C)	EXTOXNET 1996
	120 (20 °C) 104 (25 °C) 40 (50 °C)	CDPR 2007
	82.6 [0.00826 g/100 mL]	CambridgeSoft 2006

[1] Specific environmental fate parameters used in modeling are discussed in Section 3.2. Common values (e.g., molecular weight) are given in many standard references (e.g. EXTOXNET 1996; USDA/ARS 1995). Preference is given to Tomlin (2004) and other citations are given only if values differ remarkably.

[2] Recommended value (range of reported values)

[3] The U.S. EPA Dockets contain a very large amount of information compiled by U.S. EPA/OPP in the Reregistration process for carbaryl. Specific items from the dockets are cited in this risk assessment. To access the dockets, go to http://www.regulations.gov/fdmspublic/component/main, select Advanced Search -> Docket Search, and then enter the docket number in the "Docket ID" field.

Table 2: Carbaryl formulations with forestry uses covered in this risk assessment

Trade Name	Manu-facturer	Active Ingredient (% by weight)	Lbs a.i. per Unit	General Application Rates (lbs a.i./acre)	Forestry Application Rates (lbs a.i./acre for broadcast applications followed by application instructions for bark for bark applications)
			Liquid Formulations		
Sevin 4F	Bayer CropScience	43%	4 lbs a.i./gal	0.25 – 7.5 [Max CA = 16[b]]	0.75 – 1 1 gallon of 2% solution per 50 ft^2 of bark [c]
Sevin SL	Bayer CropScience	43%	4 lbs a.i./gal	0.25 – 7.5 [Max CA = 16[b]]	0.75 – 1 1 gallon of 2% solution per 50 ft^2 of bark [c]
Sevin XLR	Bayer CropScience/ Suspension	44.1%	4 lbs a.i./gal	0.25 – 7.5 [Max CA = 16[b]]	0.75 – 1 1 gallon of 2% solution per 50 ft^2 of bark [c]
			Granular Formulations		
Sevin 80 Solupak	Bayer CropScience	80%	1 lb a.i./ pack	1 – 5 [Max CA = 16[b]]	1 1 gallon of 2% solution per 50 ft^2 of bark [c]
Sevin 80 WSP (CA)	Bayer CropScience	80%	1 lb a.i./ pack	1 – 5 [Max CA = 16[b]]	1 1 gallon of 2% solution per 50 ft^2 of bark [c]
Sevin 80 WSP	Bayer CropScience	80%	1 lbs a.i./ pack	1 – 8 [Max CA = 16[b]]	0.25 – 1 [e] 1 gallon of 2% solution per 50 ft^2 of bark [c]
			Manufacturing Concentrate (for reformulation only)		
Sevin 97.5 %	Bayer CropScience [f]	97.5%	N/A	N/A	N/A
Carbaryl 99%	Burlington Scientific [f]	99%	N/A	N/A	N/A

[a] Source: www.greenbook.net unless noted otherwise
[b] In California only, up to 16 lbs a.i./acre for the control of California red scale or yellow scale.
[c] See Section 2.4.2 for a detailed discussion of mixing directions and concentrations in field solutions.
[d] Label expresses application rates from 1.25 to 6.25 lbs formulation per acre.
[e] Lower range (0.27 lb a.i/acre) for mosquito control. Upper range for mosquito control as well as the control of several other insect pests.
[f] From U.S. EPA Pesticide Product Label System. Available at http://www.epa.gov/pesticides/ pestlabels/

Table 3: Known inerts contained in commercial formulations of carbaryl that may be used in Forest Service Programs

Formulation [a]	Inerts: Name, CAS No., EPA Classification [b]	Inert % by Weight
Sevin 4F	Ethanol [CAS 64-17-5], List 4B	N.S.
Not compatible with aliphatic and aromatic solvents [e]	1,2-Propylene glycol [CAS No. 57-55-6], List 4B	N.S.
	Microfine suspension in aqueous solution [e]	N.S.
Sevin SL	Ethanol [CAS 64-17-5] , List 4B	N.S.
	1,2-Propylene glycol [CAS No. 57-55-6] , List 4B	N.S.
Sevin XLR Plus	1,2-Propylene glycol [CAS No. 57-55-6] , List 4B	N.S.
	Fine (ca. 5 micron) particulates (NOS) [d] Sticker (NOS) [d]	N.S.
Sevin 80S	Synthetic amorphous silica [CAS No. 112926-00-8], List 4A	12%
	Quartz (Silica, Crystalline) [CAS No. 14808-60-7], List 4A	0.05%
	Hydrated silica [CAS No. 63231-67-4] [c] , List 4A	N.S.
	Poly(oxypropylene)block polymer with poly(oxyethylene) [CAS No. 9003- 11-6] [c], List 4B	N.S.
	Mono-calcium salt of polymerized aryl alkylsulfonic acids [CAS No. 8061-52-7] [c], List 4B	N.S.
	Lignosulfonate, calcium salt [CAS No. 8061-52-7] [c], List 4B	N.S.
	Kaolin clay [CAS No. 1332-58-7] [c] , List 4A	N.S.
	Attapulgite clay [CAS No. 8031-18-3] [c], List 4A	N.S.
	Sodium dialkyl naphthalene sulfonate [CAS No. 53028-07-2] [c], not listed	N.S.
	Sodium dioctyl sulfosuccinate [CAS No. 577-11-7] [c], List 4B	N.S.
	Soap (sodium salt of fatty acid) [c], List 4B	N.S.
	Citric acid [CAS No. 77-92-9] [c], List 4A	N.S.
	Naphthalene sulfonic acid formaldehyde condensate, ammonium and sodium salt [CAS No. 83453-42-3] [c], not listed	N.S.
	Surfynol TG-E [c] , not listed	N.S.
Sevin 80WSP (CA) and Sevin 80WSP	Calcium silicate [CAS No. 1344-95-2], List 4A	N.S.
	Quartz (Silica, Crystalline) [CAS No. 14808-60-7], not listed	0.11%
	Diatomaceous earth [CAS No. 61790-53-2], List 4A	N.S.

[a] See Table 2 for additional information on formulations.
[b] Unless specified otherwise, information is taken from MSDS sheets at http://www.greenbook.net/. See Section 3.1.14 for a discussion of the EPA classification.
[c] Information obtained from U.S. EPA through FOIA by the Northwest Coalition for Alternatives to Pesticides. See http://www.pesticide.org/FOIA/carbaryl.html.
[d] Frank (2004)
[e] Product label available at www.GreenBook.net.

Table 4: Use of Carbaryl by Forest Service Region in 2004

Broadcast Applications

Region	Pounds	Acres	lbs/acre	Proportion (based on total pounds used)
1: Northern	0.9	7	0.13	<0.001
2: Rocky Mountain	441.5	54.5	8.1	0.39
4: Intermountain	693.4	2262	0.31	0.61
Subtotal	1135.8	2323.5	0.49	

Applications to Trees

Region	Pounds	Trees	lb/tree	
2: Rocky Mountain	356	3658	0.097	0.26
4. Intermountain	75	1243	0.06	0.05
5: Pacific Southwest	950.8	778	1.22	0.69
Subtotal	1381.8	5679	0.23	

All Applications Combined

Region	Pounds	Proportion
1: Northern	0.9	<0.001
2: Rocky Mountain	797.5	0.32
4: Intermountain	768.4	0.31
5: Pacific Southwest	950.8	0.38
Grand Total	2517.6	

Table 5: Use of Carbaryl by the Forest Service (all regions combined) from 2000 to 2004 based on applications expressed as lbs/acre

Year	Pounds Used	Acres Treated	Average Application Rate (lbs/acre)
2000	**45**	**20.5**	**2.21**
2001	**3**	**3**	**1.00**
2002	**1,207**	**8,514**	**0.14**
2003	**483**	**1,580.6**	**0.31**
2004 [b]	**1,136**	**2,323.5**	**0.49**
Total	2,874	12,441.6	0.23

Source: http://www.fs.fed.us/foresthealth/pesticide/reports.shtml

[a] Based on total pounds (all years) divided by total acres (all years).

[b] Applications for 2004 include only broadcast rates. A total of 2517.6 pounds were used in all applications combined. See Table 4 for details.

Table 6: Chemical and site parameters used in GLEAMS modeling for carbaryl

Parameter	Clay	Loam	Sand	Note/ Reference
Half-life (days)				
Aquatic Sediment		216.6		Note 1
Foliar		3.71		Note 2
Soil		12		Note 3
Water		12		Note 4
Soil $K_{o/c}$, mL/g		196		Note 3
Sediment K_d, mL/g	0.4	3.3	3.9	Note 5
Water Solubility, mg/L		32		Note 3
Foliar wash-off fraction		0.91		Note 6
Fraction applied to foliage		0.5		Note 7

Note 1 Value used by U.S. EPA/OPP 2003d in PRZM/EXAMS modeling.

Note 2 Value used by U.S. EPA/OPP 2003d in PRZM/EXAMS modeling. Represents an upper 90% confidence bound on the mean from 30 studies from which foliar half-life could be estimated (U.S. EPA/OPP 2003d, p. 64).

Note 3 Value used by U.S. EPA/OPP 2003d in PRZM/EXAMS modeling.

Note 4 Value used by U.S. EPA/OPP 2003d for hydrolysis in PRZM/EXAMS modeling. No adjustment made for photolysis, which has a half-life of about 21 days.

Note 5 Based on values given by USDA/ARS (1995). Value for silt based on silt loam and value for clay based on sandy clay loam.

Note 6 Foliar washoff of 0.91 is the value used by U.S. EPA/OPP 2003d in PRZM/EXAMS modeling.

Note 7 The fractional application to foliage is a default for liquid formulations.

Table 7: Summary of concentrations in streams based on standards GLEAMS modeling

(all units are ug/L or ppb per lb/acre applied)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0	0	0	0	0	0
10	0	0	0	0	0	0
15	0.338	44.3	0	0	0	0
20	0.634	87.2	0	0	0	0
25	0.877	126	0	0	0	0
50	1.4	233	0.00146	0.316	7.14E-06	0.000224
100	1.47	303	0.0638	17	0.0264	0.763
150	1.35	332	0.0845	24.6	0.0843	2.82
200	1.23	349	0.0879	26.8	0.139	5.47
250	1.11	361	0.0862	27	0.179	7.97

Table 8: Summary of concentrations in ponds based on standards GLEAMS modeling

(all units are ug/L or ppb per lb/acre applied)

Annual Rainfall (inches)	Clay		Loam		Sand	
	Average	Maximum	Average	Maximum	Average	Maximum
5	0	0	0	0	0	0
10	0	0	0	0	0	0
15	0.17	2.4	0	0	0	0
20	0.268	5.51	0	0	0	0
25	0.366	9.2	0	0	0	0
50	0.757	30.4	0.00106	0.0509	3.35E-06	3.77E-05
100	1.2	75.5	0.064	4.74	0.0114	0.121
150	1.42	114	0.102	9.02	0.043	0.582
200	1.52	146	0.12	11.7	0.0812	1.35
250	1.57	173	0.129	13.3	0.116	2.24

Table 9: Peak concentrations in a small stream based on Gleams-Driver simulations

(all concentrations in µg/L or ppb per lb/acre applied)			
Site	**Clay**	**Loam**	**Sand**
Dry and Warm Location	0 (0 - 2.04)	0 (0 - 1.38)	0 (0 - 1.04)
Dry and Temperate Location	0.000031 (0 - 0.019)	0 (0 - 0.011)	0 (0 - 0.005)
Dry and Cold Location	0 (0 - 0.6)	0 (0 - 0.26)	0 (0 - 0)
Average Rainfall and Warm Location	6.53 (0.27 - 34.9)	4.3 (0.1 - 26.6)	1.4 (0.005 - 14.8)
Average Rainfall and Temperate Location	6.33 (0.4 - 30.7)	4.52 (0.13 - 22.1)	1.36 (0.009 - 7.54)
Average Rainfall and Cool Location	1.65 (0.024 - 16.8)	1 (0.002 - 11.4)	0.06 (0 - 5.3)
Wet and Warm Location	3.34 (0.4 - 17.8)	1.7 (0.11 - 12.1)	0.17 (0.0025 - 5.49)
Wet and Temperate Location	1.51 (0.023 - 13.3)	0.8 (0.009 - 9.67)	0.06 (0.0003 - 4.34)
Wet and Cool Location	18 (6.63 - 33.5)	12.1 (3.7 - 23.9)	6.19 (0.5 - 10.8)

Table 10: Average concentrations in a small stream based on Gleams-Driver simulations

(all concentrations in μg/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0 (0 - 0.006)	0 (0 - 0.004)	0 (0 - 0.003)
Dry and Temperate Location	8.0E-08 (0 - 0.00006)	0 (0 - 0.00003)	0 (0 - 0.000013)
Dry and Cold Location	0 (0 - 0.0016)	0 (0 - 0.0007)	0 (0 - 0)
Average Rainfall and Warm Location	0.025 (0.0015 - 0.14)	0.016 (0.0006 - 0.1)	0.005 (0.000017 - 0.04)
Average Rainfall and Temperate Location	0.024 (0.0015 - 0.1)	0.016 (0.0006 - 0.07)	0.004 (0.000031 - 0.026)
Average Rainfall and Cool Location	0.006 (0.00007 - 0.06)	0.003 (0.00001 - 0.04)	0.00017 (0 - 0.025)
Wet and Warm Location	0.014 (0.0013 - 0.07)	0.008 (0.0004 - 0.04)	0.0006 (0.000015 - 0.016)
Wet and Temperate Location	0.007 (0.00014 - 0.06)	0.0028 (0.00006 - 0.04)	0.00024 (9.0E-07 - 0.013)
Wet and Cool Location	0.11 (0.06 - 0.18)	0.07 (0.03 - 0.12)	0.027 (0.005 - 0.05)

Table 11: Peak concentrations in a small pond based on Gleams-Driver simulations

(all concentrations in µg/L or ppb per lb/acre applied)			
Site	**Clay**	**Loam**	**Sand**
Dry and Warm Location	0 (0 - 0.8)	0 (0 - 0.5)	0 (0 - 0.4)
Dry and Temperate Location	0.000008 (0 - 0.008)	0 (0 - 0.004)	0 (0 - 0.0014)
Dry and Cold Location	0 (0 - 0.23)	0 (0 - 0.08)	0 (0 - 0)
Average Rainfall and Warm Location	3.33 (0.11 - 21.7)	2.07 (0.05 - 14.6)	0.7 (0.0024 - 6.26)
Average Rainfall and Temperate Location	3.73 (0.16 - 23.1)	2.23 (0.05 - 16.4)	0.7 (0.004 - 5.3)
Average Rainfall and Cool Location	0.8 (0.01 - 10.3)	0.5 (0.0011 - 7.12)	0.028 (0 - 4.35)
Wet and Warm Location	1.22 (0.12 - 6.88)	0.7 (0.05 - 4.46)	0.06 (0.0011 - 1.88)
Wet and Temperate Location	0.7 (0.011 - 7.27)	0.29 (0.004 - 5.09)	0.03 (0.00016 – 1.67)
Wet and Cool Location	6.21 (2.52 - 15)	3.93 (1.26 - 9.93)	1.77 (0.17 - 3.5)

Table 12: Average concentrations in a small pond based on Gleams-Driver simulations

(all concentrations in µg/L or ppb per lb/acre applied)			
Site	**Clay**	**Loam**	**Sand**
Dry and Warm Location	0 (0 - 0.04)	0 (0 - 0.012)	0 (0 - 0.009)
Dry and Temperate Location	1.2E-07 (0 - 0.0005)	0 (0 - 0.00011)	0 (0 - 0.000031)
Dry and Cold Location	0 (0 - 0.012)	0 (0 - 0.0024)	0 (0 - 0)
Average Rainfall and Warm Location	0.2 (0.008 - 1.41)	0.07 (0.0024 - 0.6)	0.024 (0.00007 – 0.25)
Average Rainfall and Temperate Location	0.24 (0.012 - 1.62)	0.09 (0.0027 - 0.7)	0.02 (0.00015 – 0.18)
Average Rainfall and Cool Location	0.06 (0.0005 - 0.6)	0.019 (0.00004 - 0.24)	0.0009 (0 - 0.13)
Wet and Warm Location	0.07 (0.007 - 0.4)	0.026 (0.0016 - 0.17)	0.0021 (0.00006 - 0.06)
Wet and Temperate Location	0.05 (0.0008 - 0.4)	0.012 (0.00022 - 0.16)	0.001 (0.000004 - 0.06)
Wet and Cool Location	0.23 (0.08 - 0.4)	0.11 (0.04 - 0.23)	0.04 (0.006 - 0.09)

Table 13: Estimated water contamination rates (WCR) based on modeling and monitoring

(all concentrations are in µg/L or ppb per lb/acre applied)

Scenario	Peak	Long-Term Average
MODELING FOR THIS RISK ASSESSMENT (1 lb a.i./acre)		
Direct Spray of Pond (Section 3.2.3.4.2) [a]	56	N/A
Pond, drift at 25 feet (Section 3.2.3.4.2) [a]	8.0	N/A
Direct Spray of Stream (Section 3.2.3.4.2) [a]	91	N/A
Stream, drift at 25 feet (Section 3.2.3.4.2) [a]	13.1	N/A
GLEAMS Stream, Section 3.2.3.4.3	27 (8 – 361)	0.2 (0.09 – 1.5)
GLEAMS, Pond, Section 3.2.3.4.3	13 (2.24 – 173)	0.4 (0.1 – 1.6)
Gleams-Driver, Stream, Section 3.2.3.4.4	6 (0.1 – 33)	0.02 (0.005 – 0.18)
Gleams-Driver, Pond, Section 3.2.3.4.4	2 (0.1 – 23)	0.1 (0.01 – 1.6)
OTHER MODELING		
U.S. EPA		
PRZM/EXAMS, Index Reservoir [b]	3.6 – 30	0.22 – 1.07
SCI-GROW (ground water) [c]	0.004	N/A
MONITORING		
NAWQA, surface water [d]	5.5	N/A
STORET, ground water [e]	0.8 – 1.0	N/A
Well water [f]	610	
Reservoirs [g]	0.043	

[a] Section 3.2.3.4.2 discusses expected concentrations in terms of the nominal application rate of 1 lb a.i./acre. The values for direct spray and drift are taken from Worksheet 10a (direct spray and drift as 25 feet for a pond) and Worksheet 10b (direct spray and drift as 25 feet for a stream) adjusted to WRC values based on the application rate of 0.75 lbs/acre.

[b] From U.S. EPA/OPP 2003d, Table 7, p. 19. Values adjusted to WCR values by dividing by the modeled application rate and the number of application used in the modeling.

[c] From U.S. EPA/OPP 2003e, Table 10, p. 47. Values adjusted to WCR values by dividing by the modeled application rate and the number of application used in the modeling.

[d] From U.S. EPA/OPP 2003e, Table 10, p. 47. Values not associated with application rate.

[e] From U.S. EPA/OPP 2003d, p. 11 - 13. Values not associated with application rate.

[f] From U.S. EPA/OPP 2003d, p. 11, summarizing Jacoby et al. (1992). Not associated with an application rate.

[g] From U.S. EPA/OPP 2003d, p. 13, survey of reservoirs jointly with USGS. Not associated with an application rate.

Table 14: Concentrations of carbaryl in surface water used in this risk assessment

(see Section 3.2.3.4.7 for discussion)

Typical Application Rate:	**0.75**	**lb/acre**
	Peak Concentration (ppb or µg/L)	**Longer-term Concentration (ppb or µg/L)**
Central	15	0.225
Lower	1.6	0.075
Upper	44	1.5

Water contamination rate [a]	**mg/L per lb/acre applied**	
	Peak Concentration (mg/L or ppm per lb/acre)	**Longer-term Concentration (mg/L or ppm per lb/acre)**
Central	0.02	0.0003
Lower	0.002	0.0001
Upper	0.033	0.002

[a] Water contamination rates – concentrations in units of mg a.i./L expected at an application rate of 1 lb a.i./acre. Units of mg a.i./L are used in the EXCEL workbook that accompanies this risk assessment.

Table 15:U.S. EPA Dose-Response Assessments for Human Health

Exposure Scenario	Point of Departure (mg/kg/day)	Uncertainty/FQPA Safety Factors	RfD/MOE [a]	Study and Toxicological Effect
Acute Dietary	1.1 ($BMDL_{10}$)	Uf_A = 10x Uf_H = 10x FQPA = 1x	Acute RfD = 0.01	U.S. EPA/OPP 2007d, brain AChE inhibition in post-natal day 11 (PND 11) pups
Chronic	Due to the rapid recovery of ChE activity, the acute exposure from carbaryl is the main duration of concern and therefore a chronic assessment is not appropriate for carbaryl.			
Incidental Oral	1.1 ($BMDL_{10}$)	Uf_A = 10x Uf_H = 10x FQPA = 1x	MOE = 100	Same as acute dietary
Dermal (All durations)	86	Uf_A = 10x Uf_H = 10x FQPA = 1x	MOE = 100 (adult) MOE = 180 (children)	Rat Adult Dermal Study (MRID 45630601), Brain ChE inhibition most sensitive, BMD10= 49.35 mg/kg and BMDL10= 30.56 mg/kg. Adjusted by 2.8x to account for rat skin permeability compared to human skin (MRID 47151902).
Inhalation (All durations)	1.1 ($BMDL_{10}$)	Uf_A = 10x Uf_H = 10x FQPA = 1x	MOE = 100	Same as acute dietary
Cancer	Classification: "Likely to be carcinogenic in humans" $Q1^* = 8.75 \times 10^{-4}$ $(mg/kg/day)^{-1}$ based on incidence of hemangiosarcomas in mice.			

[a] Modified from the U.S. EPA/OPP (2007a), Table 4, p. 10

Key:

$BMDL_{10}$: Lower 95% confidence limit of the benchmark dose associated with a 10% response.

MOE: margin of exposure.

Uf_A: Uncertainty factor for extrapolating from animals to human.

Uf_H: Uncertainty factor for sensitive subgroups in the human population.

FQPA: Uncertainty factor for considerations under the Food Quality Protection Act.

Table 16: Estimates of Dose-Severity Relationships for Carbaryl in Humans

NOTE: The dose-severity relationships detailed in this table and discussed in Section 3.3.5 should not be interpreted as suggesting that exposures above the RfD of 0.01 mg/kg bw are acceptable.

Dose (mg/kg bw) [a]	Corresponding Hazard Quotient [b]	Organism (number of individuals): Effect	Reference
0.01	1	Human Equivalent Dose: Based on a $BMDL_{10}$ of 1.1 mg/kg in 11 day old rats after gavage exposure with an uncertainty factor of 100. No adverse effects anticipated in any individuals.	EPA/OPP 2007a
0.06	6	Humans (5): No effects attributable to 6 wk exposure.	Wills et al. 1968
0.1	10	Human Equivalent Dose: Chronic feeding study in rats with a NOAEL of 9.6 mg/kg bw/day and an uncertainty factor of 100. No adverse effects anticipated in any individuals.	U.S. EPA/ORD 2002
0.12	12	Humans (6): Decrease in ability of renal tubules to reabsorb amino acids over 6 wk exposure.	Wills et al. 1968
0.2	20	Rats: The estimated human dose is based on the LOAEL (liver and kidney pathology) of 15.6 mg/kg bw/day from chronic feeding study used by U.S. EPA/ORD to derived the chronic RfD of 0.1 mg/kg bw/day. LOAEL divided by the uncertainty factor of 100 – i.e., 0.156 mg/kg bw/day ≈ 0.2 mg/kg bw/day.	U.S. EPA/ORD 2002
0.55	N/A [c]	Humans: Sporadic inhibition of AChE activity but no overt signs or symptoms of toxicity after occupational exposure.	Best and Murray 1962
0.5, 1, 2	50, 100, 200	Humans (2): Single oral doses to two individual per dose. No AChE inhibition and no signs or symptoms of toxicity after single oral dose.	Wills et al. 1968
2.8	280	Human: Violent epigastric pain followed by profuse sweating. Treatment with atropine (1 mg) resulted in complete recovery within 2 hours.	Hayes 1982
5.45	545	Human: Nausea, lightheadedness, and weakness. Treatment with atropine (4.8 mg) resulted in nearly complete recovery within 3 hours and no effects on following day.	Hayes 1982
90	9000	Sheep: Lowest reported LD_{50} value in mammals.	WHO 1994
1,000	100,000	Monkey: LD_{50} value in monkeys is >1,000 mg/kg.	WHO 1994
5,700	570,000	Human: Death after suicidal ingestion.	Farago 1969

[a] The RfD values from U.S. EPA/ORD (2002) and EPA/OPP (2007a) are intended as estimates of doses in humans. The animal LOAEL from EPA/OPP (2007a) is divided by the uncertainty factor of 100 to estimate a human dose. Doses from the studies by Best and Murray (1962), Hayes (1982) and Wills et al. (1968) involve human exposures.

[b] All Hazard Quotients are based on the RfD of 0.01 mg/kg bw/day derived by the U.S. EPA/OPP (2007a).

See Section 3.3.2 for details.

[c] The dose estimate of 0.055 mg/kg bw is based on urinary excretion of 1-naphthol in workers. The accuracy of the estimated dose cannot be determined. The detail on follow-up observations appears marginal.

Table 17: Acute LD_{50} Values of Carbaryl in Various Species of Birds

Species	LD50 (mg/kg bw by gavage)	Body Weight in kg (Range)	Reference [a]
Mallard Duck (*Anas platyrhynchos*)	>2,564	0.9 (0.815 – 1.06)	Hudson et al. 1984
Canada Goose (*Branta canadensis*)	1,790	3.8 (3.0 – 4.7)	Hudson et al. 1984
Ring-necked Pheasant, ♂ (*Phasianus colchicus*)	>2,000	1.3	Hudson et al. 1984
Ring-necked Pheasant, ♀ (*Phasianus colchicus*)	707	0.95	Hudson et al. 1984
Sharp-tailed grouse (*Tympanuchus phasianellus*)	1,240 (780 – 1,700)	0.89 (0.817 – 0.953)	Mount and Oehme 1981
California quail (*Lophortyx californicus*)	>2000	0.5 (0.468 – 0.620)	Hudson et al. 1984
Rock Dove (*Columba livia*)	2,000 (1,000 – 3,000)	0.35 (0.340 – 0.369)	Hudson et al. 1984
Chicks, 7 to 14 days old [NOS]	197	N/A	Sherman and Ross 1961
Red-winged blackbird (*Agelaius phoeniceus*)	56	0.0526 (0.0415 – 0.0636)	Schafer et al. 1983
Starlings (*Sturnus vulgaris*)	16	0.0823 (0.0799 – 0.0847)	Schafer et al. 1983

[a] Reference for toxicity value. All body weight values are taken from Dunning (1993).

Table 18: Summary of modeled concentrations in the entire 60 inch soil column

(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	0.00308	0.0433	0.00266	0.0404	0.00264	0.0404
10	0.00339	0.0433	0.00304	0.0404	0.00284	0.0404
15	0.00333	0.0431	0.00298	0.0404	0.0028	0.0404
20	0.00326	0.0428	0.00295	0.0404	0.00276	0.0404
25	0.00319	0.0424	0.00292	0.0404	0.00274	0.0404
50	0.00282	0.0399	0.00283	0.0404	0.0028	0.0404
100	0.00217	0.0337	0.00275	0.0398	0.00308	0.0404
150	0.00165	0.0267	0.00271	0.0392	0.00327	0.0404
200	0.00124	0.0262	0.0027	0.0386	0.00332	0.0404
250	0.000912	0.0262	0.00268	0.0381	0.00328	0.0404

Table 19: Summary of modeled concentrations in the top 12 inches of the soil column

(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	0.0154	0.217	0.0133	0.202	0.0132	0.202
10	0.0169	0.217	0.0152	0.202	0.0142	0.202
15	0.0166	0.215	0.0149	0.202	0.014	0.202
20	0.0163	0.214	0.0147	0.202	0.0137	0.202
25	0.0159	0.212	0.0146	0.202	0.0135	0.202
50	0.0141	0.2	0.0141	0.202	0.0123	0.199
100	0.0109	0.168	0.0134	0.199	0.0102	0.188
150	0.00824	0.133	0.0129	0.195	0.00857	0.175
200	0.0062	0.131	0.0125	0.192	0.00736	0.162
250	0.00456	0.131	0.0122	0.189	0.00647	0.151

Table 20: Summary of toxicity values used in the ecological risk assessment

(all amounts expressed as a.i.).

Organism Group/Duration	Endpoint	Toxicity Value	Reference
Terrestrial Animals			
Acute			
Non-canine Mammals	NOAEL	4 mg/kg bw	See Section 4.3.2.1
Canine Mammals	NOAEL	4 mg/kg bw	Same as non-canids
Birds (mallard)	NOAEL	21 mg/kg bw	Same as chronic value
Honey Bee	LD_{50}	1.2 mg/kg bw	U.S. EPA/OPP 2003d, MRID 05004151
Longer-term			
Non-canine Mammals	NOAEL	4 mg/kg bw	See Section 4.3.2.1
Canine Mammals	NOAEL	4 mg/kg bw	Same as non-canids
Birds	NOAEL	21 mg/kg bw/day	ACC263701 U.S. EPA/OPP 2003d
Aquatic Animals			
Acute			
Amphibians			
Sensitive	NOEC (brain AChE)	0.006 mg/L	Same value as fish [a]
Tolerant	NOEC (brain AChE)	0.03 mg/L	Same value as fish [a]
Fish Sensitive (Rainbow trout)	NOEC (brain AChE)	0.006 mg/L	Ferrari et al. 2004a
Tolerant (Squawfish)	NOEC (brain AChE)	0.03 mg/L	Beyers and Sikoski 1994
Invertebrates			
Sensitive (*Leptodora kindtii*)	LC_{50}	0.0035 mg/L	Sakamoto et al. 2005
Tolerant (Eastern oyster)	EC_{50}	2.7 mg/L	U.S. EPA/OPP 2003d
Longer-term			
Amphibians			
Sensitive (Salamander)	NOEC: developmental	0.0005 mg/L	Rohr et al. 2003
Tolerant	NOEC (brain AChE)	0.03 mg/L	Same value as fish [a]
Fish Sensitive (Rainbow trout)	NOEC (brain AChE)	0.006 mg/L	Ferrari et al. 2004a
Tolerant (Squawfish)	NOEC (brain AChE)	0.03 mg/L	Beyers and Sikoski 1994
Invertebrates			
Sensitive (*Daphnia magna*)	NOEC (reproductive)	0.0015 mg/L	U.S. EPA/OPP 2003d
Tolerant (midge larvae)	NOEC (emergence)	0.5 mg/L	U.S. EPA/OPP 2003d
Aquatic Plants			
Algae [b]			
Green algae	NOEC	0.29 mg/L	U.S. EPA/OPP 2003d
Macrophytes	No data		

[a] See Section 4.3.3.2 for discussion.
[b] Data are available on only one species, *Pseudokirchneriella subcaptitata*. In the worksheets, this value is used for both sensitive and tolerant species.

APPENDICES

Appendix 1: Chemical Properties and Environmental Fate

Appendix 2: Mammals, Acute Toxicity

Appendix 3: Mammals, Effects After Repeated Administration

Appendix 4: Toxicity to Birds

Appendix 5: Toxicity to Terrestrial Invertebrates

Appendix 6: Terrestrial Field Studies

Appendix 7: Toxicity to Fish

Appendix 8: Toxicity to Amphibians

Appendix 9: Toxicity to Reptiles

Appendix 10: Toxicity to Aquatic Invertebrates

Appendix 11: Toxicity to Aquatic Plants and Microorganisms

Appendix 12: Aquatic Field and Mesocosm Studies

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl

Data Summary	Reference
Aquatic Sediment Halftimes	
The greatest effect of redox potential was found with carbaryl. Although rapid dissipation occurred under aerobic conditions t1/2 = 1.8-4.9 days, carbaryl degradable much more slowly under anaerobic conditions: t1/2 = 125-746 days. The sorption coefficient consistently increased with time.	Bondarenko and Gan 2004
Dislodgeable Foliar Residues (DFR)	
Carbaryl applied to cabbage and lettuce crops in a field in the San Joaquin Valley, near Porterville, CA, at a rate of 2.0 lbs active ingredient/acre (lb a.i./A) using a tractor-mounted boom sprayer. This application rate is equivalent to 22.42 μg/cm^2. At 1 day after treatment, samples were collected using four popular foliar dislodging techniques to determine their relative dislodging efficiency; three of the techniques gave similar results, whereas a fourth gave marginally lower results. Sample were defined as 40 leaf punches equivalent to 400 cm^2. DFR Values in μg a.i./sample Cabbage: 276 to 411 μg a.i./sample 0.69 to 1.03 μg/cm^2 Equivalent to a proportion of 0.031 to 0.046 of application rate. Lettuce: 1913 to 2478 μg a.i./sample 4.78 to 6.20 μg/cm^2 Equivalent to a proportion of 0.21 to 0.28 of application rate.	Bruce et al 2006
Carbaryl applied to cabbage in CA at a rate of 2.0 lbs a.i./acre (22.42 μg/cm^2). Residues were log-normally distributed with a mean of 511 μg a.i./sample with a sample consisting of 400 cm^2. The DRF of 511 μg a.i./sample corresponds to 1.28 μg/cm^2 or a proportion of 0.057 of the application rate. Very similar to Bruce et al. 2006.	Korpalski et al 2005
A multiple-intensity rainfall simulator was used to determine the effects of rainfall intensity and amount on concentrations of carbaryl (Sevin XLS Plus) washed from soybean plants. Two hours after carbaryl was applied at 1.12 kg/ha, 25 mm of rain was applied at intensities of 13.0, 27.4, 53.8, or 105.1 mm/hr. About 67% of the carbaryl on the plants was washed off by 25 mm of rain. Rainfall amount had a greater effect on carbaryl concentrations in washoff than rainfall intensity.	Willis et al 1996

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl
(continued)

Data Summary	Reference
A liquid carbaryl product (41.2% a.i.; '7' Carbaryl Insecticide, Monterey Chemical, U.S.A.) was applied at label rates ranging from 0.1 1 to 0.21% a.i. to trees, shrubs, and herbaceous plants on residential and commercial properties in California. Carbaryl was monitored in the spray mixtures, air, surface waters, plant foliage, fruits and vegetables in the sprayed areas. Foliar dislodgeable residues ranged from 1.54 - 7.12 $\mu g/cm^2$. The specific application rates are not given.	Walters et al 2003
Hydrolysis	
The influence of clay preparation methods on the sorption and hydrolysis of carbaryl by K+-saturated reference smectite SWy-2 was studied. Each preparation of mineral fractions manifested significantly different abilities to hydrolyze carbaryl to 1-naphthol, decreasing in the order whole clay > heavy fraction >> clay-sed. > light clay > claycent. The extent of 1-naphthol disappearance from solution, accompanied by a progressive darkening of the clay, followed the order whole clay > heavy fraction > > > light clay > clay-sed. > clay-cent. Using ring labeled [14C]carbaryl, ~61% and 15% of the total 14C activity added to the whole clay and light fraction, respectively, remained unextractable.	Arroyo et al 2004
Photolysis	
The behavior of carbaryl photodegradation in the presence of ionic and non-ionic surfactants was studied. Carbaryl completely degrades in water after ca. 30 min irradiation, following a pseudo-first order kinetics (Pramauro et al. 1997)	Bianco et al 1999

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl
(continued)

Data Summary	Reference
Carbaryl in a pesticide mixture studied in four water types: Ultra-pure water (MQW), river water (RW), filtered river water (FRW), and seawater (SW). Experiment lasted 6 months. Carbaryl half-lives calculated from linear regression curves: Darkness t1/2 (days) at 6°C: MQW = No degradation observed, RW = 31, FRW = 45, SW = 22. t1/2 (days) at 22°C: MQW = 37, RW = 11, FRW = <2, SW = <2 Natural Sunlight t1/2 (days): RW = 9, SW = 13	Lartiges and Garrigues 1995
Soil Degradation/Dissipation	
Treated 0.79 ha fan-shaped field with 9.6% slope in a small watershed (North Appalachian Experimental Watershed at Coshocton, Ohio). Silt loam soil: 21% sand, 63% silt, 16% clay, and 1.7%. Carbaryl granules (20% a.i.) banded into corn seed furrows at rate of 5.03 kg/ha a.i. in spring 1973. Soil samples collected on day of application and 5, 12, 25, 39, 62, and 116 days after application. Carbaryl remained stable in soil for 25 to >116 days at different points in the field and then decayed rapidly: 95% disappeared in 135 days. Lag periods indicated that degradation from soil was primarily microbiological. Runoff water and sediments accounted for only 5.77 g (0.14%) of the 4 kg of carbaryl applied to the soil. Moreover, >90% of runoff loss occurred in a single rainfall 19 days after application. Even lesser amounts of carbaryl were transported from the field in runoff solids. Investigators conclude: high-volume rainfall occurring shortly after carbaryl application in the field can generate a low-level transport of the pesticide to nontarget areas.	Caro et al. 1974

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl
(continued)

Data Summary	Reference
Plots within wet and dry sites in boreal (south central Alaska), temperate (north western North Carolina), and Mediterranean (east central California) ecosystems were sprayed with 2.0 % aqueous carbaryl (Sevin,SI [41.2%]; Rhone-Poulenc, NC) using a backpack sprayer, on 9 June 1993. Controls were untreated sites. Soil cores from the three sites were analyzed at 1, 30, 60, 90, 365, and 483 days after applications. The highest levels of residues were found in the upper inch of soil plots; persisting for 90 days. When soil cores had little or no litter, the upper soil layer had higher levels of carbaryl. Minimal amounts of carbaryl moved downward within any site. All sites, except Alaska dry and North Carolina wet, had carbaryl levels exceeding 20 ppm in the upper layer of soil at 90 days. Measurable carbaryl levels were present in the North Carolina dry site and California wet and dry sites 1 yr after application. The decreasing order of carbaryl persistence was North Carolina dry > California wet > California dry > Alaska wet > North Carolina wet > Alaska dry. Trace amounts of 1-naphthol were found occasionally, but not conjugated metabolites.	Hastings et al 1998
Laboratory study. Three types of soil spiked with 2 ppm carbaryl. Degradation was rapid in clay as compared with clay loam and sandy clay. Degradation in clay loam and sandy clay appeared to follow first-order curves. Half-lives not given, but plots of %carbaryl remaining vs. time for the three soil types.	Thapar et al 1995

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl
(continued)

Data Summary	Reference
Soil Binding (Kd, Ko/c)	
Twenty two soils from Australia and five soils from Pakistan representing a range of organic C contents and various ecosystems in Australia. Organic C in these soils ranged from 2.8 - 70.1 g/kg, pH from 4.3 - 8.6, and clay contents from 12 -755 g/kg. Lowest OC = soil Pk10; 2.8 g/kg. Highest OC = soil Pk6; 8.6 g/kg. Carbaryl (>99% pure) had linear sorption isotherms on these soils. Kp (L kg-1) values ranged from 1.0 (soil Pk10) to 59.7 (soil Pk6). Koc (L kg-1) values ranged from 189(soil Mt. Mary; OC=10.2 g/kg) to 4318 (soil Pk6). Models for predicting Koc Carbaryl using aryl C with O-aryl or carboxyl C are given.	Ahmad et al 2001
The potential of 5 different surfactants to enhance release of carbaryl from contaminated (88 mg/ kg soil) soil (Pakistan; clay content = 252 g/kg, OC = 22 g/kg) was studied. A significant amount of release (up to 32%) was contributed by the surfactants. The authors noted that at concentration above 10 g /L, the surfactants did not further increase the release of carbaryl possibly due to the formation of large micelles which clogged the soil micropores.	Ahmad et al 2004

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl *(continued)*

Data Summary	**Reference**
Technical grade carbaryl. Organic Carbon (%) of four soils from India: Lateritic soils Bolpur = 0.234 Nalhati = 0.675 Alluvial soils Barokoddi = 0.990 Dudherkuthi = 0.640 Values of Freundlich parameters for the sorption of carbaryl on soils at 30°C: Adsorption Desorption Soil K 1 /n K l/n Bolpur 0.308 1.554 1.216 1.428 Nalhati 2.175 1.385 6.429 1.409 Barokodali 2.490 1.447 10.016 1.624 Dudherkuthi 1.916 2.099 3.792 2.491 The values of K and l/n showed a decreasing sequence of the adsorption capacity of soils for carbay1 as Barokodali > Nalhati>Dudherkuthi>Bolpur, which was the same order as the organic matter content of the soils. The absence of rapid initial increase of adsorption indicated that interaction between carbaryl and soil samples was of a kind other than ion exchange and the equilibrium seemed to be fully attained within 3 hr.	Jana and Das 1997
Koc = 300 L/kg, t1/2 = 10 days, solubility in water = 120 mg/L (Wauchope et al. 1992) OC (g/kg) Clay(%) Kf Koc Kd t1/2 Red Bay Topsoil = 15.2 14 5.14 338 5.07 9 Red Bay Subsoil = 3.9 31 0.56 144 0.44 18 Astatula Topsoil = 8.0 1 4.72 590 4.42 8 Astatula Subsoil = 2.0 1 1.34 671 0.90 13 Mineralization rate coefficients given.	Nkedi-kizza and Brown 1998

Appendix 1: Laboratory and Simulation Studies on the Environmental Fate of Carbaryl
(continued)

Data Summary	Reference
Water Degradation/Dissipation	
Dissipation/degradation halftime in artificial ponds of 0.36 days.	Hanazato and Yasuno 1990b
Dissipation in streams after forestry applications at a rate of 0.84 kg/ha (0.75 lb/acre). Peak concentrations after spraying were 0.93 to 7.8 µg/L in brooks and 0.44 to 2.0 µg/L in rivers. An atypical peak of 16 µg/L was measured in one stream. Dissipation constants ranged from 0.005 to 0.068 h-1 with a mean of 0.025 h-1. This corresponds to halftimes of 28 (10 to 138) hours or about 1 (0.5 to 5.75) days.	Stanley and Trial 1980

Appendix 2: Acute toxicity to Experimental Mammals

Species	Exposure	Response	Reference
ORAL			
Rats, Gavage			
Rat; Male, 60 days old, Long–Evans from Charles River Laboratories (Raleigh, NC).	0, 25, 50, 75, and 150 mg/kg carbaryl (>99% purity; Chem Services, West Chester, PA) in corn oil. Dose–response curves for cholinesterase (ChE) inhibition produced by carbaryl were determined at 4 h after dosing with 0, 10, 30, 50, 100, or 175 mg/kg carbaryl (>99% purity; Chem Services, West Chester, PA) in a corn oil vehicle.	Treatment with carbaryl resulted in an acute hypothermic response followed by a delayed elevation in core temperature that persisted for at least one day after injection. There was a dose-dependent response in the magnitude of the temperature increase. The higher doses of carbaryl (75 and 150 mg/kg) yielded signs of acute cholinergic over-stimulation. Most animals displayed excessive salivation, lacrimation, diarrhea, chewing, twitching, and apparent muscle weakness. Motor activity was reduced during the night following treatment at the highest dose of carbaryl. Carbaryl at the dose of 75 mg/kg induced strong tremors, head nodding and myoclonic jerks (150 mg/kg). One rat treated with 75 mg/kg of carbaryl died 30 min post dose after showing tremors. Carbaryl produced significant decreases in ChE activity in erythrocytes, plasma, and brain tissues.	Gordon et al. 2006

Appendix 2: Acute toxicity to Experimental Mammals *(continued)*

Species	Exposure	Response	Reference
Rat; Male, 60 days old, Long-Evans hooded from Charles River Laboratories (Raleigh, NC)	0, 20,75, 150 mg/kg carbaryl (99%; Rhone-Poulenc AG Co., Research Triangle Park, NC) in corn oil.	Treatment-related effects at 20 mg/kg carbaryl: 1. autonomic - salivation, lacrimation, and defecation (decreased); 2. activity - motor activity (decreased) and rears (decreased); 3. neuromuscular - gait changes 4. sensorimotor - tail-pinch response (decreased) and touch response (decreased); 5. reactivity - arousal (decreased); 6. tremors, chewing, and hypothermia. Recovery was evident by 24 hr, except for the following effects (dose levels in parentheses), which were still observed: motor activity (decreased) (20, 75 and 150 mg/kg), tremors (l50 mg/kg) and chewing (150 mg/kg). Effect on motor activity (decreased) (150 mg/kg) was still observed at 72 hr after dosing. None of the effects continued to 1 week after dosing. At 24 hr after dosing at the 150 mg/kg, treatment level wt loss was the greatest (9.6%) At 24 hr there was 0% mortality.	Moser 1995
Rats, adult Sprague-Dawley males (6-8 months old)	Oral administration of 100 mg/kg carbaryl (Ortho Liquid Sevin 27% in water) followed by intraperitoneal injection of 0, 20, 35, or 70 mg/kg.	Maximal cholinergic signs of toxicity 1 hour after treatment included salivation, respiratory distress, muscle tremors, and weakness; inhibition of carboxylesterase activities in brain, liver, and plasma observed 1 hour after treatment.	Ehrich et al. 1992
Other species.			
Cats, mice, monkeys	Unknown	LD_{50}s for mammals ranged from 100 mg/kg for cats and mice to 2000 mg/kg for monkeys. LD_{50} for pigs is >1500 mg/kg	CCME (1999a)

Appendix 2: Acute toxicity to Experimental Mammals *(continued)*

Species	Exposure	Response	Reference
DERMAL			
Black-footed Ferret	The potential for relay toxicity determined by feeding carbaryl-treated prairie dogs to ferrets. Adult prairie dogs were treated topically with 2.5 g of commercial 5% carbaryl dust sold as flea powder. After 14 days prairie dogs were killed and fed to ferrets.	Analysis of ferret blood cholinesterase (ChE), prairie dog brain ChE, and hepatic carbaryl concentration. There was no difference between pre- and post-exposure blood ChE activity, nor did treated prairie dog brain ChE differ significantly from controls. Hepatic carbaryl concentrations were less than detection limits (50 ppb).	Orst et al 1998
Rat; Wistar, Male, 3 months old	11 mg/cm^2 and 22 mg/cm^2 carbaryl (99.0% purity; Institute of Organic Industrial Chemistry in Warsaw) suspended in an emulsion of gum arabic, olive oil and water was applied to the tail skin for 4 hr/day for 4 wks.	The body mass of all animals, both in the experimental and control groups, increased about 70g during studies lasting 28 days. Degenerative changes observed at 11 mg/cm^2: lungs and brain 22 mg/cm^2: liver, kidneys, lungs, heart, and brain	Tos-luty et al. 2001a
Rat; Wistar, male, 200-300 g	^{14}C-carbaryl in ethyl alcohol (with activity of 670 kBq/ml containing 1.67 mg of carbaryl (preparation per 1cm^2 of the tail skin was 74.4 kBq (0.19 mg of carbaryl)) was applied to the skin of the tail for 4 h daily. One group was exposed once, one group twice, and one group three times. Control animals were not exposed to skin penetration.	At a single exposure, carbaryl was absorbed at the rate of 0.15 µg/cm^2 during 4 h. The rates of carbaryl absorbed during exposures repeated twice or three times were smaller: 0.02 µg/cm^2 and 0.012 µg/cm^2, respectively Directly after exposure, as well as 6 h and 20 h after application, carbaryl was detected in the skin at the sites of application and in the skin at the distance of 2 cm from exposure site. It was also detected in the brain. liver, kidney, heart, lungs, plasma, all blood cells, erythrocytes, and leukocytes.	Tos-luty et al. 2001b

Appendix 2: Acute toxicity to Experimental Mammals *(continued)*

INTRAPERITONEAL			
Mouse; strain not identified	Single IP dose of 0, 0 (solvent control), and 7 mg/ kg body wt Sevin (100%pure).	Induced structural chromosomal aberrations in mouse spleen cells, with maximum effect 6 h after treatment. The principal type of aberration induced in mouse spleen cells was the single break with chromatid deletions and fragments, and the frequency of tetraploid cells increased.	Amer et al. 1996
Mouse; Balb/c, Female, 6-10 wks old, from Charles River Japan, Inc.	Subcutaneous injection of 0 and 1.0 mg/0.1 ml/mouse carbaryl (CAS No. 63-25-2). Peritoneal macrophages were obtained from the mice 1 d after treatment.	Carbaryl inhibited lipopolysaccharide (LPS)-induced NO production in vitro. Carbaryl did not significantly effect production of LPS-induced TNF-a or NO production in peritoneal macrophages	
Rat; Albino, Male, Adult, 250-350 g	1. Single IP dose of 0 (vehicle control) and 50 mg/kg carbaryl (99.7% pure, Riedel-de Haen; Seelze, Germany). 2. Subacute IP dose of 0 (vehicle control) and 10 mg/kg carabaryl (99.7% pure, Riedel-de Haen; Seelze, Germany) daily for 14 days.	1. A single IP dose of 50 mg/kg: inhibition (56.38%) of brain AChE activity, suppression (55.95%) of plasma BuChE activity, and decrease (26.36%) in platelet uptake of 5-HT. No significant effect on brain MAO-A activity. 2. Exposure of rats to a daily IP dose of 10 mg/kg for 14 days: no significant inhibition of activities of brain AChE and plasma BuChE; no significant effect on brain MAO-A activity or platelet 5-HT uptake.	Sachana et al. 2001

Appendix 2: Acute toxicity to Experimental Mammals *(continued)*

INHALATION			
Rat; Crl:CD BR, Male, 5 wk old, from Charles River Breeding Laboratories (Kingston, N .Y.)	nose-only inhalation exposures, for 6 h/d, 5 d/wk for 2 wk to mean concentrations of 0 (air only), 0 (acetone only), 36, 137, and 335 mg/m^3 aerosolized carbaryl (99.3% purity; E. I. Du Pont de Nemours and Co., Experimental Station, Wilmington, Del.) in acetone.	Inhibition of humoral immune function was observed by dose-dependent decreases in spleen cell number, AFC/lO^6 splenocytes, AFC/spleen, and serum levels of SRBC-specific IgM antibody. Significant decreases of 33, 57, and 22% in spleen cell number, AFC/spleen, and thymus weight, respectively, were observed at the 335 mg/m^3 exposure level Body weight not significantly affected. Signs of neurotoxicity were initially observed in some animals following the 137 and 335 mg/m^3 exposures. The severity and number of signs decreased with daily carbaryl exposures. The neurotoxic signs included tremors, salivation, diarrhea, slow righting reflex, abnormal gait, and decreased muscle tone.	Ladics et al. 1994

Appendix 3: Mammals, Effects After Repeated Administration

Species	Exposure	Response	Reference
Short Term Multiple Gavage (other than developmental studies)			
Rat; Brown Norway, Female, 3 months old, 10 per group	Rats were gavaged for 2 weeks with 0, 2, 10, or 50 mg/kg body wt/day carbaryl in corn oil (99% pure carbaryl from Chem Service. West Chester. PA). Rats were then sensitized with a subcutaneous injection of house dust mite antigen in aluminum hydroxide adjuvant 3 days after the beginning of carbaryl exposure and challenged with antigen via the trachea 1 day after the final carbaryl ingestion.	2 days after challenge, antigen-specific cell proliferation in pulmonary lymph nodes was significantly higher in the 50 mg/kg group, while antigen-specific splenocyte proliferation was decreased in groups dosed with 2, 10, and 50 mg/kg carbaryl. Total protein and lymphocyte number in bronchoalveolar lavage (BAL) fluid were also increased in the 50 mg/kg group. 7 days after challenge, immune-mediated pulmonary inflammation (eosinophils), antigen-specific immunoglobulin (Ig) E level in serum, and antigen-specific IgE and IgA levels in BAL fluid were significantly elevated in the 50 mg/kg group. No apparent change was observed for lactate dehydrogenase and eosinophil peroxidase in BAL fluid, while the number of BAL macrophages were decreased in the 10 and 5O mg/kg carbaryl groups. Serum IgA and BAL IgG levels were unaffected by carbaryl treatment In summary, systemic immune suppression was found in rats treated for 2 weeks with doses of carbaryl ranging from 2 to 50 mg/kg/day, while prolonged pulmonary inflammatory responses to HDM and elevated HDM-specific IgE responses were observed in rats exposed to 50 mg/kg/day carbaryl.	Dong et al. 1998

Appendix 3: Mammals, Effects After Repeated Administration *(continued)*

Species	Exposure	Response	Reference
Rat; Male, 90 days old, Long-Evans strain from Charles River Laboratories (Raleigh, NC)	Rats were administered 0, 25, and 75 mg/kg carbaryl (>99% purity from Chem Services) by oral gavage at either 09:00 or 15:00 h (EST).	Core body temperature and motor activity monitored before and after dosing showed an effect of carbaryl treatment. The hypothermic maximum for both low and high doses was greater when carbaryl was administered at 09:00h than at 15:00 h There was a dose-dependent increase in temperature index with dose of carbaryl. Rats dosed at 09:00 h with 25 mg/kg carbaryl had a significant 25% decrease in motor activity. The same dose administered at 15:00 h had no significant effect on motor activity. Both 09:00 and 15:00 h dosing with 75 mg/kg carbaryl led to ~ 50% reduction in motor activity.	Gordon and Mack 2001
Rat; Wistar Albino, Male, 60-70 g, from Industrial Toxicology Research Centre (Lucknow)	0 (peanut oil control), 50 mg, and 100 mg/kg body wt carbaryl (technical grade, 99.20% pure; Paushak Limited, Baroda) in peanut oil p.o. 5 days/wk for 90 days.	No clinical signs of toxicity were observed in the treated rats except lethargy (compared to controls). Significant decrease in body wt gain after 60 days in 100 mg/kg body weight group. No change in the weights of testes, accessory sex organs, or epididymides in any of the test groups. Testicular enzyme activity was significantly affected: reductions in SDH and G6PDH activity at 100 mg/kg body wt; increases in γGT and LDH activity at 50 and 100 mg/kg body wt. Significant decrease in total epididymal sperm count and percent sperm motility at both doses. Significant increase in percent morphological abnormalities in spermatozoa head, neck and tail at both doses. Moderate to marked histopathological changes in the testes at both doses.	Pant et al. 1995

Appendix 3: Mammals, Effects After Repeated Administration *(continued)*

Species	Exposure	Response	Reference
Rat; Druckery Albino, Male, Young (~40g) and Adult (~125g) from Industrial Toxicology Research Centre (Lucknow)	0 (peanut oil control), 50 mg, and 100 mg/kg body wt carbaryl (technical grade, 99.20% pure; Paushak Limited, Baroda) in peanut oil orally (not specified) 5 days/wk for 60 days.	No overt toxicity or mortality was observed. Dose and age-related decreases in body weight gain were observed at 50 and 200 mg/kg. No change occurred at 25 mg/kg. Absolute weights of testes, epididymis, seminal vesicle, ventral prostate and coagulating gland were significantly decreased at 100 mg/kg in young rats; no effect was evident at 25 or 50 mg/kg. Relative organ weights were not affected at any dose. Significant dose and age-dependent decrease in sperm motility and sperm count only at 50 and 100 mg/kg. Significant dose and age-related increase in abnormal sperm only at 50 and 100 mg/kg. **The authors conclude a 'No observed effect level' of 25 mg/kg body wt. in young and adult rats for sperm toxicity was demonstrated.**	Pant et al. 1996

Short Term Dietary			
Mouse; Meadow Jumping (*Zapus hudsanius*), Male and Female, Adults from a captive breeding colony established in 1997 from adults collected from Big Horn County in southeastern Montana	1) Male and female mice were deprived of food for 24 hr prior to testing, then fed wheat-bran flakes containing either 0, 2, or 20% carbaryl (AI) by weight (Sevin 4 oil, Rhone-Poulene Ag Co., Research Triangle Park, NC; 20%carbaryl by weight). After 7 days of exposure, maximal running speeds (km/hr) were determined by timing the animals as they ran along a microprocessor-controlled rectangular racetrack fitted with photocells and timers. 2) Sperm-positive females were fed bran containing 0 or 2% carbaryl until parturition. Following birth, observations were made on behavioral interactions between mothers and their pups including grooming and cannibalism.	1) Animals exposed to 2 or 20% carbaryl exhibited more random, jerky movements within the racetrack and would frequently bump against the walls. There was a significant effect of carbaryl concentration on running speeds ($F_{2,42}$ = 8.92, P <0.01). Control subjects exhibited the fastest running speed, followed in decreasing order by the 2% and 20% groups. 2) No apparent differences in the grooming of pups by treated females compared to controls were observed. With respect to cannibalism, only (10%) of the control mice giving birth consumed their young. In contrast, a significantly higher number (N =7; 70%) of the mice fed on bran containing 2% carbaryl ate their young (X^2 = 7.3, P<0.01) A dose of 2% corresponds to 20,000 ppm. Assuming a food consumption of about 15% of body weight per day, this would correspond to about 3,000 mg/kg bw/day.	Punzo 2003
Subchronic Dietary (15 days to 90 days)			
Rats; Swiss Albino, Male	0, 1.01 mg carbaryl/kg, and l0.3 mg carbaryl/kg was administered p.o. by dropping dose into the mouths of rats every day for 3.5 months (carbaryl (1-naphthyl methylcarbamate); 99% technical purity obtained from Hektas Firm, Kocaeli, Turkey). The rats were then immunized sc with tetanus toxoid (10 lf/0.2 mL) mixed with an equal volume of Freund's complete adjuvant 20 day before terminating the exposure.	No mortalities and no adverse signs were observed following the daily exposure to carbaryl. At the 1.01 mg carbaryl/kg treatment level, no significant effect was observed on total white blood cells, red blood cell counts, thrombocytes, hemoglobin, % lymphocytes, monocytes, granulocytes, or IgG and IgM concentrations against tetanus toxoid. At the 10.1 mg/kg/day carbaryl treatment level, only lymphocyte counts decreased.	Akay et al. 1999

Appendix 3: Mammals, Effects After Repeated Administration *(continued)*

Species	Exposure/Response	Reference
Teratology Studies		
Rat; Sprague-Dawley, Pregnant	Pregnant rats dosed (p.o.) with 0, 6, 12, and 25 mg/kg/day carbaryl from gestation day 14 to postnatal day 7. Fetotoxicity (reduced litter size) observed at 25 mg/kg/day. Fetal brain cholinesterase (ChE) inhibited during gestation.	McDaniel et al. 1997
Reproduction Studies		
Dams and pups (NOS)	Dams gavaged with 0, 6, 12, or 25 mg/kg/day carbaryl from gestation day 14 to postnatal day 7, after which pups were gavaged postnatal day 7-day 42. Other dams were treated from gestation day 14 to postnatal day7. While dam blood contained dose-proportional carbaryl and 1-naphthol, milk had measurable carbaryl only at 25°C. Milk protein levels were increased proportional to dose, up to 15%. There were no biologically significant changes in the immunotoxicity group. There were no changes in reproductive function of males or females treated as juveniles. Necropsy sperm endpoints were unaffected. Male organ weights and structure were unchanged by exposure.	Chapin et al 1997
Pig	NOEL for pigs fed carbaryl throughout a gestation cycle = 4 mg/kg bw/day. LOEL for reduced litter size and increased stillbirths in pigs = 8 mg/kg bw/day.	Earl et al. 1973; Smalley et al. 1969 (as cited in CCME 1999a)
Mouse; Rabbit	Rabbits and mice fed 150 mg/kg bw per day over the course of a reproductive cycle had decreased weight gain and increased maternal mortality.	Murray et al. 1979
Rats	Drinking water, 3 mg/L, from 5 days prior to mating through to 20 days after birth of offspring. Decrease in size of growth plate and reduced density of bone. Suggestive of inhibition of ossification.	Rafael et al. 2001

Appendix 4: Toxicity to Birds

Species	Exposure	Effects	Reference
Single Dose Gavage/Capsules			
Red-legged partridge (*Alectoris rufa* cross); Adult, Male	200 mg/kg carbaryl (99% purity; Embetec Crop Protection, Yorkshire, U.K.) given orally in gelatin capsules 1 hr after birds had been treated with corn oil alone or a single oral dose of 167mg/kg malathion in corn oil.	Oral administration of 200 mg/kg carbaryl was lethal to 4 out of 12 partridges pretreated with 167 mg/kg malathion. Death occurred 2 to 3 hr after dosing with carbaryl. A further 6 out of 12 birds showed symptoms of ChE poisoning. Only 2 of the 12 malathion-pretreated birds showed no visible signs of toxicity. By contrast, birds given either malathion or carbaryl alone showed no visible symptoms of toxicity. In birds pretreated with corn oil, carbaryl administration led to a 75% inhibition of serum BuChE activity 1hr later and an 81% depression 3 hr later. In birds pretreated with corn oil, carbaryl administration led to a significant reduction (56%) in brain AChE activity.	Johnston et al. 1994

Appendix 4: Toxicity to Birds *(continued)*

Acute Dietary			
Turkey (species not given)	0 or 200 mg/kg carbaryl (99% purity; Z.Ch. Organika-Azot) was given in fodder for 3 days. After the end of carbaryl treatment and again after day 109, all the birds were immunized with the mesogenic Roakin strain of the Newcastle disease virus (NDV).	Levels of gammaglobulin and ceruloplasmine in blood serum in turkeys pre-treated with carbaryl were lower at all sampling days after exposure to NDV; some days the difference was significant. The intra-cellular ability to kill germs by granulocytes, phagocytic activity of leukocytes, and the activity of lysozyme were all lowered after exposure to NDV; some days the difference was significant. The level of specific antibodies for the Newcastle virus was higher (not significant) in the controls compared to the treated birds. A significantly lower reactivity of lymphocytes to the specific mitogen - Newcastle virus - was observed throughout the experiment in the treated birds.	Wojcik and Swiecicka-Grabowska 2004
Acute - Other Exposure Routes			
Mallard eggs	Direct application to eggs.	LC_{50} is 36 times higher than field application rate. Few details. Marginal use.	Hoffman and Albers 1984
Blue rock pigeon (*Columba livia*)	One-time intramuscular injection of 0 or 900 mg/kg body weight carbaryl (50% W.P.) in distilled water.	The number of erythrocytes (min/mm^3) in blood samples from treated birds decreased by 21.67%. The amount of hemoglobin (g/dl) in blood samples from treated birds decreased significantly. There was a non-significant decrease in packed cell volume in blood samples from treated birds.	Sharma and Saxena 1997
Longer Term			
Chicken	1) Fed 180 mg/kg bw/day as a mixture of kaolin powder and Sevin for 60 days. 2) Fed 540 mg/kg bw/day for 35 days.	1) No Effect 2) 100% mortality	Nir et al. 1966, as cited in CCME 1999a

Appendix 4: Toxicity to Birds *(continued)*

Blue rock pigeon (*Columba livia*)	Intramuscular injections of 0 or 225 mg/kg body weight carbaryl (50% W.P.) in distilled water were given on Days 1, 7, 14, and 21 of the exposure period.	Tremors and excessive salivation were observed in birds after the second week of treatment. The number of erythrocytes (min/mm^3) in blood samples from treated birds significantly decreased at Days 7 and 14. The amount of hemoglobin (g/dl) in blood samples from treated birds decreased significantly after 28 days. There was a non-significant decrease in packed cell volume in blood samples from treated birds.	Sharma and Saxena 1997
Reproduction Studies			
Japanese Quail	Carbaryl at dietary concentrations of 0, 50, 150, 300, 600, 900, and 1200 ppm (mg/kg feed) for 14 weeks.	Decreased body weight at 900 and 1200 ppm. Relative kidney weights increased at concentrations of 150 ppm and above. No significant differences in growth of F1 offspring. Slight but statistically insignificant decrease in egg production and hatchability at 600 ppm and higher.	Bursian and Edens, 1977

Appendix 5: Toxicity to Terrestrial Invertebrates

Grouped by bees, earthworms, and other and then alphabetically by author within each group.

Application	Observations	Reference
Bees		
Africanized honeybees (*Apis mellifera*) were fed 0 or 1.5 μ1 Sevin (70.94% a.i. carbaryl) in sucrose.	Sevin disrupted the learning (proboscis conditioning) of honey bees. The authors recorded responses to an unconditioned stimulus to examine whether Sevin influenced the motor systems rather than learning per se. Bees pre-exposed to Sevin seldom responded to the unconditioned stimulus.	Abramson et al 1999
Honey bee	LD_{50} = 26 mg/kg bw (no additional details)	Deo et al. 1988
Honey bees (*Apis mellifera*) were treated on abdomen with serial dilutions of carbaryl in acetone.	LD_{50} = 0.232 μg/μL (0.5 μL/bee) = 0.464 μg/bee. Assuming a body weight of 0. 093 g (USDA/APHIS 1993), 5 mg/kg bw.	Ellis et al. 1997
Honeybees (*Apis mellifera*); Trout Lily bees (*Andrena erythronii* (females), Alfalfa Leafcutting bees (*Megachile rotundata* (females),and Bumblebees (*Bombus terricola* (workers) were treated on mesoscutum with carbaryl (technical grade) in acetone.	**48 hr LD_{50}in μg a.i./g body weight**: Honeybee = **2.72** (2.36, 3.02) Trout Lily Bee = **9.42** (7.09, 11.53) Alfalfa Leafcutting Bee = **21.06** (17.63, 25.44) Bumblebee = **268.8** (no C.L., since regression not significant) Relative susceptibility based on parallel line probit analysis of 48 hr mortality data (in units of μg a.i./g body weight) relative to honeybee: Honeybee = 1.0 Trout Lily Bee = 0.262 Leafcutting Bee = 0.105 Bumblebee = 0.006 The second largest bee, **honeybee, was the most susceptible**, the smallest bee, leafcutting bee, was the third-most susceptible, while the largest, bumblebee, was the least susceptible.	Helson et al. 1994
Honeybees (*Apis mellifera*)	Carbaryl in pollen at concentrations of 10 and 100 mg a.i./kg pollen fed to different bee colonies. A clear dose-response increase in mortality. Cannot, however, calculate incidence because the number of bees in each colony is not specified. Carbaryl apparently stable in pollen for at least 10 weeks.	Moffett et al. 1970
Alfalfa Leafcutting bees (*Megachile rotundata*) (adult females) were fed honey with 2 mg of plain bran or commercially formulated carbaryl bran bait (2% a.i.) for 4 days. Cells collected from nest boxes had egg provisions treated with 2 mg carbaryl bran bait (2% a.i.), 1 mg of carbaryl bran bait (2% a.i.), 2	Adults fed honey solution containing carbaryl bran bait showed no effect on any fitness parameter: nesting days, cells per day, % offspring survival, or total investment in offspring (mg), or in offspring weight or sex ratio. Larvae fed contaminated provisions gained as much weight as those fed uncontaminated provisions.	Peach et al. 1995

Appendix 6: Terrestrial Invertebrates *(continued)*

Application	Observations	Reference
mg plain wheat bran, or stirred to simulate the disturbance of the bran addition.		
Honeybee (*Apis indica* and *Apis mellifera*) foragers were inoculated by dip or injection with different bacteria species (isolated from *A. inidica*) that had previously been shown to metabolize carbaryl. *Indica* bees were then topically exposed to 0.2 μg/bee and *mellifera* to 0.4 μg/bee. Water and acetone controls used.	Increase in percent mortality to carbaryl exposure in antibiotic pre-treated *indica* bees compared to that in control *indica* bees. Significant increase in tolerance to carbaryl, as reflected in time mortality responses up to 24 hr, due to bacterial inoculation in both species of honeybee. The application of mixed culture to bees resulted in higher tolerance than the individual isolates. In *mellifera* , there was a significant difference in mean **24 hr LD_{50} value; (0.298 and 0.257μg/bee)** between the two modes of inoculation. All the bacterial inoculations also showed significant increases in LD_{50} values over controls (water treatment). [Assuming a body weight of 0. 093 g (USDA/APHIS 1993), the LD_{50} of 0.257 μg/bee corresponds to about 2.76 mg/kg bw, virtually identical with value from Helson et al. 1994.] The application of mixed culture to bees induced higher tolerance than the individual isolates.	Sharma and Nath 1996
Earthworms		
Earthworms *Eisinia fetida*, *Eudrilus eugeniae*, *Perionyx excavatus,* and *Allolobophora tuberculata*. Contact test with *Eisinia* only: 2 days carbaryl exposure Soil Test with all: 14 days carbaryl exposure.	In *Eisinia*, soil exposure to carbaryl was less toxic than contact exposure, which the authors note was expected because of the quick breakdown of carbaryl to 1-naphthol. This breakdown product was less toxic to *Eisinia*, based on soil test results, LC_{50} = 723 mg/kg. However, *Eisinia* was more sensitive to carbaryl at low concentration in soil compared to contact tests. In the soil tests, sensitivity to carbaryl at low concentration was *Eudrilus* > *Perionyx* > *Allolobophora* > *Eisinia* **Contact LC_{50}:** *Eisinia* = 0.825E-03 mg/kg bw **Soil LC_{50} (mg/kg soil):** *Eisinia* = 0.103E-02 *Eudrilus* = 0.947E-05 *Perionyx* = 0.829E-03 *Allolobophora* = 0.277E-04 **Note: These values are discordant with all other soil LC_{50} that have been reported. See especially Heimbach 1984 and Neuhauser et al. 1986. Reason(s) for difference are not apparent.**	Callahan et al. 1994
Eisenia andrei, *in vitro* assays	IC_{50} values for inhibition of acetylthiocholine of 5.75 x 10-9.	Caselli et al.

Appendix 6: Terrestrial Invertebrates *(continued)*

<table>
<tr><th>Application</th><th>Observations</th><th>Reference</th></tr>
<tr><td>of cholinesterase inhibition</td><td>M. Corresponding value for inhibition of proprionylthiocholine was 4.79 x 10-9 M.</td><td>2006</td></tr>
<tr><td>Lumbricus terrestris</td><td>Six week LC_{50} (concentration in bedding) of 33 ppm (mg/kg) (Table 2). Note that this value is much higher than soil LC50 values reported above by Callahan et al. 1994.</td><td>Cathey 1982</td></tr>
<tr><td>Eisenia fetida</td><td>LC_{50} = 8.3 µg/cm^2, filter paper contact assay</td><td>Edwards and Bater 1992</td></tr>
<tr><td>Earthworms (Metaphire posthuma) were exposed to 0, 0.125, 0.25, and 0.50 ppm carbaryl (technical grade; Union Carbide Corporation, Bhopal, India) for 5, 10, 20, 40 and 80 min in behavioral (immersion in carbaryl) studies (locomotion and geotaxis).

In reproductive studies (exposure to soil spiked with carbaryl), earthworms were exposed to 0, 0.125, 0.25, 0.50, 1.0, and 2.0 ppm carbaryl.</td><td><u>Behavior Studies</u>
At 0.125ppm exposure for 20 min or 40 min, locomotion was significantly reduced by more than half.
At 0.25ppm and 0.5ppm, exposure for 5 min significantly reduced locomotion, but at longer exposure periods the earthworms did not move at all.

Dose-dependent and exposure time-dependent increases in burrowing times were observed at all the other concentrations tested. The maximum time was taken by earthworms exposed to 0.5ppm for 80 min.

<u>Reproductive Studies</u>
Sperm head abnormalities were observed at all the concentrations tested

Cocoon production was inhibited at all concentrations; there was no cocoon production at 2.0ppm.

Normal hatching occurred at 0.125 and 0.25. Delay in hatching and non-viability was observed at 0.5, 1.0, and 2.0 ppm.</td><td>Gupta and Saxena 2003</td></tr>
<tr><td>Eisenia foetida</td><td>14-Day LC_{50} values determined by 3 different methods:
Contact filter paper: 3.0 µg/cm^2
Artificial Soil: 174 mg/kg soil
Artisol (silica) Test: 151 mg/kg silica</td><td>Heimbach 1984</td></tr>
<tr><td>Earthworms (Pheretima spp.) were exposed to a commercial formulation of carbaryl (850 g/kg a.i.) for 24 hr, 48 hr, or 7 days. Control used.</td><td>LC_{50} in mg/kg soil:
24 hr = 77.2
48 hr = 15.7
7 day = 9.0</td><td>Mostert et al. 2002</td></tr>
<tr><td>Eisenia foetida</td><td>Contact Assay:
14 day $LC_{50:}$ 0.014 mg/cm^2 applied to soil surface.
Soil Incorporation Assay:
14 day LC_{50}: 106 mg/kg soil.</td><td>Neuhauser et al. 1985</td></tr>
<tr><td>Comparative toxicity in four species</td><td>
<table>
<tr><td>Contact Assay</td><td></td></tr>
<tr><td>Species</td><td>LC_{50} mg/cm^2</td></tr>
<tr><td>Allolobophora tuberculata</td><td>0.0005</td></tr>
<tr><td>Eisenia fetida</td><td>0.014</td></tr>
<tr><td>Eudrilus eugeniae</td><td>0.0005</td></tr>
<tr><td>Perionyx excavatus</td><td>0.0095</td></tr>
</table>
<table>
<tr><td>Artificial Soil Assay</td><td></td></tr>
</table>
</td><td>Neuhauser et al. 1986</td></tr>
</table>

Appendix 6: Terrestrial Invertebrates *(continued)*

Application	Observations	Reference
	Species / LC_{50} mg/kg soil *Allolobophora tuberculata* 22 *Eisenia fetida* 106 *Eudrilus eugeniae* 119 *Perionyx excavatus* 263	
Eisenia foetida and *Lumbricus rubellus*	48-hour LC_{50}s in contact/filter paper assay. *Eisenia foetida*: 9 (4.3-19) µg/cm^2 *Lumbricus rubellus*: 0.28 (0.09-0.84) µg/cm^2.	Roberts and Dorough 1984
Earthworms (*Lumbricus terrestris*) were exposed to 0, 15.5, and 62 mg/kg Sevin (½ and 2x label rate) in soil for 48 hr.	Earthworm movement from the treated side of the test chamber to the untreated side occurred as a result of the presence of carbaryl. As concentration increased, earthworm avoidance tended to increase. Regression analysis showed a positive correlation ($r^2 = 0.60$) between earthworm avoidance and pesticide label rate.	Slimak 1997
Earthworms (*Eisenia foetida; Allolobophora caliginosa; Allolobophora chlorotica; Lumbricus rubellus*)	Direct exposure to aqueous solutions for 30 minutes with an 80 observation period. LC_{50} in mg/L water: *E. foetida* = 200-800 mg/L *A. caliginosa* = 3.1 – 6.3 mg/L *A. chlorotica* = ca. 200 mg/L *L. rubellus* = 25 – 50 mg/L	Stenersen 1979
Earthworms (*Eisenia foetida; Allolobophora caliginosa; Allolobophora chlorotica; Lumbricus rubellus*)	Soil exposures at concentrations from 4 to 64 ppm. No mortality in *E. foetida*. 100% mortality in *A. caliginosa* and *L. rubellus* after 2 to 3 days at 4 ppm. 100% mortality in *A. chlorotica* at 8 ppm after 7 days. 50% mortality in *A. chlorotica* at 4 ppm over 14 days	Stenersen 1979
Earthworms (*Eisenia fetida andrei*) were exposed to 0, 0.05, 0.1, 0.5, 1, and 3 μg/cm^2 carbaryl in a contact test for 48 hr.	**5 day LC_{50} = 3.4 μg/cm^2** Significant inhibition of the lysozyme activity detected in the cytosol (CL) but significant increase in cytolytic activity starting at 0.1 μg/cm^2. Significant inhibition of phagocytosis starting at 0.5 μg/cm^2.	Ville et al. 1997
OTHER		
Colpoclypeus florus (beneficial parsitoid)	Direct spray with 30 ppm solution caused 74% mortality in 48 hours and 150 ppm caused 100% mortality in the same period.	Brunner et al. 2001
Trichogramma platneri (beneficial parsitoid)	Direct spray with 30 ppm solution caused 79% mortality in 48 hours and 150 ppm caused 98% mortality in the same period.	Brunner et al. 2001
Soil microarthropods (*Collembola* spp.) were exposed to 0.26% and 0.625% carbaryl (Carbaryl 50 WP; Excel Industries Ltd, India) in sterilized sandy loam for 24 hr.	Acetylcholinesterase activity was significantly inhibited: 0.26% carbaryl =52.40% inhibition 0.625% carbaryl = 61.60% inhibition	Chakravorty et al. 1995

Appendix 6: Terrestrial Invertebrates *(continued)*

Application	Observations	Reference
Two-spotted spider mites (*Tetranychus urticae*) were reared on bean plants sprayed with 0 or 600 ppm carbaryl, and were then observed on leaves treated with dicofol or amitraz	In dicofol bioassays, there was no significant difference between mites pre-exposed to carbaryl and controls in the tendency to feed and stand longer off treated areas. In amitraz bioassays, pre-exposure to carbay1had the opposite effect. It increased the propensity of mites to feed and stand off amitraz-treated areas, resulting in increased avoidance of amitraz.	Dombrowski et al. 1994
Asian lady beetle (*Harmonia axyridis*)	Complete inhibition of egg hatch in Petri assays at application rates equivalent to1.97 kg/ha (1.75 lb/acre). Adverse effects in field trials at the same rate.	Galvan et al. 2005
Potato leafhopper (target), *Reduviolus americoferus* (preditor), and tarnished plant bug (non-pest alternate prey)	LC_{50}s based on concentrations in solution for direct spray. Potato leafhopper: 15.4 mg/L Tarnished plant bug: 73.3 mg/L *R. americoferus*: 173.9	Martinez and Pienkowski 1983
Spring wasp (*Tiphia vernalis*, parasitoid)	4-day soil treatments: 0.5X equivalent to 4 mg/kg (eq. to application rate of 4 lb/acre). See Table 1. Decrease in survival of *T. vernalis* progeny.	Oliver et al. 2005
Spring wasp (*Tiphia vernalis*, parasitoid)	Turf core bioassay (foliar exposure): 8.96 kg/ha (8 lbs/acre). Increased mortality: a factor of about 2 over controls at 48 hours. A greater response in males than females at 24 hours.	Oliver et al. 2006
Brown snails (*Helix aspersa*) dietary exposures for 10 days.	LC_{50} = >10,003 ppm EC_{50} = 5,003 ppm (95% C.L. = 3678, 4803) For the sublethal effect of extended edematous body with drooping eyestalk: NOAEL= 626 ppm LOAEL = 2,502 ppm For mortality: NOAEL = 2,502 ppm LOAEL = 10,003 ppm The authors suggest that the relative ineffectiveness of carbaryl may have been due in part to aversion of the spiked food by the snails.	Schuytema et al 1994
European corn borer (*Ostrinia nubilalis*)	Larvae exposed via contaminated diet. 96-hour LC_{50} of 5.3 ppm. 18 day LC_{50} of 4.2 ppm.	Trisyono and Chippendale 1997
Lady beetle (*Coleomegilla maculata*)	Eggs exposed by dipping in solutions of carbaryl. Complete egg mortality at 1400 mg/L.	Trisyono et al. 2000
Southern pine beetle (*Dendroctonus frontalis*), bw 2.12 mg	Topical application LD_{50} values: 24 h: 136.35 mg/kg 48 h: 25.8 mg/kg	Zhong et al. 1995
Spruce beetle (*Dendroctonus furipennis*) , bw 15.4 mg	Topical application LD_{50} values: 24 h: 8.7 mg/kg 48 h: 4.22 mg/kg	Zhong et al. 1995

Appendix 6: Summary of Terrestrial Field or Field Simulation Studies

Application Rate	Observations	Reference
Carbaryl (Sevin 50 WP, Rhone-Poulenc, NC)at 12 and 60 g/100L was hand sprayed onto apple trees in three apple orchards near Corvallis, OR in 1994 and 1995. Unsprayed trees were controls.	Twelve families, 26 genera, and 30 identifiable spider species were found in surveys of apple trees. In 1994, full field rates of carbaryl (60 g/100 L) significantly suppressed spider population densities (25-75% mortality). 12 g/100L had no effect. In 1995, no effect on spider populations were observed at either rate.	Bajwa and Aliniazee 2001
Carbaryl (Sevin 80% + NR440 oil) at 0.38 ± 1.45 oil (0.32 lb a.i./100 gal) applied in August 1984 with a high-volume oscillating boom to four rows (15 trees each) of 20-yr-old Eureka lemon trees. Treated rows were separated by three rows of unsprayed trees that served as controls.	Of the four pesticides tested, only carbaryl residue caused high initial mortality to *Cryptolaemus montrouzieri* (48-hr LC_{50} = 0.803 $\mu g/cm^2$; for three remaining beneficials (*Aphytis melinus* 48-hr LC_{50} = 0.767 $\mu g/cm^2$, *Euseius stipulatus* 48-hr LC_{50} = 1.905 $\mu g/cm^2$, and *Metaphyscus helvolus* 48-hr LC_{50} not provided) mortality related to carbaryl residue decreased to<50% after 3 days. [Note: This study concerns the relative toxicity of the dislodgeable residue of four agents used to control California red scale in citrus groves to nontarget species; however, the dislodgeable residue values are not provided except as toxicity values.]	Bellows and Morse 1988
Mixture of 13% carbaryl (a.i.) and 87% cucuritacin (bait) applied to 260 ha treatment blocks at a rate of 0.0699 kg/ha [0.062 lb a.i./acre] for control of corn rootworm beetle. Applications in Iowa and South Dakota. Observations for up to 4 weeks post application.	Greatest apparent adverse effect on ground dwelling spiders. No substantial impact on staphylinid abundance. Decrease in beetle (Carabidae), ants (Formicidae), and lacewings (Chrysopidae) at some but not all sites. No adverse effects and some beneficial effects on canopy spiders.	Boetel et al. 2005
Carbaryl (Sevin SL; Aventis, NJ) at 6.10 kg a.i./ha (approx 6 lb a.i./acre) sprayed on plots of mixed stands of tall fescue with 25-50% flowering white clover cover at the University of Kentucky's Spindletop Research Farm near Lexington, KY.	Bumble bee (*Bombus impatiens*) colonies were confined on the plots after residues had dried, with effects on colony vitality evaluated after 14 days. Colony vitality adversely affected: fewer worker bees, honey pots, and brood chambers were present in hives from treated plots. Worker biomass and colony weights were also reduced. Two of the four colonies had no live brood or adults. Significantly reduced foraging activity on treated plots. Foraging endemic bumble bees did not avoid sprayed plots relative to untreated plots (significant).	Gels et al 2002

Appendix 6: Terrestrial Field Studies *(continued)*

Application Rate	Observations	Reference
Mixed community of soil arthropods. Treatment of plots (about 1000 m^2) of ponderosa pine with carbaryl at 5.22 g/ m^2 (52.2 kg/ha or 46.5 lb/acre) or 26.1 g/m^2 (216 kg/ha or 192 lb/acre).	Soil residues of 498 ppm at 46.5 lb/acre and 2960 ppm at 192 lb/acre. Substantial decrease in collembolan and gamasid mite populations at DAT 10. Decreases in collembolans persisted at DAT 138.	Hoy and Shea 1981
8.96 kg/ha (8 lb/acre) applied to turf.	Reduced earthworm populations over a 20 week post-application period.	Potter et al. 1990
Granular carbaryl (Sevin 7 G, 7.15% a.i.; Lebanon Chemical, PA) was applied at a rate of 4.5 kg/ha (4 lb/acre) to plots in mixed oak-pine and oak forests in central New Jersey. Untreated areas were controls.	The diversity and abundance of forest arthropods taken in pitfall traps for 12 wk after treatment was assessed. <u>Mixed Oak-Pine Forest</u> Total number of arthropod taxa, total number of individual arthropods , and total number of *Collembola* were reduced in treatment samples relative to controls within 1 wk of application and remained lower at least 12 wk after the application. Total number of *Formicidae* was lower in the treatment plots after application, but not significantly depressed until 12 wk after treatment. There was a significant reduction in both total number of ground spider taxa and total number of spiders at 1and 2 wk post treatment, respectively. Significant differences were also detected at 12 wk after the application. <u>Oak Forest</u> Total number of arthropod taxa, total number of individual arthropods , total number of *Collembola*, and total number of *Formicidae* were reduced in treatment samples relative to controls within 1 wk of application and remained lower at least 12 wk after the application. Total number of ground spider taxa was reduced only at 8 wk post treatment. Total number of spiders was significantly reduced after 2 wk, not after 4 wk, but then again significantly reduced at 8 and 12 wk post treatment.	Schulze et al. 2001

Appendix 6: Terrestrial Field Studies *(continued)*

Application Rate	Observations	Reference
Carbaryl (Sevin 80A; Rhone-Poulenc, NC) at 567 g carbaryl/378 L water/0.45 ha (1.26 kg/ha or 1.12 lb/acre) was applied with a commercial air-blast sprayer to orange trees at the Citrus Research and Education Center, University of Florida in 1995. Unsprayed trees were controls.	Mortality of adult parasitic wasps (*Aphytis holoxanthus*) after 24 hr exposure to carbaryl residues on treated orange leaves at various sampling intervals up to 31 days post treatment was assessed. Wasps were dead after 4 to 5 hr of exposure to carbary1 residues on leaves that were collected 4 hr, and 1, 2, and 3 days post treatment. Wasp mortality on carbaryl residues was 100% through day 10 and declined to control levels by day 27. Surviving wasps after day 14 appeared healthy. Quantification of dislodgeable residues on treated orange leaves was simultaneously assessed.	Rehman et al 1999
Carbaryl (Sevin 80S) at 115.0 g a.i./l00L was applied using a vertical oscillating boom sprayer to plots of orange and lemon trees at the Agricultural Experiment Station in Riverside, CA, in 1987 and 1988.	There was a significant increase in non-target Citrus red mite (*Panonychus citri*) densities were observed in both years. The increased levels persisted 6-8 months after treatment.	Walker and Aitken 1996

Appendix 7: Toxicity to Fish

Species	Nature of Exposure	Exposure Time	Effects	Reference
Channelfish (*Nuria denricus*)	Carbaryl concentrations of 0.05 to 100 ppm		5 ppm and higher: abnormal swimming behavior and decreased survival. 0.5 ppm NAEL.(NOAEC) 24-h LC_{50}: 52.4 mg/L 96-h LC_{50}: 34.7 mg/L 504-h LC_{50}: 12.59 mg/L [additional time value specified]	Abbasi and Soni 1991
Fresh-water catfish (*Mystus vittatus*), six healthy juveniles/ concentration	30-100 mg/carbaryl 50% a.i.(50WP, Union Carbide India Ltd) dissolved in 1 L water	24, 48, and 72 hours	100% mortality within 72 hrs at 32.5 ppm; **72-hr LC_{50} = 17.5 ppm**; no mortality at ≤12.5 ppm (sublethal concentrations accelerated swimming activity and increased the frequency of respiration/ gill movements in response to increased concentrations of carbaryl)	Arunachalam et al. 1980
Fresh-water catfish (*Mystus vittatus*), three juveniles/ concentration	fish reared individually in concentrations of 5, 7.5, 10, or 12.5 ppm carbaryl (controls reared in fresh water)	27 days	Decrease in feeding rate and growth rate (from 10.15 mg/g/day in freshwater to 2.84 mg/g/day at 12.5 ppm).	Arunachalam et al. 1980
Spike-tailed paradise fish (*Macropodus cupanus*) – obligate air-breather	Concentrations of 1 ppm to 5 ppm	24-96 hours	No mortality at any concentration at 24 hours. At 96 hours, LC_{50} of 3.5 ppm. No mortality at 2.5 ppm.	Arunachalam and Palanichamy 1982
Spike-tailed paradise fish (*Macropodus cupanus*) – obligate air-breather	fish reared individually in concentrations of 1, 1.5, 2.0, or 2.5 ppm carbaryl (controls reared in fresh water)	26 days	Clear dose-related decrease in food conversion efficiency at concentration from 1 to 2.5 ppm.	Arunachalam and Palanichamy 1982
Green snakehead *Channa punctatus*	Concentrations of 1 ppm to 8 ppm	24-96 hours	NOEC = 5 ppm. 96 hour LC_{50} = 6 ppm	Arunachalam et al. 1985
Green snakehead *Channa punctatus*	fish reared individually in concentrations of 1, 1.5, 2.0, or 2.5 ppm carbaryl (controls reared in fresh water)	26 days	Dose-related decreases in oxygen consumption, feeding rate and growth rate at all concentrations.	Arunachalam et al. 1985

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Carp (4 species: *Labeo rohita; Cirrhina mrigala; Cyprinus carpio; Catla catala;*	Range of test concentrations not specified. Fish observed daily. Observations on Day 4 used to calculate 96 hour LC_{50} values.	30 days	96-hour LC_{50} values *Labeo rohita*: 1.87 mg/L *Cirrhina mrigala*: 1.37 mg/L *Cyprinus carpio*: 2.0 mg/L *Catla catala*: 1.42 mg/L 30-day MATC (NOEC) values for all four species were in the range of 0.052-0.078 mg/L.	Bansal et al. 1980
Tilapia mossambica	Static bioassay	48 hours	LC50 = 5.495 (4.4-6.59) mg/L Gives slope but does not specify the concentration transformation on which the slope is based.	Basha et al. 1983
Rainbow Trout (*Oncorynchus mykiss*); Larval	Static-renewal acute toxicity test. Nominal concentrations: 0 (solvent (acetone) control), 188, 375, and 750 µg/liter carbaryl (Chem Services, Inc., West Chester. PA)	24 hr and 96 hr	Cholinesterase (ChE) activity decreased significantly ($P < 0.0001$) with increasing concentration. Mean inhibition of ChE activity ranged 14-38% at 24 hr, 32-41% at 96 hr, and 7- 14 % following a 48-hr recovery period. MChR binding was not significantly affected. Receptor affinity (K_D) did not vary significantly with increasing carbaryl concentrations and exposure durations. Exposure caused significant changes in swimming speed, and these changes were positively correlated with changes in brain ChE activity ($r2 = 0.7057$. $P = 0.0006$).	Beauvais et al. 2001
Colorado Squawfish (*Ptychocheilus lucius*)	Flow-through acute toxicity test.	24 hr	Cholinesterase inhibition (ChE) NOEC = 29.3 µg/L LOEC = 49.1 µg/L	Beyers and Sikoski 1994

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Mesolarval, metalarval, and juvenile Colorado Squawfish (*Ptychocheilus lucius*) and Bonytail (*Gila elegans*)	Range-finding, 4 day renewal-acute, and 32 day early life stage (ELS) tests were conducted with technical carbaryl (1-naphthyl methylcarbamate, 99%, Rhone-Poulenc, Research Triangle Park, NC) The lowest concentration lethal to all test organisms in 24 h was the highest test concentration used in 4 day renewal-acute tests.	4 days (96 hr) and 32 days	**96 hr LC_{50} in mg/L:** Colorado squawfish = 1.31 (95% C.L. = 1.23, 1.4) Bonytail = 2.02 exposed (95% C.L. = 1.78, 2.25) 32 day ELS: NOEC: 445 µg/L for Colorado squawfish and 650 µg/L for bonytail. LOEC: 866 µg/L for Colorado squawfish and 1240 µg/L for bonytail. Threshold concentrations as estimated by linear-plateau regression were 364 µg/L for Colorado squawfish and and 217 µg/L for bonytail Typically, growth was as sensitive or more sensitive than survival as a measure of toxic effects.	Beyers et al. 1994

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Mesolarval, metalarval, and juvenile Colorado Squawfish (*Ptychocheilus lucius*) and Bonytail (*Gila elegans*)	4-day renewal-acute test using Sevin.4-Oil (a carbaryl formulation containing 49% carbaryl and petroleum distillates) (Rhone-Poulenc, Research Triangle Park, NC)	4 days	**96 hr LC_{50} in mg/L:** Colorado squawfish = 3.81 (95% C.L. = 2.87, 3.52) Bonytail = 3.31 (95% C.L. = 3.06, 3.55) The authors state that the toxicity of Sevin-4-Oil (49% carbaryl) was approximately one-half that of carbaryl, as outlined in the previous study in this table. The ratio of median lethal concentrations of carbaryl to Sevin-4-Oil was 0.840 and 1.24 for Colorado squawfish and bonytail, respectively. The authors state that ratios between 0.5 and 1.5 are considered within the range of normal experimental variation; therefore, no synergistic or antagonistic toxic effects due to formulation of carbaryl as Sevin-6 Oil were observed.	Beyers et al. 1994
Sole (*Solea solea*)	Enzymatic extract derived from tissue homogenate was treated with 10^{-4} - 10^{-6} M carbaryl (Technical grade; Rhone-Poulenc).	1 hr	7.8×10^{-6} M caused 50% acetylcholinesterase inhibition.	Bocquene et al. 1995
Fathead minnow (*Pimephales promelas*)	Full life-cycle flow-through bioassay, concentrations of 0.008, 0.017, 0.062, 0.21, and 0.68 mg/L	9 months	0.68 mg/L: decreased survival and no reproduction. 0.008 mg/L: decreased survival in hatchlings. This effect was probably not attributable to carbaryl because the effect was not seen at 0.017, 0.062, 0.21 mg/L.	Carlson 1972

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Medaka; Juvenile	Static test conditions. Measured concentrations: 0, 2.5, 5.1, 7.0, 9.4 mg/L carbaryl (99% Technical Grade, Union Carbide, New York, NY).	1) 24 hr for toxicity test 2) 48 hr for electrophysiological and predator/prey tests	1) Toxicity test: 24 hr LC50 = 9.4 mg/L 2) Electrophysiological test: Treated fish were slow to react to handling and displayed rapid body spasms when stimulated. Significant increase in neuro-muscular delay. Significantly more responsive to touch at lower concentrations, and less responsive in near lethal concentrations. Significant increase in response to stimuli rate (R/S) after 24 hr only at 7.0 mg/L. At 9.4 mg/L R/S was 72% at 24 hr but decreased to 33% at 48 hr. Predator/prey test: There were no differences between control groups and exposed prey (treated Medaka) at 2.5 or 7.0 mg/L. At 9.3 mg/L there was an increase in consumption time of treated Medaka by bluegill predators.	Carlson et al. 1998
Bluegill sunfish	Static	96 hours	LC_{50} = 5.9 mg/L	Carter and Graves 1972
Mosquitofish	Static	96 hours	LC_{50} = 1.4 mg/L	Carter and Graves 1972
Channel catfish	Static	24 hours	LC_{50} = 11.5 mg/L	Carter and Graves 1972
Zebrafish	Fertilized eggs were exposed to nominal concentrations 1-100 µg/ml carbaryl.	4 hours post fertilization (hpf) to 28 hpf	All embryos died at concentrations of 50 µg/ml (50 ppm) and greater. Growth arrest was observed at 30 µg/ml (30 ppm) and pericardial edema was observed at 10 µg/ml (10 ppm). No gross abnormality was observed at concentrations below 10 µg/ml (10 ppm).	Cheng et al. 2004

Appendix 7: Toxicity to Fish *(continued)*

<table>
<tr><th>Species</th><th>Nature of Exposure</th><th>Exposure Time</th><th>Effects</th><th>Reference</th></tr>
<tr><td>Carp, Asian (Cyprinus carpio)</td><td>Static</td><td>96 hours</td><td>LC_{50} = 3.7 mg/L
Longer term exposures lead to kidney damage.</td><td>Dhanapakiam and Premlatha 1994</td></tr>
<tr><td>Rainbow trout (Salmo gairdneri)</td><td>Static</td><td>96 hours</td><td>LC_{50} = 4.3 (3.65-5.59) mg/L</td><td>Douglas et al. 1986</td></tr>
<tr><td>Fathead minnow (Pimephales promelas), Bonytail chub (Gila elegans), Colorado squawfish (Ptychocheilus lucius), and Razorback sucker (Xyrauchen texanus)</td><td>Test concentrations not specified in publication. Control and solvent control used. Carbaryl, 99.7% a.i.</td><td>7 days</td><td>IC_{25} (Inhibition Concentration, integrating growth/survival effects)
in mg/L:
Squawfish = 1.33
Sucker = 2.06
Minnow = 0.42
Chub = 0.25

Squawfish and sucker IC25 significantly greater than minnow and chub.</td><td>Dwyer et al. 1999</td></tr>
<tr><td>Comparative LC_{50} study of 19 species. See column 4.

Note: Several of the tested species are marine.</td><td>Static, 99.7% purity</td><td>96-hour</td><td><table><tr><th>Species</th><th>LC_{50}</th></tr><tr><td>Fathead minnow</td><td>5.21</td></tr><tr><td>Sheepshead minnow</td><td>4.36</td></tr><tr><td>Rainbow trout</td><td>1.88</td></tr><tr><td>Atlantic sturgeon</td><td><0.8</td></tr><tr><td>Shortnose sturgeon</td><td>1.81</td></tr><tr><td>Razorback sucker</td><td>4.35</td></tr><tr><td>Bonytail chub</td><td>3.49</td></tr><tr><td>Cape Fear shiner</td><td>4.51</td></tr><tr><td>Colorado pikeminnow</td><td>3.07</td></tr><tr><td>Spotfin chub</td><td>3.41</td></tr><tr><td>Desert pupfish</td><td>7.71</td></tr><tr><td>Leon Springs pupfish</td><td>4.54</td></tr><tr><td>Fountain darter</td><td>2.02</td></tr><tr><td>Greenthroat darter</td><td>2.14</td></tr><tr><td>Gila topminnow</td><td>>3.0</td></tr><tr><td>Apache trout</td><td>1.54</td></tr><tr><td>Greenback cutthroat trout</td><td>1.55</td></tr><tr><td>Lahontan cutthroat trout</td><td>2.25</td></tr></table></td><td>Dwyer et al. 2005a</td></tr>
<tr><td>Comparative IC_{25} (growth) study. See column 4.</td><td>Static renewal, 99.7% purity</td><td>7-days</td><td><table><tr><th>Species</th><th>IC_{25}</th></tr><tr><td>Fathead minnow</td><td>0.42</td></tr><tr><td>Razorback sucker</td><td>2.06</td></tr><tr><td>Bonytail chub</td><td>0.25</td></tr><tr><td>Colorado pikeminnow</td><td>1.33</td></tr><tr><td></td><td></td></tr></table></td><td>Dwyer et al. 2005a</td></tr>
</table>

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Rainbow Trout (*Oncorynchus mykiss*); Juvenile	Static conditions. Carbary1(99.0% purity, Chem Service, West Chester, PA, USA) dissolved in acetone. Test concentrations not given.	96 hr	**96 hr LC_{50} = 5.40 mg/L** (95% C.L. = 4.27-6.18) **IC_{50}** (inhibition of trout brain cholinesterase) **= 0.019 mg/L**	Ferrari et al 2004a
Goldfish (*Carassius auratus*); Juvenile	Static conditions. Nominal concentrations: 9.0, 11.0, 14.0, 17.0 and 21.0 mg/L carbaryl (99.0% purity, Chem Service, West Chester, Pennsylvania) dissolved in acetone.		Brain ChE showed 86% inhibition at its LC_{50}. The estimated IC_{50} of the goldfish brain cholinesterase was 2.62 mg/L. Recovery from carbaryl inhibition occurred within 1 week. Signs of toxicity (at the beginning of the treatment at median lethal concentrations): bursts of swimming and loss of equilibrium, with a further short-term compensation causing reduced locomotion. **96 hr LC_{50}= 13.86 mg/L** (95% C.L. = 12.1-15.9) **NOEC = 9.0 mg/L**	Ferrari et al. 2004b

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Guppy (*Poecilia reticulata*) and Zebrafish (*Brachydanio rerio*)	Semi-static conditions. Nominal concentrations (guppy): 0 (DMSO solvent control), 2.99, 5.97, 11.94, 23.88, and 47.76 µmol/L carbary1 (99% pure; Chebios, Roma, Italy); (zebrafish): 0 (DMSO solvent control), 4.48, 8.96, 17.91, 35.82, and 71.64 µmol/L carbary1. Measured concentrations (guppy): 2.39, 4.33, 8.05, 14.89, and 33.01 µmol/L carbary1; (zebrafish): 3.90, 7.21, 14.66, 26.83, and 48.37 µmol/L carbary1	96 hr	In the guppy, the highest concentration (33.01 µmol/L; equiv to 6.6 mg/L @ MW=201.2) caused rapid loss of equilibrium, associated with spiral swimming behavior. After a few hours, guppies became hypoactive and all died within a 24-48 h exposure period. Similar responses, with reduced mortality, were observed at lower concentrations after 3 or 4 days exposure. Exposure of the zebrafish at similar concentrations (specifics not given) caused only minor hypoactivity. Four out of ten zebrafish survived exposure to the highest concentration (48.37 µmol/L, equiv to 9.7 mg/L). 96 hr LC_{50}: Guppy = 12.5 µmol/L (2.5 mg/L) Zebrafish = 46.8 µmol/L (9.4 mg/L)	Gallo et al. 1995
Air-breathing Catfish (*Hepteropneus tes fossilis*)	Static bioassay. For determination of LC_{50}: 0, 15, 17.5, 20, 22.5, and 25 ppm carbaryl (WDP 50%) in distilled water. For food utilization and respiratory metabolism studies: not given.	LC_{50} = 96 hr Food utilization = 15 days	**LC_{50} = 19.99 ppm** (95% C.L. = 17.92, 22.29) Feeding rate, and absorption and conversion of food of exposed fish significantly decreased. Oxygen consumption and surfacing frequency increased in exposed fish. Statistical significance not given.	James and Sampath 1994

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Cold water species; (*Oncorhyncus mykiss*), Apache trout (*Oncorhynchus apache*), and Lahontan cutthroat trout (*Oncorhynchus clarki henshawi*)	Static acute toxicity tests. Carbaryl in acetone. 0, 0 (solvent control), 0.5, 0.8, 1.3, 2.2 and 3.6 mg/L. Carbaryl appear as concentrations in one of the tables, but are not given under Methods.	96 hr	Decreased numbers of muscarinic cholinergic receptors (MChR) in rainbow trout brain at 2.2 and 3.6 mg/L. This effect was not observed in Lahontan or Apache trout brain, because there were no survivors at 2.2 or 3.6 mg/L.	Jones et al. 1998
Fathead minnow (*Pimephales promelas*), Bonytail chub (*Gila elegans*), Colorado squawfish (*Ptychocheilus lucius*), and Razorback sucker (*Xyrauchen texanus*)	Static acute toxicity tests. Carbaryl in acetone. Two citations are given as source for procedures. 0, 0 (solvent control), 0.5, 0.8, 1.3, 2.2 and 3.6 mg/L carbaryl appear as concentrations in one of the tables, but are not given under Methods.	96 hr	Decreased numbers of muscarinic cholinergic receptors (MChR) in fathead minnow at 3.6 and 6.0 mg/L. Decreased numbers of MChR in razorback sucker at 6.0 mg/L. Decreased numbers of MChR in bonytail chub at 3.6 mg/L. Increased numbers of MChR in Colorado squawfish at 2.2 mg/L.	Jones et al. 1998
Catfish (*Clarius butrachus*)	0 and 15.3 ppm Sevin (carbaryl forumlation; 50% WDP powder, Bhopal Pesticides, Bhopal, India)	24 hr, then for 48 hr intervals until 168 hr	Serum glucose levels were significantly increased in treated fish throughout the exposure period. Serum alkaline phosphotase levels showed insignificant changes after 24 hr, thereafter significant elevation was observed in treated fish. Serum total bilirubin levels were significantly increased in treated fish throughout the exposure period.	Jyothi and Narayan 1999

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Catfish (*Clarius butrachus*)	0 and 15.3 ppm of the commercial formulation of carbaryl, sevin (Bhopal Pesticides).	24 hr, then for 48 hr intervals until 168 hr	**96 hr LC_{50}** for carbaryl of **46 ppm** was determined according to probit analysis; the authors are not clear whether this was done in the current study or at an earlier time. Significant depletion in serum cholesterol levels in treated fish throughout the exposure period.	Jyothi and Narayan 2001
Carp (*Cyprinus carpio*)	Assays on egg hatchability and 96 hr LC_{50}s for different life-stages. Duration period for eggs not specified but included sufficient time for all viable eggs to hatch.	96-h for LC_{50}s	No eggs hatched at 5 mg/L. Reduces egg hatching at 0.5 mg/L and higher. LC50s: Eggs: 1.19 mg/L Larvae: 2.86 mg/L Fry 3.30 mg/L	Kaur and Dhawan 1996
Carp (*Cirrhina Mrigala*)	0 (tap water control), 0.002 and 0.01 mg /L Sevin (carbaryl 50% WP; l-napthyl-N-methyl carbamnate). Concentrations were made in terms of the pesticide commercial formulation and not in terms of active ingredient of pure pesticide.	60 days	During both the preparatory and pre-spawning phases of reproduction, both treatment levels significantly reduced the protein and lipid contents of flesh, liver and gonads of males and females. The decline was greater at 0.01 mg/L than at 0.002 mg/L. Significant decrease in gonadal-somatic index, ova diameter, absolute fecundity, running fecundity, fertilization rate, hatchability and survival of eggs at both treatment levels.	Kaur and Dhawan 1996
Striped bass (*Morone saxatilis*)	Saline water using proportional diluters (constant concentrations) rather than static renewal.	96 hours	96-hr LC_{50} 1 mg/L	Korn and Earnest 1974
Mozambique Tilapia (*Sarotherodon mossambicus*)	Static bioassay	Up to 3 days	LC_{50} Values 24-h: 13 mg/L 48-h: 10 mg/L 72-h: 8 mg/L	Koundinya and Ramamurthi 1980a.

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Mozambique Tilapia (*Sarotherodon mossambicus*)	4 mg/L	30 days	Increased RBC count and hemoglobin.	Koundinya and Ramamurthi 1980b.
Guppy (*Lebistes reticulatus* a.k.a. *Poecilia reticulate*)	Static exposures	4 days	LC_{50} Values 24-h: 5 mg/L 48-h: 4.6 mg/L 72-h: 4.6 mg/L 96-h: 4.6 mg/L	Manna and Ghosh 1987
Rainbow trout (*Oncorynchus mykiss*)	Static exposures to fish reared on different diets.	4 days	LC_{50} Values from 0.935 to 1.74 mg/L for fish on different diets. None of the differences are statistically significant	Marking et al. 1984
Green snakehead (*Channa punctatus*)	Static renewal exposures	4 days	LC_{50} Values 24-h: 29 mg/L 48-h: 23 mg/L 72-h: 18 mg/L 96-h: 14 mg/L	Mishra et al. 1991
Mosquitofish (*Gambusia affinis*)	Static (no renewal noted). Fish were collected from a ditch and not reared in the laboratory.	4 days	96 h LC_{50}: 204 mg/L	Naqvi and Hawkins 1988
Striped bass (*Morone saxatilis*)	Static. No renewal specified	4 days	96 h LC_{50} values in mg/L Fresh water: 0.76 (0.5-0.11) Saline water (1%): 2.3 (1.8-3.0)	Palawski et al. 1985
Fathead minnow (*Pimephales promelas*)	Flow-through proportional diluters	4 days	96-h LC_{50}: 5.01 mg/L	Phipps and Holcombe 1985
Goldfish (*Carassius auratus*)	Flow-through proportional diluters	4 days	96-h LC_{50}: 16.7 mg/L	Phipps and Holcombe 1985
Channel catfish (*Ictalurus punctatus*)	Flow-through proportional diluters	4 days	96-h LC_{50}: 12.4 mg/L	Phipps and Holcombe 1985
Bluegill sunfish (*Lepomis macrochirus*)	Flow-through proportional diluters	4 days	96-h LC_{50}: 6.97 mg/L	Phipps and Holcombe 1985
Rainbow trout (*Salmo gairdneri*)	Flow-through proportional diluters	4 days	96-h LC_{50}: 0.86 mg/L	Phipps and Holcombe 1985

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Brook trout (*Salvelinus fontinalis*),	Appears to be static.	4 days	LC_{50} Values 24-h: 1.83 mg/L 48-h: 1.5mg/L 72-h: 1.15 mg/L; 1.64 mg/L 96-h: 1.07 mg/L; 1.45 mg/L The replicate values for 72 and 96 hours were conducted using somewhat larger fish.	Post and Schroeder 1971
Rainbow trout (*Salmo gairdnerii*)	Appears to be static.	4 days	LC_{50} Values 96-h: 1.5 mg/L	Post and Schroeder 1971
Cutthroat trout (*Salmo clarki*)	Appears to be static.	4 days	LC_{50} Values 72-h: 2 mg/L 96-h: 1.5 mg/L; 2.1 mg/L The replicate values 96 hours were conducted using somewhat larger fish.	Post and Schroeder 1971
Coho salmon (*Oncorhyn-chus kisutch*)	Appears to be static.	4 days	LC_{50} Values 24-h: 2.95 mg/L 48-h: 2.7mg/L 72-h: 1.7 mg/L 96-h: 1.3 mg/L	Post and Schroeder 1971
Carp (*Cirrhina mrigala)*	Static	4-days	96 h LC_{50} values TGAI: 2.5 (1.9-3.2) mg/L 85%WP: 5.7 (5.5-5.9) mg/L 50% WP: 5.9 (5.7-6.3) mg/L All values expressed as a.i.	Rao et al. 1984
Green snakehead (*Channa punctatus*)	Static	1-Days	96 hr LC_{50}: 8.71 mg/L	Rao et al. 1985

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Freshwater cold and warm water species; Some saltwater species. See column 4.	Freshwater static acute toxicity tests. Saltwater static acute toxicity tests.	12, 24, 48, 72, and 96 hr	12 and 24 hr LC50s were also reported, as were 95% C.L.s. **96 hr LC_{50} in mg/L:** <u>Cold water</u> Rainbow trout = **1.9** Apache trout = **1.5** Greenback cutthroat = **1.6** Lahontan trout = **2.3** <u>Warm water</u> Fathead minnow = **5.2** Bonytail chub = **3.5** CO pikeminnow = **3.1** Razorback sucker = **4.4** <u>Euryhaline</u> Sheepshead minnow = **4.4** Leon Springs pupfish = **4.5** Desert pupfish = **7.2** Fish exposed to higher concentrations of carbaryl were immobilized. Fish dying from carbaryl exposure generally exhibited arched backs. gaping mouths, and flared gills and fins.	Sappington et al. 2001
Catfish (*Clarius butrachus*)	0 (solvent control), 1.0, 2.0, and 4.0 mg/L carbaryl (technical grade, 99% purity, Rallis India Ltd.)	96 hr and 15 days	Changes in body color (from pinkish gray to dark gray), opercular movement, surfacing and swimming. Significant alterations in the levels of some biochemical indices (total protein, inorganic phosphate, glucose, cholesterol, lactic acid) as well as in the activities of some key enzymes (LDH, acid and alkaline phosphatases, GOT, and GPT) in the serum of catfish at all three treatments and for both exposure periods.	Sharma 1999
Green snakehead *Channa punctatus*	Wild caught. No indication of renewal.	4 days	LC_{50} Values 24-h: 21.2 mg/L 48-h: 20.5 mg/L 72-h: 20.02 mg/L 96-h: 19.5 mg/L	Singh et al. 1984

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Stinging catfish (*Heteropneustes fossilis)*	Wild caught. No indication of renewal.	4 days	LC_{50} Values 24-h: 22.95 mg/L 48-h: 22.3 mg/L 72-h: 21.45 mg/L 96-h: 20.1 mg/L	Singh et al. 1984
Banded Gourami (*Colisa fasciatus*); Adult	0, 8.0, 8.5, 9.0 and 9.5 mg/L carbaryl (1-naphthyl-N-methylcarbamate) (purity 99%) for toxicity assay. 0, 4.0, 6.0 and 8.0 mg/L carbaryl (99% purity) for biochemical assay.	96 hr	24 hr LC_{50} = 9.04 mg/L. 96 hr LC_{50} = 8.00 mg/L. (95% C.L.= 7.78, 8.15) Glycogen, pyruvate, and total protein content decreased while lactate content increased in liver and muscle tissues.	Singh et al. 2004
Green snakehead (*Channa punctatus*)	Wild caught. Renewal not specified.	4 Days	96 hr LC_{50} = 15 mg/L. NOEC: 10 mg/L	Thakur and Sahai 1994
Striped snakehead (*Channa striatus*)	Wild caught. Renewal not specified.	4 Days	96 hr LC_{50} = 17.5 mg/L. NOEC: 12 mg/L	Thakur and Sahai 1994
Sucker head (*Garra gotyla*)	Wild caught. Renewal not specified.	4 Days	96 hr LC_{50} = 7.5 mg/L. NOEC: 2.5 mg/L	Thakur and Sahai 1994
Rohu carp (*Labeo rohita*)	Source of fish N.S. Flow-through system.	4 Days	96 hr LC_{50} = 4.6 mg/L (0.5 g bw). 96 hr LC_{50} = 7.75 mg/L (4.5 g bw).	Tilak et al. 1980

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Zebrafish (*Danio rerio*); Eggs and embryos	A stock solution of 16 ml of Sevin to 3000 ml of aged water was established and used to mix four dilutions, in which eggs were kept until they hatched: Dilution 1 (1/250 stock to aged tapwater Dilution 2 (1/500 stock to aged tapwater) Dilution 3 (1/750 stock to aged tapwater Dilution 4 (1/1000 stock to aged tapwater). Control was aged tapwater.	Each egg was observed every 24 hr until all eggs had hatched; last hatch was at 144 days.	The highest overall mortality rate (31 %) was in Dilution 1. The lowest mortality rate (15%) occurred in Dilutions 3 and 4. The control had a mortality rate of 19% and Dilution 2 had a rate of 33%. Sevin had a significant effect on embryo size from the time the eggs were laid until they hatched. Embryos in the highest concentration, Dilution 1, developed more slowly and hatched later than the controls and eggs in other dilutions. Embryos were smaller than the controls even at the lowest concentration.	Todd and VanLeeuwen 2002
Carp (*Cyprinus carpio*)	Collected from fish pond. Renewal not specified	4 Days	LC_{50} Values 24-h: 13.51 mg/L 48-h: 11.74 mg/L 72-h: 10.36 mg/L	Toor and Daur 1974
Catfish (*Clarias batrachus*)	Wild caught. Static exposures.	4 Days	TGAI LC_{50} Values 24-h: 61.1 mg/L 48-h: 53.6 mg/L 72-h: 48.6 mg/L 96-h: 46.9 mg/L Formulation (NOS) LC_{50} Values 24-h: 163 mg/L 48-h: 134 mg/L 72-h: 123 mg/L 96-h: 108 mg/L	Tripathi and Shukla 1988
Carp (*Cyprinus carpio*)	Static	4 Days	96 h LC_{50}: 2 mg/L	Verma et al. 1981
Catfish (*Saccobranchus fossilis*)	Static. Wild caught.	4 Days	TGAI LC_{50} Values 24-h: 23 mg/L 48-h: 21 mg/L 72-h: 20 mg/L 96-h: 20 mg/L	Verma et al. 1982
Carp *Cirrhina mrigala*	Hatchery reared. Static.	4 Days	96 h LC_{50}: 1.94 mg/L	Verma et al. 1984

Appendix 7: Toxicity to Fish *(continued)*

Species	Nature of Exposure	Exposure Time	Effects	Reference
Carp *Cirrhina mrigala*	Hatchery reared. Static.	60 days	NOEC for growth and survival: 0.087 – 0.1086 mg/L	Verma et al. 1984
Cutthroat trout (*Salmo clarki*)	Static. Hatchery reared	4 Days	96-h LC_{50} Value pH 6.5: 5.0 mg/L pH 7.5: 3.95 mg/L pH 7.8: 3.95 mg/L pH 8.5: 0.97 mg/L	Woodward and Mauck 1980

Appendix 8: Toxicity to Amphibians

Species	Exposure	Effects	Reference
ACUTE			
Green frog (*Rana clamitans*); Tadpoles	96 hr static test. 0, 0 (solvent control), 3.5, 5.0, 7.2, 10.3, 14.7, 21.0, and 30.0 mg/L carbaryl (technical-grade; Rhone-Poulenc, NC) at three different temperatures.	After 48 hr, average survival was significantly different at each temperature. Lower concentrations (3.5,5.0,7.2, and 10.3 mg/L) were not significantly different from controls, and survival at these concentrations exceeded 94%. Survival was significantly affected by an interaction between temperature and concentration. **96 hr LC50** (95% CL) **in mg/L:** 17°C (62°F) = **22.02** (20.62, 23.52) 22°C (72°F) = **17.36** (16.24, 18.56) 27°C (81°F) = **11.32** (10.42, 12.29)	Boone and Bridges 1999
Plains leopard frog (*Rana blairi*)	0, 0 (solvent control), 3.5, 5.0, and 7.5 mg/L carbaryl (99.7% purity, technical-grade; Rhone-Poulenc, NC) for 96 hr.	Carbaryl caused a nearly 90% reduction in tadpole activity at the lowest concentration compared to the controls. Time spent being active by the tadpoles was significantly lower at all three concentrations.	Bridges 1997
Southern leopard frog (*Rana sphenocephala*) tadpoles and adult red-spotted newts (*Notophthalmus viridescens*)	0 or 2.5 mg/L carbaryl (technical grade) for 24 hr.	Treated tadpole activity significantly decreased. Treated newt activity decreased, but not significantly After 24 hr, predation rates were lowest when both newts and tadpoles were simultaneously either exposed or not exposed, and were greatest when newts and tadpoles were not exposed simultaneously.	Bridges 1999a
Gray tree frog (*Hyla versicolor*); tadpoles	0, 0 (solvent control), 1.25 and 2.50 mg/L carbaryl for 24 hr.	At 1.25 mg/L, tadpole activity was unaffected. At 2.50 mg/L, tadpole activity was significantly decreased.	Bridges 1999b
Southern leopard frog (*Rana sphenocephala*), five developmental stages	0, 0 (solvent control), 0.16, 0.40, or 1.0 mg/L carbaryl	**96 hr LC50 = 10.6 mg/L** Hatching success and embryo survival unaffected at any treatment level, regardless of life stage exposure. Metamorphs exposed throughout the tadpole stage and throughout development (egg, embryo, tadpole) experienced significant mortality at all treatment levels.	Bridges 2000

Appendix 8: Toxicity to Amphibians *(continued)*

Species	Exposure	Effects	Reference
Red-legged frog (*Rana aurora*), yellow-legged frog (*R. boylii*), spotted frog (*R. pretiosa*), wood frog (*R. sylvatica*), Pickeral frog (*R. palustris*), plains leopard frog (*R. blairi*), northern leopard frog (*R. clamitans*), crayfish frog (*R. areolata*), 10 populations of Southern leopard frog (*Rana Sphenocephala*)	Survival time assays in egg masses exposed to carbaryl at 30 mg/L. Changes in tail movement assayed at 2.5 mg/L.	Based on survival time in egg masses, the most sensitive species was the wood frog and the least sensitive species was the red-legged frog. Significant differences were apparent in different populations of the southern leopard frog.	Bridges and Semlitsch 1999
Southern leopard frog (*Rana Sphenocephala*) tadpoles	Time to death assayed at 30 mg/L in full- and half-sibling families.	Smaller tadpoles more tolerant than larger tadpoles. Significant variations among different families.	Bridges and Semlitsch 2001
Southern leopard frog (*Rana sphenocephala*), tadpoles	Test concentrations of 0 to 28 mg/L with solvent (acetone) control. Static.	96 hr LC_{50} = 8.4 (7.4-9.6) mg/L.	Bridges et al. 2002
Bullfrog tadpole (*Lithobates catesbeianus*)	Static exposures	96 hr LC_{50} = 7.6 mg/L	Carter and Graves 1972
Boreal toad (*Bufo boreas*)	Carbaryl (97% a.i.; Rhone-Poulenc, NC)	96 hr LC_{50} = 12.3 mg/L	Dwyer et al. 2005a
African Clawed frog (*Xenopus laevis*)	Carbaryl (NOS)	Embryos: 24-hr LC_{50}: 4.7 mg/L. Minor abnormalities at concentrations < 1 mg/L. Gross abnormalities as 10 mg/L. Tadpoles: 0.1 ppm, erratic swimming in about half of the organisms. 1 ppm, erratic swimming with severe incoordination. 10 ppm, severe incoordination or no activity.	Elliott-Feeley and Armstrong 1982
Argentine toad (*Bufo arenarum*)	Static conditions. Carbary1(99.0% purity, Chem Service, West Chester, PA, USA) for 96 hr. Test concentrations not given.	**96 hr LC_{50} = 24.64 mg/L** (95% C.L. = 17.68, 34.77) **IC_{50}** (inhibition of tadpole cholinesterase) **= 7.58 mg/L**	Ferrari et al 2004a

Appendix 8: Toxicity to Amphibians *(continued)*

Species	Exposure	Effects	Reference
Indian green frog (*Rana hexadactyla*)	Static bioassay (with 24 h renewal) with wild caught organisms.	24 h LC_{50}: 150 mg/L 96 h LC_{50}: 55.34 mg/L	Khangarot et al. 1985
Bullfrog (*Rana tigrina*)	Acute lethal bioassay and sublethal exposures to 0.1, 0.5, 1.2, and 5 mg/L	96 h LC_{50}: 6.2 mg/L Sublethal effects as low as 0.1 mg/L: concentration related decreases in absorption efficiency and food conversion efficiency. No clear NOEC. No significant effect on duration of metamorphosis.	Marian et al. 1983
Tiger frog (*Rana tigrina*)	Intraperitoneal injection of Sevin (50% W.D.P.) at doses of 500 to 700 mg/kg bw.	**96 hr LD_{50} = 640 mg Sevin/kg bw** NOAEL = 400 mg Sevin/kg bw Effect on protein levels assessed. The paper is not clear but the doses appear to be expressed as the Sevin formulation.	Sampath et al 1995
Tiger frog (*Rana tigrina*); tadpoles	Static renewal test. Control and 8 different concentrations (not given) of carbaryl for 96 hr.	**96 hr LC_{50} = 5.68 ppm** Effect of carbaryl at 10, 20, and 30% of LC50 on excretion of NH_3-N and urea-N assessed. Significant effect at all levels.	Sampath et al 2002
Common frog (*Rana tigrina*)	Intraperitoneal injection of Sevin (50% W.D.P.) At different concentrations (not given).	Effect on lipid metabolism. No statistical analysis of data.	Sampath and Elango 1997
Gray tree frog (*Hyla versicolor*)-tadpoles; African clawed frog (*Xenopus laevis*) - embryos and tadpoles	0.24, 0.81, 2.7, 9.0, and 30 mg/L carbaryl (99.7% a.i.; Rhone-Poulenc, NC)	**96 hr LC_{50} in mg/L:** **Clawed frog tadpole = 1.73** **Tree frog tadpole = 2.47** **Clawed frog embryo = 15.25** **96 hr LC_{50} = 6.2 mg/L** in *Rana tigrina* tadpoles (Marian et al. 1983) After 1 day exposure, carbaryl significantly increased swimming activity in clawed frogs at 1.25 and 1.76 mg/L Irradiation of 7.5 mg/L carbaryl resulted in 100% mortality in clawed frog embryos on Day 1 compared to 0% mortality at 7.5 mg/L non-irradiated carbaryl.	Zaga et al 1998

Longer Term			
Green frog (*Rana clamitans*), free-swimming tadpoles (low density: 20 tadpoles/1000 L or high density: 60 tadpoles/1000 L)	Carbaryl as liquid Sevin (21.3%) at nominal concentration of 3.5 mg/L added 0, 1, 2, or 3 times at 14-day intervals to 1.85 m in diameter ponds (1480 L man-made aquatic communities) from July 27-August 24	Frequency of exposure to carbaryl significantly accelerated the rate of development of the tadpoles, compared with controls, and the effect of frequency varied according to the density of the ponds: *the majority of metamorphs and the most developed tadpoles came from high-density ponds exposed to carbaryl 3 times*. Dose frequency had no significant effect on tadpole mass or survival.	Boone et al. 2001
Various species including Southern leopard frog (*Rana sphenocephala*), plains leopard frog (*R. blairi*), and the Woodhouse toad (*Bufo woodhousii*)	Mesocosm (artificial ponds). High and low population density mesocosms used at each concentration: 0, 3.5 mg a.i./L, 5.0 mg a.i./L, or 7.0 mg a.i./L for 77 days.	The only adverse effect was a concentration related increase in time to metamorphosis. Increased survival in Woodhouse toads at highest concentration and increased survival in high-density ponds relative to low density ponds at highest concentration.	Boone and Semlitsch 2002
Gray tree frog (*Hyla versicolor*); tadpoles	1)Nominal concentrations: 0, 0 (solvent control), 0.045, and 0.090 mg/L carbaryl (99.8% purity, technical-grade; Rhone-Poulenc, NC for 10 days. 2) Nominal concentrations: 0, 0 (solvent control), 1.0, 2.1, 4.2, and 8.3 mg/L carbaryl for 16 days. 3) Nominal concentrations: 0, 0 (solvent control), 0.07, 0.14, 0.27 and 0.54 mg/L carbaryl for 16 days.	1)Organisms test in the presence and absence of caged predators (salamanders). Survival of tadpoles remained high until day 5 when it decreased significantly at both treatment levels – 8% of controls at 0.09 mg/L and 40% of controls (with predators) and 3% of control mortality (with predators) at 0.05 mg/L. Greater mortality with predator induced stress. 2)After 16 d, survival at all treatments was significantly lower than the controls. Predators did not affect survivorship. Decrease in activity was dose related. 3) After 10 d, survival at all treatments was significantly lower than the controls. Predator cues increase carbaryl lethality by a factor of 4.	Relyea and Mills 2001

Appendix 8: Toxicity to Amphibians *(continued)*

Leopard frog (*Rana pipiens*), Green frog (*Rana clamitans*), Bullfrog (*Rana catesbeiana*), Gray tree frog (*Hyla versicolor*), American toad (*Bufo americanus*); tadpoles	0, 1, and 2 mg/L a.i. Sevin for 16 days.	Mortality was not significantly affected at either concentration for any species. Growth Leopard frog: significantly reduced at both concentrations. Gray tree frog: significantly reduced at 2 mg/L. Bullfrog: significantly reduced at 2 mg/L. Green frog and American toad not affected.	Relyea 2004a
Streamside salamander (*Ambystoma barbouri*)	0, (solvent control), 0.5, 5.0, and 50 μg/L carbaryl (99% pure; ChemService, PA) for 37 days.	Larval survival significantly reduced at 50 μg/L. Delayed hatching at 5 and 50 μg/L. Significant (p=0.044) developmental effects but these do not appear to have been concentration related. An increase in larval activity at 50 μg/L. The paper involves a large number of statistical tests and comparisons. The only clear NOEC is 0.5 µg/L or 0.0005 mg/L.	Rohr et al. 2003

Appendix 9: Toxicity to Reptiles

Species	Exposure	Effects	Reference
Reptiles			
Leopard tortoise (*Geochelone pardalis*), 1-2 years old	Dermal application of carbaryl dust once a week for 3 weeks. Precise exposure conditions not specified.	Decreased food consumption, reduced defecation, diarrhea, and skin irritation were observed as transient (<1 hr) effects. Eye irritation was observed for 2 hrs after exposure.	Burridge et al 2002
Neonates of four aquatic/semi-aquatic snakes: Black swamp snake (*Seminatrix pygaea*), southern watersnake (*Nerodia fasciata*), diamondback water snake (*Nerodia rhombifer*), and brown watersnake (*Nerodia taxispilota*)	Snakes collected from uncontaminated wetlands and neonates born in captivity. Carbaryl concentrations of 0 (control), 2.5 mg/L and 5.0 mg/L.	Concentration-related decrement in maximum swimming velocity in all four species. No statistically significant differences among species based on relative changes from controls.	Hopkins and Winne 2006
Black swamp snake (*Seminatrix pygaea*) and Diamondback water snake (*Nerodia rhombifer*)	0, 2.5 and 5.0 mg/L Sevin for 48 hrs.	Swimming velocity was reduced for both swamp and water snake at 5.0 mg/L, but significant only for swamp snake.	Hopkins et al. 2005

Appendix 10: Toxicity to Aquatic Invertebrates

Note: Freshwater species followed by saltwater species in separate tables. Tables sorted by author.

Freshwater Species	Exposure	Effects	Reference
Malanopsis dufouri (Snail)	96 hours	LC_{50} at 15 °C: 14.87 mg/L LC_{50} at 22 °C: 12.8 mg/L LC_{50} at 29 °C: 10.1 mg/L	Almar et al. 1988
Procambarus clarkia (Crayfish)	96 hours	Dechlorinated tap water 0.4 mg/L: 0% mortality 0.8 mg/L: 40% mortality 1.6 mg/L: 80% mortality Lake water 0.4 mg/L: 0% mortality 0.8 mg/L: 20% mortality 1.6 mg/L: 40% mortality	Andreu-Molinere et al. 1986
Water flea (*Daphnia longicephala*)	0 (solvent control), 0.1, 0.32, 1.0 and 3.2 μg/L.	3 day old Daphnia: Body length was negatively correlated with toxicant concentrations and concentrations of 1 µg/L and higher caused significantly reduced body length. Relative crest height was significantly decreased by carbaryl at a concentration of 3.2 µg/liter. Adult daphnia: there was a negative correlation between body length or first brood size and carbaryl concentration; there was no affect on age at first reproduction. However, in the presence of kairomone, released by a Daphnia predator *Anisops gratus*, body length and first brood size both increased with increasing carbaryl concentrations. Significant decrease in reproduction rate at 0.32 μg/L with or without predator stress.	Barry 1999
Prawn (*Machrobrachium malcolmsonii*)	21 day chronic test. 0, 5.15, 7.73, and 15.47 μg/L a.i. of Sevin (50% a.i. carbaryl; M/S. Gujarat Agro Industries, India).	Significant effects on biochemical metabolism in the hemolymph, brain, hepatopancreas, gills and muscle of treated prawns.	Bhavan and Geraldine 2002
Zebra mussel (*Dreissena polymorpha*)	0 or 100 ng/L carbaryl.	Significant and maximum inhibition of AchE was achieved after 24 hr and maintained until end of exposure at 96 hr.	Binelli et al. 2006

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Crawfish, White River	Static	96-h LC_{50} = 0.5 mg/L	Carter and Graves 1972
Mussel (*Utterbackia imbecillis*); Larvae (glochidia)	Carbaryl as Sevin. (Garden Tech; 22.5% active ingredient: TechPac)	**Cited 24 hr LC_{50} in mg/L:** **Amphipod** (Gammarus lacustris) = **0.04** (Technical grade; Sanders 1969) **Chironomid** (C. thummi) = **0.127** (Technical grade; Fisher and Lohner 1986) **Cladoceran** (Daphnia magna) = **22.9** (Technical grade; Lejczak 1977) **Bivalve** (Utterbackia imbecillis) = **30.1** (Technical grade; Johnson et al. 1993) **<u>This study:</u>** **24 hr LC_{50} in mg/L:** **Bivalve** (Utterbackia imbecillis) = **7.9** (Sevin;) **NOEC (representing amount of a.i.) = 3.49 mg/L**	Conners and Black 2004 Review
Lugworm (*Arenicola marina*)	Carbary; (99%)	48 hour LC_{50} = 7.2 (5.7 – 9.0) mg/L	Conti 1987
Water flea (*Daphnia pulex*)	1) 0(solvent control), 5, and 40 ppb carbaryl (>99% grade chemical; Wako Pure Ltd.) for 5, 30, and 50 min 2) 0, 1 ppb carbaryl for 24 hr. 3) 0, 100 ppb carbaryl for 10 to 20 min. in predator/prey test.	1) Swimming behaviors were significantly changed. The largest number of changes and the largest range in significant responses were at the highest dosage, 40 ppb (acutely toxic to adults within about 1 hr). 2) Significant changes in swimming behavior after exposure for 24 hr. 3) Significant tendency for treated Daphnia to be eaten first by bluegill sunfish. Treatment induced "spinning," an easily observable change in swimming behavior.	Dodson et al. 1995
Water flea (*Ceriodaphnia dubia*)	7 day survival and reproduction test. Test concentrations not given. Control and solvent control used. Carbaryl, 99.7% a.i. (Rhone-Poulenc, Research Triangle Park, NC).	**IC_{25}** (Inhibition Concentration, reproduction and survival) = **<0.33 mg/L**	Dwyer et al. 2005b

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Paramecium multimicro-nucleatum	24 hours	24-hour LC_{50} = 93 mg/L	Edmiston et al. 1985
Midge larvae (*Chironomus riparius*)	Carbaryl, 99.7% purity, 24 hours	24-hour LC_{50} values 0.106 mg/L at pH 4 0.133 mg/L at pH 6 0.127 mg/L at pH 8	Fisher and Lohner 1986
Daphnia magna	Specified only as Sevin. Concentrations from 0.00016 to 0.1 mg/L	LC_{50} = 0.0011 mg/L	Gaaboub et al. 1975
Mosquito larvae (*Culex pipiens*)	Specified only as Sevin. Concentrations from 0.0005 to 0.008 mg/L	LC_{50} = 0.17 mg/L	Gaaboub et al. 1975
Water flea *(Daphnia ambigua)*	Concentrations of 0, 1, 2, 3, 4 and 5 µg/L carbaryl or 10 hour exposures to 5 µg/L at various stages in life cycle. Carbaryl > 99% pure.	5 µg/L x 10 h: No damage to eggs. Growth and eggs reproduction diminished. Effect most substantial in 1st instars. Long-term (NOS): 1 µg/L: NOEC 2 µg/L: Reduced survival, growth, and reproduction.	Hanazato 1991b
Water flea (*Daphnia ambigua*)	0, 1, 2, 3, 4 and 5 μg/L carbaryl (>99% grade chemical; Wako Pure Ltd.)	At higher carbaryl concentrations, 4 and 5 μg/L, no individuals survived to the third instar. Daphnia did not develop helmets in response to carbaryl at low (sublethal) concentrations of 1-3 μg/L. Carbaryl enhanced the development of high helmets and prolonged the maintenance period of the helmets over instars in the presence of *Chaoborus*.	Hanazato 1995
Four daphnid species	Carbaryl (>99%) for 8-14 hours at concentrations of 0, 5, 10, 15, 20, 25, and 30 µg/L.	Different morphologic responses among the different species of daphnids. Some effects noted at lowest concentration tested. The results do not lend themselves to quantitative estimates of differences in sensitivity among the daphnid species.	Hanazato and Dodson 1993

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Water flea (*Daphnia pulex*)	Neonates (<24-h old) born in high or low O_2 medium were reared in 0, 5, 10, 15, and 20 μg /L carbaryl (>99% grade chemical; Waka Pure Ltd.).	A concentration of 10 μg /L or higher reduced growth rate, adult body length, number of eggs produced, time taken to mature, and survivorship. Effects were more marked in the low oxygen condition than in high oxygen.	Hanazato and Dodson 1995
Damselfly larvae (*Xathocnemis zealandica* and *Austrolestes colensonis*)	Collected species in wild. 48 hour exposures	48 hr-LC_{50}s *Xathocnemis zealandica*:0.6 mg/L *Austrolestes colensonis*: 3.13 mg/L	Hardersen and Wratten 1999
Damselfly (*Xathocnemis zealandica*); larvae	Larvae were reared in to 0, 1, 10, and 100 ppb formulation of carbaryl 80W, Nufarm in water for 67 days.	Significant reduction in emergence at the 100 ppb level only (> 90%); caused by high mortality early in the test. Days to 90% emergence was not affected at the 1 and 10 ppb levels. The lower carbaryl concentrations did not affect emergence success but increased the developmental speed slightly. controls. Adult damselflies from the 10 ppb level had increase in fluctuating asymmetry (FA) level in cell patterns in wings but the FA level for wing length did not show any differences compared to controls. Carbaryl had a half-life of approximately 12 days in water.	Hardersen and Wratten 1998
Freshwater Shrimp (*Paratya compressa improvisa*), *Moina macropcopa* (Cladocera) and *Daphnia magna* (Cladocera)	Static 48-hour exposures	48-hr LC_{50}s (read from graph in Fig 1) D. magna: 0.011-0.012 mg/L *P. compressa*: 0.02 mg/L *M. macrocopa*: 0.2 mg/L	Hatakeyama and Sugaya 1989
Bivalve (*Corbicula striatella*)	Organisms used in bioassays collected in the field.	LC_{50} values: 24 h: 35.9 mg/L 48 h: 16.2 mg/L 72 h: 9.9 mg/L 96 h: 5.1 mg/L	Jadhav et al. 1996

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Penaeid prawn (*Metapenaeus monoceros*)	Carbaryl (99%), static. 96 hour exposure period and 10 day recovery period	96 h LC_{50}: 0.025 mg/L After sublethal exposures to 8.3 µg/L (0.0083 mg/L), significant inhibition in AChE activity in nerve tissue, midgut gland, gill, and muscle which persisted throughout the 10-day recovery period. **This long recovery period is unlike the patterns seen in mammals and fish.**	Jayaprada and Rao 1991
Midge (*Chironomus riparius*)	0 or 40 ppb carbaryl (>99% purity, Chem Services, PA) for 1 hr, then transferred to clean water for 0, 2, 6, 12, and 24 hr before 2nd 40 ppb treatment.	EC_{20} (effect in 20% after 1 hr) (physiological endpoint=figure eight upon stimulation) = 40 ppb. Midges exposed for two 1 hr periods showed significantly fewer symptoms of intoxication than when exposed continuously for 2 hr, if recovery in clean water was provided for 6 or more hours. Recovery times that were less than 6 hr produced essentially additive toxicity. AChE activity was also measured.	Kallander et al 1997
Crab (*Paratelphusa masoniana*)	Static (no renewal) LC_{50} assays.	24 h LC_{50} = 1.1 mg/L. 96 h LC_{50} = 1 mg/L. No strong temporal relationship. This may be due to lack of renewal of carbaryl in test system.	Kaushik and Kumar 1993
Crab (*Paratelphusa masoniana*)	Static bioassay test. 0 or 0.252 mg/L carbaryl for 1 month.	Treatment level was derived as 1/4 the 96-hr LC_{50} described in Kaushik and Killmar 1993. Initially, crabs became agitated for 4-5 hours and attempted to evade the media, after which they settled in the bottom of the aquaria; this behavior was not seen in the control crabs. Changes in midgut were assessed during the exposure period.	Kaushik and Kumar 1998

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

<table>
<tr><th>Freshwater Species</th><th>Exposure</th><th>Effects</th><th>Reference</th></tr>
<tr><td>Midge larvae (Chironomus riparius)</td><td>Static bioassays at pH 4, 6, and 8 and temperatures of 10°C, 20°C, and 30°C</td><td><table><tr><th>pH</th><th>Temp.</th><th>EC_{50} mg/L</th></tr><tr><td>4</td><td>10°C</td><td>0.133</td></tr><tr><td></td><td>20°C</td><td>0.110</td></tr><tr><td></td><td>30°C</td><td>0.061</td></tr><tr><td>6</td><td>10°C</td><td>0.133</td></tr><tr><td></td><td>20°C</td><td>0.110</td></tr><tr><td></td><td>30°C</td><td>0.071</td></tr><tr><td>8</td><td>10°C</td><td>0.096</td></tr><tr><td></td><td>20°C</td><td>0.128</td></tr><tr><td></td><td>30°C</td><td>0.107</td></tr></table></td><td>Lohner and Fisher 1990

Add text note in WP file next</td></tr>
<tr><td>Amphipod (Hyalella azteca)</td><td>Fed and starved amphipods were exposed to carbaryl (Rhone-Poulenc Agricultural Co, NC).</td><td>However. starved amphipods were more sensitive (significantly) than fed amphipods.

24 hr LC_{50} in μg/L:
48 hr of starvation = 7.0
72 hr of starvation = 6.0
96 hr of starvation = 6.5

24 hr LC_{50} in μg/L:
48 hr of feeding = 12.5
72 hr of feeding = 10.5
96 hr of feeding = 11.5</td><td>McNulty et al 1999</td></tr>
<tr><td>Six Mussel species: Leptodea fragilis, Utterbackia imbecillis, Lampsilis cardium, Lampsilis siliquoidea, Megalonaias nervosa, and Ligumia subrostrata; Larvae (glochidia). Two standard test organisms: Ceriodaphnia dubia and Daphnia magna.</td><td>Carbaryl (Rhone-Poulenc, Research Triangle Park, NC).</td><td>24 hr LC_{50} in mg/L:
L. fragilis = 9.1
M. nervosa = 27.4
L. siliquoidea = 31.1
L. cardium = 33.9
U. imbecillis = 40.2
L. subrostrata = 43.1

C. dubia = 0.1
D. magna = 1.9

NOEC in mg/L:
L. fragilis = 3.5
U. imbecillis = 3.6
L. subrostrata = 5.2
M. nervosa = <6.0
L. cardium = 9.3
L. siliquoidea = <16.7

C. dubia = 0.05
D. magna = 2.15</td><td>Milam et al 2005</td></tr>
</table>

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Snail (*Pomacea patula*)	Nominal concentrations: 0 (solvent control), 8.5, 10.8, 13.5. 17.0. and 2 1.5 μg/mL carbaryl (99%; Sigma).	**96 hr LC_{50} = 14.6 μg/mL:** (95 % C.L. = 13.2,16.3) Bioconcentration factors: **BCF_{ss} = 2.97** **BCF_{l} = 1.35** The **elimination constant (k_{el})** was obtained by linear regression analysis (**k_{el} = - 0.675**; r2 = 0.999). (Snails exposed to sublethal concentration (0.1 of LC_{50}) for 72 h). The transfer of snails to carbaryl-free water after 72 h of exposure was followed by rapid monophasicelimination with a **half-life = 1.0 hr.** ACHase activity was also examined.	Mora et al 2000
Freshwater prawn (*Macrobrachium dayanum*)	Wild caught prawn. Aeration during exposure. Static with no renewal specified in materials and methods.	LC_{50} values: 24 h: 0.0513 mg/L 48 h: 0.0438 mg/L 72 h: 0.0391 mg/L 96 h: 0.0352 mg/L	Omkar and Murti 1985 This may have been static renewal as in Omar and Shukla 1985 below. Not clear.
Freshwater prawn (*Macrobrachium dayanum*)	Wild caught prawn. Aeration during exposure. Static renewal every 24 hours.	LC_{50} values: 24 h: 0.033 mg/L 48 h: 0.027 mg/L 72 h: 0.024 mg/L 96 h: 0.019 mg/L	Omar and Shukla 1985
Water flea (*Ceriodaphnia dubia*)	Technical grade carbaryl	96 h LC_{50}: 0.0116 mg/L 96 h IC_{50} for Reproduction: 0.008 mg/L NOEC: 0.00106 mg/L	Oris et al. 1991
Amphipod (*Gammarus italicus* and *Echinogammarus tibaldii*)	Static conditions. Six concentrations of carbaryl (99% purity) after initial range-finding tests.	**96 hr LC_{50}** (95% CL) **in mg/L:** *G. italicus* = 0.0280 (0.025, 0.031) *E. tibaldii* = 0.0065 (0.0057, 0.0076)	Pantani et al 1997

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Crab (*Paratelphusa jacquemontii*)	Static exposures. Compound specified as sevimol.	LC_{50} values: 24 h: 0.0098 mg/L 48 h: 0.0065 mg/L 72 h: 0.0054 mg/L 96 h: 0.0042 mg/L Not clear if the values refer to a.i. or formulation. Should not use in any analysis	Patil et al. 1992
Mayfly (*Ameletus* sp.), Caddisfly (*Brachycentrus americanus*), Stonefly (*Calineuria californica*), Mayfly (*Cinygma* sp.), *Lepidostoma unicolor*, Caddisfly (*Psychoglypha* sp. early and late instar); Larvae and Nymphs	Formulated carbaryl (Clean Crop®, Platte Chemical, NE), an emulsifiable concentrate (EC) 43% a.i., w/v.	Organisms that would maximize diversity in functional feeding strategy, life history, and taxonomy were chosen to represent a stream community. **96 hr LC50** (95% CL) **in μg/L:** ***Cinygma* sp. =11.1** (7.7-13.9) ***C. californica* =17.3** (14.06-20.2) ***Ameletus* sp. =20.4** ***L. unicolor* =29.0** (19.5-37.0) ***Psychoglypha* sp. early =30.1** (25.0-40.4) ***B. americanus* =41.2** (37.6-50.5) ***Psychoglypha* sp. late =61.0** (55.6-68.54) LC1 values were used in calculation of hazardous concentration to 5% of the stream macroinvertebrate community (HC5) based on the lower 95% confidence limit (HC5/95). The hazardous concentration (HC5/95) ranged from 0.43 to 0.66 μg/L. Signs of toxicity include knockdown, moribund states, and death, were examined for *Cinygma* sp. and *C. californica*, with severity and time of appearance being a function of dose.	Peterson et al. 2001b

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Mayfly (*Cinygma sp.*) and Stonefly (*Calineuria calfornica*); Nymphs	Exposures: 15, 30, and 60 min., then nymphs transferred to clean water for the remainder of the 96 hr test period. *C. calfornica* treated with 17.3, 173, and 1,730 μg/L carbaryl. *Cinygma* treated with 10.2, 102, 204, 408, and 1,020 μg/L carbaryl. Formulated carbaryl (Clean Crop®, Platte Chemical, NE), an emulsifiable concentrate (EC) 43% a.i., w/v.	**96 hr LC_{50}** (95% CL) **in μg/L:** 15 min exposure Mayfly = 848 Stonefly = 50% mortality not reached 30 min exposure Mayfly = 220 Stonefly = 50% mortality not reached 60 min exposure **Mayfly = 165.0** (124, 232) **Stonefly = 1,139.4** (370, 15410) % mortality values at 96 h after 15, 30, or 60 min exposures increased as exposure time increased for both organisms. Mayfly had 100% mortality for all three exposure times at the 1,020 μg/L level. LC50 values for the 60 min exposure were significantly different between species , with **mayfly more sensitive than stonefly**.	Peterson et al. 2001a
Crayfish (*Oronectes immunis*); Snail (*Aplexa hypnorum*)	Flow-through proportional diluters.	96-hr LC_{50} (95% CL) in mg/L: Crayfish: 2.87 (1.55, 5.32) Snail: > 27	Phipps and Holcombe 1985
Mosquito larvae (*Culex pipiens* and *Aedes caspius*)	Duration and other experimental conditions not specified	LC_{50} values: *Culex pipiens*: 4.56 (4.07-5.09) mg/L *Aedes caspius*: 4.79 (4.18-5.43) mg/L	Riad et al. 1992
Stonefly naiad (*Pteronarcys californica*)	Static bioassays	LC_{50} values: 24 h: 0.030 mg/L 48 h: 0.013 mg/L 96 h: 0.0048 mg/L	Sanders and Cope 1968
Cladocerans (Bosmina species *B. longirostris and B. fatalis*), and their predator, Giant water flea (*Leptodora kindtii*)	0 (solvent control), 1.22, 1.95, 3.12, 5.00, 8.00, 12.80, and 24.48 μg/L carbaryl (>99% purity; Wako Chemical, Japan) for 24 hr.	**24-hr LC_{50}** (95% CL) **in μg/L:** ***B. fatalis*** **= 4.1** (2.0, 6.5) ***B. longirostris*** **= 8.6** (6.1, 13.2) ***L. kindtii*** **= 3.5** (1.2, 7.5)	Sakamoto et al 2005

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Dragonflies eggs (*Anax nigrofasciatus nigrofasciatus, Anax parthenope julius* and *Orthetrum albistylurn speciosum*)	Exposure of fertilized eggs to concentrations ranging from 0 to 1000 ppb	Carbaryl inhibited hatching, and the sensitivity of the ova to carbaryl was greater in the order of *A. parthenope julius*, *A. nigrofasciatus* and *0. speciosum*. In *A. parthenope julius*, 40 ppb resulted in embryo mortality with no hatching. This is an abstract with little detail. No full publication was encountered in the literature.	Shishido et al. 2001
Snail (*Lymnaea stagnali*)	2000 μg/L carbaryl for 1 yr.	Reduced growth, delayed egg laying, and increased mortality.	Sedge and Bluzat 1983 (as cited in Canadian Envtl Quality Guidelines 1999)
Dragonfly nymphs (*Brachythermis contaminata*)	Static. Wild caught. Carbaryl characterized only as a 10% WDP formulation.	24 hour LC_{50}: 0.000014 mg/L. 48 hour LC_{50}: 0.000011 mg/L. 72 hour LC_{50}: 0.00000084 mg/L. 96 hour LC_{50}: 0.00000069 mg/L. Estimated NOEC: $1.729x10^{-6}$ ppm or about 0.000002 ppm.	Shukla and Mishra 1980
Prawn (*Macrobrachium lamarrei*)	Static. Wild caught.	LC50 values: 24 hour: 0.0489 mg/L. 48 hour: 0.0408 mg/L. 72 hour: 0.0427 mg/L. 96 hour: 0.0403 mg/L.	Shukla and Omkar 1984
Water scorpion (*Ranatra elongata*)	Static. Wild caught.	96 hr LC_{50} = 0.623 mg/L	Shukla et al. 1982
Dragonfly larvae (*Anax nigrofasciatus nigrofasciatus, Anax parthenope julius* and *Orthetrum albistylurn speciosum*)	N.S.	Carbaryl inhibited hatching, and the sensitivity of the ova to carbaryl was greater in the order of *A. julius*, *A. nigrofasciatus* and *0. speciosum*. Effective concentration for *0. speciosum* was 40 ppb.	Shishido et al. 2001 Publication as abstract only.
Snail (*Lymnaea acuminata*) pest species	Wild caught. Aeration during. Does not specify renewal or static.	LC_{50}s 48 hours: 14 mg/L 72 hours: 5.6 mg/L 96 hours: 4.5 mg/L 168 hours: 0.78 mg/L 240 hours: 0.44 mg/L	Singh and Agarwal 1981

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Snail (*Pila globosa*) pest species	Wild caught. Aeration during. Does not specify renewal or static.	LC_{50}s 24 hours: 58 mg/L 48 hours: 48.5 mg/L 72 hours: 41 mg/L 96 hours: 36.5 mg/L 168 hours: 27 mg/L 240 hours: 23.5 mg/L	Singh and Agarwal 1981
Snail (*Lymnaea acuminata*) pest species	Wild caught. Aeration during. Does not specify renewal or static.	LC_{50}s 48 hours: 14 mg/L 72 hours: 7 mg/L 96 hours: 4.4 mg/L 120 hours: 2.4 mg/L 144 hours: 1.2 mg/L	Singh and Agarwal 1983
Sludge worm (*Tubifex tubifex*)	Laboratory reared. Static renewal.	96 h LC_{50}: 0.05 mg/L Decrease protein, carbohydrate, and lipids at concentration of 0.01 mg/L and higher.	Suseela et al. 1994
Snail (*Lymnaea acuminata*)	0, 3.0, 6.0, 9.0, and 12.0 mg/L carbaryl for 96 hr.	Glycogen, pyruvate, lactate, and lactic dehydrogenase activity in hepatopancreas, and ovotestis were significantly affected. Cited from Srivastava and Singh 2001: **24 hr LC50 = 20.05 mg/L** **96 hr LC50 = 14.19 mg/L**	Tripathi and Singh 2002
Snail (*Lymnaea acuminata*)	0, 3.0, 6.0, 9.0, and 12.0 mg/Lcarbaryl for 96 hr.	Levels of total protein in hepatopancreas and ovotestis tissues were significantly altered at 6, 9, and 12 mg/L. Levels of free amino acid and nucleic acids (DNA & RNA) and protease activity in hepatopancreas and ovotestis tissues were significantly altered at all treatment levels.	Tripathi and Singh 2003b

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Freshwater Species	Exposure	Effects	Reference
Snail (*Lymnaea acuminata*)	Nominal concentrations: 0, 1.0, 3.0, 6.0, and 9.0 mg/Lcarbaryl (Technical grade) for 28 days.	Number of eggs after 96 hrs and number of hatched eggs significantly reduced at 1.0 and 3.0 mg/L. No eggs were laid at 6.0 and 9.0 mg/L. Survivability was significantly reduced at 7, 14, 21, and 28 days after hatching at 1.0 and 3.0 mg/L. No significant effect observed on number of egg masses or hatching period. The activities of AChE, SDH, cytochrome oxidase and phosphatases (acid & alkaline) in nervous, ovatestis and hepatopancreas tissues were significantly inhibited.	Tripathi and Singh 2003a
Stonefly naiad (*Pteronarcys badia*)	Wild caught. Static	TGAI 96-h LC_{50} Value pH 6.5: 0.011 mg/L pH 7.5: 0.013 mg/L pH 8.5: 0.029 mg/L	Woodward and Mauck 1980
Amphipod (*Gammarus pseudolimnaeus*)	Wild caught. Static	TGAI 96-h LC_{50} Value pH 6.5: 0.013 mg/L pH 7.5: 0.007 mg/L pH 8.5: 0.0072 mg/L	Woodward and Mauck 1980

Saltwater Species	Exposure	Effects	Reference
Mussel (*Mytilus edulis*)		1 hr EC50 (abnormal development) = 5.3 - 24 mg/L, depending on the initial development stage: mussels were most sensitive immediately after fertilization, and sensitivity decreased as mussels matured.	Armstrong and Millemann 1974 (as cited in Canadian Envtl Quality Guidelines 1999)
Brine shrimp (*Artemia salina*); 24, 48, and 72 hr old	24 hr static toxicity test. 0, 0 (solvent control), and 0.5-500 μmol/L carbaryl (>97% purity; Germany).	24 hr LC_{50} (95% CL) at different ages: 24-hr old = 137.00 μmol/L (27 mg/L) 48-hr old = 29.40 μmol/L (5.9 mg/L) 72-hr old = 1.74 μmol/L (0.35 mg/L) Differences are statistically significant. The lethal action of carbaryl was completely prevented by pretreatment with atropine.	Barahona and Sanchez-Fortun 1999

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Saltwater Species	Exposure	Effects	Reference
Oyster (*Crassostrea gigas*)	Enzymatic extract derived from tissue homogenate was treated with 10^{-4} - 10^{-6} M carbaryl (Technical grade; Rhone-Poulenc) for 1 hr.	1.50 x 10^{-7} M caused 50% acetylcholinsterase inhibition. Note: 1.50 x 10^{-7} M is equivalent to 0.15 µM or 0.03 mg/L.	Bocquene et al. 1995
Prawn (*Palaemon serratus*)	Enzymatic extract derived from tissue homogenate was treated with 10^{-4} - 10^{-6} M carbaryl (Technical grade; Rhone-Poulenc) for 1 hr.	1.70 x 10^{-7} M caused 50% acetylcholinsterase inhibition. Note: 1.70 x 10^{-7} M is equivalent to 0.17 µM or 0.034 mg/L.	Bocquene et al. 1995
Dungeness crab (*Cancer magister*)	Exposure conditions not specified	**24-hr LC_{50} = 76 μg/L**	Buchanan et al 1970, as cited in Barahona and Sanchez-Fortun 1999
Hard Clam (*Mercenaria mercenaria*)	Concentrations (a.i.) of 0.02 to 10 mg/L.	Decrease egg development at 2 ppm and above. Study not well-detailed.	Davis and Hidu 1969
Eastern oyster (*Crassostrea virginica*)	Concentrations (a.i.) of 0.02 to 10 mg/L.	Decrease larval growth at 2 ppm and above. Study not well-detailed.	Davis and Hidu 1969
Mussel (*Mytilus edulis*)	Nominal concentrations: 0-10 mg/L carbaryl (98% pure; Alltech) for 72 hr.	**Log K_{ow} = 2.36** **EC_{50}** (feeding rate) = **41.6 μmol/L** (8.4 mg/L); expressed as concentration in water **EC_{50}** (feeding rate) = **50.0 μmol/kg** (1 mg/kg) **wet weight**; expressed as concentration in tissue **Bioconcentration Factor**: Predicted = 2.1 Observed = **2.4** Carbaryl reduced feeding rate in a simple concentration-related manner. Within the range of concentrations shown to have an adverse effect on feeding rate, the activity of AChE was severely reduced. The authors felt that the shape and slope of the concentration response curve and the WEC50 suggested that carbaryl was acting as a narcotic, although when toxicity was expressed in terms of tissue concentration there was evidence of a small enhancement over narcotic behavior.	Donkin et al. 1997

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Saltwater Species	Exposure	Effects	Reference
Sea urchin (*Pseudoachinus magellanicus*)		**12 hr EC_{50}** (increased developmental abnormalities) = was 0.0063 mg/L	Hernandez et al. 1990 (as cited in Canadian Envtl Quality Guidelines 1999)
Sand shrimp (*Crangon septemspinosa*)	Carbaryl at 27.5 mg/L during a 53 hr EC50 test.	53 hr EC50 (immobility) = 27.5 mg/L	McLeese et al. 1979 (as cited in Canadian Envtl Quality Guidelines 1999)
Sea urchin (*Paracentrotus lividus*); Gametes, embryos, and larvae	10^{-3}, 10^{-4}, 10^{-5}, 10^{-6}, and 10^{-7} M carbaryl	Morphological. biochemical, histochemical and immuno-histochemical analyses were performed both during embryo and larval development. For the morphological effects on fertilization and first cleavages, the effective concentration was 10^{-4}; for further stages, concentrations between 10^{-5} and 10^{-7} M were effective. 10^{-3} M totally arrested development.	Pesando et al 2003
Amphipod (*Gammarus lacustris*)	Unknown	**24-hr LC_{50} = 0.040 ppm**	Pimentel 1971, as cited in Barahona and Sanchez-Fortun 1999
Dungeness crab (*Cancer magister*)	Unknown	**LC_{50} = 0.60-0.63 ppm**	Pimentel 1971, as cited in Barahona and Sanchez-Fortun 1999
Ghost shrimp (*Callianassa affinis*)	Unknown	**24-hr LC_{50} =0.13 ppm**	Pimentel 1971, as cited in Barahona and Sanchez-Fortun 1999
Mud shrimp (*Upogebia pugettensis*)	Unknown	**24-hr LC_{50} =0.04-0.13 ppm**	Pimentel 1971, as cited in Barahona and Sanchez-Fortun 1999
Red crayfish (*Procambarus clarki*)	Unknown	**LC_{50} =3 ppm**	Pimentel 1971 (as cited in Barahona and Sanchez-Fortun 1999

Appendix 10: Toxicity to Aquatic Invertebrates *(continued)*

Saltwater Species	Exposure	Effects	Reference
Shore crab (species not given)		**LC_{50} = 0.27-0.71 ppm**	Pimentel 1971, as cited in Barahona and Sanchez-Fortun 1999
Penaeid prawn (*Metapenaeus monoceros*)	4 days, static renewal	LC_{50} : 0.0249 (0.0237 – 0.0261)mg/L:	Reddy and Rao 1992
Mussels (*Mytilus galloprovincialis*) and European flat oysters (*Ostrea edulis*).	Carbaryl (Sigma-Aldrich, Italy). Inhibition measured with *in vitro* tissue preparations. No *in vivo* exposures.	Significant inhibition of ChE activity was observed in gills of mussels and oysters: **IC_{50}** (ChE activity in gills): **Mussel = 6.14 x 10^{-7} M** (0.12 mg/L) **Oyster = 1.37 x 10^{-6} M** (0.27 mg/L)	Valbonesi et al 2003

Appendix 11: Toxicity to Aquatic Microorganisms and Plants

Species	Exposure	Effects	Reference
Blue-green algae: cyanobacterium (*Nostoc muscorum*)	Concentrations of 5, 10, 25 or 50 mg/L carbaryl (99%) added to cultures on 6th day (exponential phase) of growth. Treatment lasted for 96 hrs followed by repetitive washing with distilled water.	Dose-related, significant stimulation of glutathione reductase and superoxide dismutase at ≥10 mg/L. NOAEL = 5 mg/L	Bhunia et al. 1993
Cyanobacterium (*Nostoc muscorum*)	Qn the 6th day of growth (at exponential phase) carbaryl (99%; Union Carbide) was added at 0, 5, 10, 25, 50, and 75 mg/L for 96 hr.	At 10 and 25 mg/L carbaryl the growth of the cyanobacteria was significantly decreased, but at 50 mg/L severe reduction in growth was observed. Lethal dose of carbaryl was found to be 75 rng/L. Chlorophyll *a* content was significantly reduced and respiration rate significantly increased in a dose-dependent manner at all levels (10, 25, 50) except 5 mg/L. Nitrogenase, nitrate reductase, and glutamine synthetase activities were significantly reduced in a dose-dependent manner at all levels (10, 25, 50) except 5 mg/L. **NOAEL = 5 mg/L**	Bhunia et al 1994
Green alga (*Chlorella pyrenoidosa*)		Population reduced by 30%. MIC = 0.1 ppm.	Christie 1969 (as cited in Padhy and Mohapatra 2001)

Appendix 11: Toxicity to Aquatic Microorganisms and Plants *(continued)*

<table>
<tr><th>Species</th><th>Exposure</th><th>Effects</th><th>Reference</th></tr>
<tr><td>Cyanobacteria Anabeana, Nostoc, Calothrix, Scytonema, and Westiellopsis. (10 spp)</td><td>0.1, 0.5, 1, 2, 5, 10, 20, 50, 100, 200, 300, and 500 ppm Sevin (carbaryl 50% WP) for 15 days.</td><td>EC_{50} (inhibition of growth) in ppm:
A. variabilis 5.1
A. fertilissima 7.4
N. sphaericum 9.0
Westiellopsis sp 9.6
N. linckia 15.4
S. multiramosum 18.3
N. muscorum 22.5
Scytonema sp 22.7
C. parietina 28.1
C. sp 50.9

Chlorophyll a content in the treated cyanobacteria was decreased by 48-55%.</td><td>Das and Adhikary 1996</td></tr>
<tr><td>Bacteria Photobacterium phosphoreum, Spirillum volutans, and Bacillus cereus</td><td>Sevin.</td><td>EC_{50} (light output by P. phosphoreum) = 63 mg/L

MEC_{90} (loss of 90% motility of S. volutans) = 89 mg/L

Minimum concentration that inhibited growth in B. cereus (18 hr 37°C) = 70 mg/L</td><td>Ghosh et al 1997</td></tr>
<tr><td>Ciliate (Colpoda aspera)</td><td>Sanmakou wettable powder (75% carbaryl)</td><td>EC_{50} = 46.9 mg/L
MIC (minimum inhibitory concentration) against Alcaligenes faecalis = >2000 mg/L

72 hr LC_{50} for Tetrahymena pyriformis in pure culture = 25- 50 mg/L (Nistar et al. 1981).

24 hr LC_{50} for Paramecium multimicronucleatum = 28 mg/L (Edmistom et al. 1985)

2 hr LC_{50} for Euplotes sp. = 28 mg/L (Weber et al 1982)</td><td>Kakiichi et al 1996</td></tr>
<tr><td>3 species of cyanobacteria</td><td>92% purity</td><td><table><tr><th>Species</th><th>EC_{50}</th><th>LOEC</th><th>NOEC</th></tr><tr><td>Anabaena flos-aquae</td><td>4.00</td><td>2.5</td><td>1</td></tr><tr><td>Microcystis flos-aquae</td><td>2.12</td><td>0.25</td><td>0.1</td></tr><tr><td>Microcystis aeruginosa</td><td>1.26</td><td>0.2</td><td>0.1</td></tr></table></td><td>Ma et al. 2006</td></tr>
</table>

Appendix 11: Toxicity to Aquatic Microorganisms and Plants *(continued)*

<table>
<tr><th>Species</th><th>Exposure</th><th>Effects</th><th>Reference</th></tr>
<tr><td>5 species of green algae</td><td>92% purity</td><td>
<table>
<tr><td>Species</td><td>EC_{50}</td><td>LOEC</td><td>NOEC</td></tr>
<tr><td>Selenastrum capricornutum</td><td>3.60</td><td>0.5</td><td>0.2</td></tr>
<tr><td>Scenedesmus quadricauda</td><td>6.10</td><td>1</td><td>0.5</td></tr>
<tr><td>Scenedesmus obliquus</td><td>2.80</td><td>0.5</td><td>0.2</td></tr>
<tr><td>Chlorella vulgaris</td><td>2.56</td><td>0.5</td><td>0.2</td></tr>
<tr><td>Chlorella pyrenoidosa</td><td>4.18</td><td>0.5</td><td>0.2</td></tr>
</table>
</td><td>Ma et al. 2006</td></tr>
<tr><td>Cyanobacterium (Anabaena sp. PCC 7120)(Nostoc muscorum)</td><td></td><td>LC_{50} in ppm:
In liquid culture:
Cultured in C -N medium = 26.92
Cultured in C + N medium = 28.84

LC25, LC75, and LC100 given.

The effect of urea, potash, and superphosphate on the toxicity of carbaryl was examined.</td><td>Padh 2001</td></tr>
<tr><td>Cyanobacterium (Anabaena sp. PCC 7120)(Nostoc muscorum)</td><td>Sevin 50W (Union Carbide, India):
0, 20, 40, 60 and 80 ppm in
C-N medium
0, 20, 40, 60, 80, and 100 ppm in C+N medium.</td><td>LC_{50} in ppm:
In liquid culture:
Cultured in C -N medium = 26.92
Cultured in C + N medium = 28.84
In agar media:
Cultured in C -N medium = 23.99
Cultured in C + N medium = 31.62

MIC (minimum inhibitory concentration) = 10 ppm.

100 ppm in C - N medium and 120 ppm carbaryl in C + N medium were confirmed as the lethal concentrations (LC100).

Effects on nitrogen fixation and the frequency of heterocysts was examined.

Growth inhibition of general cyanobacteria at 50 ppm (Muralikrishan and Venkateswarulu 1984).</td><td>Padhy and Mohapatra 2001</td></tr>
</table>

Appendix 11: Toxicity to Aquatic Microorganisms and Plants *(continued)*

Species	Exposure	Effects	Reference
Diatom (*Cyclotella meneghiana* and *Nitzchia* sp); Green algae (*Scenedesmus quadricauda* and *Sclenastrum capricornutum*); Cyanobacteria unicellular (*Microscystis aeruginosa*); Cyanobacteria filamentous (*Pseudoanabaena* sp and *Oscillatoria* sp); Cyanobacteria filamentous (nitrogen-fixing) (*Aphanizomenon flos-aquae* and *Anabaena inaequalis*); and Duckweed (*Lemna minor*)	3.667 mg/L Sevin 80S. (Expected Environ-mental Concen-tration).	Significant percent inhibition (% inhibition of ^{14}C uptake for algae and 7-day growth for duckweed): Algae *C. meneghiana* = 35 *Nitzchia* sp = 58 *S. quadricauda* = 67 *S. capricornutum* = 68 Cyanobacteria *Oscillatoria* sp = 56 *Pseudoanabaena* sp = 70 *A. inaequalis* = 73 *M. aeruginosa* = 76 *A. flos-aquae* = 86 Duckweed *Lemna minor* = 33	Peterson et al 1994
Diatom (marine; *Coscinodiscus concinnus*)	0.05 mg/L carbaryl.	46% growth inhibition.	Ramachandran et al. 1980 (as cited in Peterson et al 1994)
Green alga *Scenedesmus*	0.1 ppm carbaryl.	^{14}C assimilation stimulated.	Stadnyk et al. 1971 (as cited in Padhy and Mohapatra 2001)
Ciliated Protozoa, *Spirostomum teres*	24 hours	24 h LC_{50}: 3.34 mg/L	Twagilmana et al. 1998
Cyanobacterium (*Nostoc muscorum*)		Inhibition of growth at 120 ppm.	Vaishampayan 1985 (as cited in Padhy and Mohapatra 2001)

Appendix 12: Aquatic Field and Microcosm Studies

Application	Observations	Reference
Four single-engine fixed-wing aircraft were used to apply Sevin-4-Oil (40.5%carbaryl; Rhone-Poulenc, NC) at a rate of 560 g a.i./ha (July 1991) and 448 g a.i./ha (July 1993) to rangeland on both sides of the Little Missouri River, ND.	1991 An impact site was established ~1 river-km upstream from the downstream extent of the pesticide application, and a reference site ~3.6 river-km upstream of the impact site. Maximum mean carbaryl concentration in the Little Missouri occurred ~1hr after application = 85. 1 μg/L. There was a significant increase in variability of invertebrate drift (number of invertebrates per 100 m^3 water passing through drift nets) at the impact site during the 3 hr immediately following pesticide application. Subsequent collections during the day of pesticide application showed that the increase in invertebrate drift was transient and undetectable after the first sampling interval. Ephemeroptera, especially Heptageniidae, were the only taxa affected by pesticide application 1993 An impact site was established ~3.6 river-km upstream from the downstream extent of the pesticide application, and a reference site ~3.2 river-km upstream of the impact site. Maximum mean carbaryl concentration in the Little Missouri occurred ~2hr after application = 12.6 μg/L. No increase in invertebrate drift was observed after pesticide application. The relative change in brain AChE activity of fish flathead chub (*Platygobio gracilis*) at reference and impact sites was not significantly different after pesticide application in either year.	Beyers et al. 1995
0, 3.5, or 7.0 mg a.i./L (liquid Sevin, 21.3% carbaryl) was applied to cattle tank mesocosm ponds (water, leaf litter, and plankton from natural ponds) with bullfrog (*Rana catesbeiana*) tadpoles and no predators, or bullfrog tadpoles with red-spotted newts (*Notophthalmus viridescens*), bluegill sunfish (*Lepomis macrochirus*), or crayfish (*Orconectes* sp.).	Carbaryl negatively affected predator survival by eliminating crayfish from all ponds, and by eliminating bluegill sunfish from ponds exposed to the highest concentration of carbaryl; carbaryl exposure did not effect survival of red-spotted newts. High concentrations of carbaryl reduced tadpole survival regardless of whether predators survived carbaryl exposure or not. Presence of crayfish and newts reduced tadpole survival, while bluegill sunfish appeared to facilitate bullfrog tadpole survival. Presence of carbaryl stimulated bullfrog tadpole mass and development.	Boone and Semlitsch 2003

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
Green frog (*Rana clamitans*) tadpoles reared at low and high density were exposed to 0 or 3.5 mg a.i./L (liquid Sevin, 21.3% carbaryl) zero, one, two, or three times at 14 day intervals in artificial aquatic communities (water, leaf litter, and plankton from natural ponds in outdoor cattle tank mesocosm ponds).	No frogs reached metamorphosis in control ponds and all (except one frog) that did were from low-density ponds; additionally, only those low density ponds exposed to carbaryl early in tadpole development produced metamorphs. Low density ponds that were dosed once early in development produced more metamorphs than ponds that were exposed to carbaryl once mid and late development at either density. The tadpole density, dose treatment, and their interaction did not have a significant effect on tadpole survival. "Bridges (C. Bridges, unpublished data) found no difference between the effects of the commercial formulation of carbaryl (Sevin) and technical-grade carbaryl in laboratory mortality studies with amphibians."	Boone and Bridges 2003
0 or 2.5 mg/L liquid Sevin (21.3% carbaryl) was applied to cattle tank mesocosm ponds (water, leaf litter, and plankton from natural ponds) with green frog (*Rana clamitans*) tadpoles.	Tadpole development and mass was stimulated by presence of carbaryl. Tadpole survival was not affected by carbaryl. Cladoceran (zooplankton) levels were significantly reduced at 7 and 21 days after treatment.	Boone et al 2005
0.5 mg/L carbaryl (Wake Pure Chemical, Japan) was applied to mesocosm tanks maintained with plankton and low or high predacious copepod (*Mesocyclops pehpeiensis*) densities. Control tanks had no carbaryl and no predators.	Cladocerans were eliminated by carbaryl at both predator densities. Density of rotifers increased after carbaryl elimination of cladocerans at low predator density but not at high predator density. No decrease in predator density was observed after application. The number of trophic interactions per species was not affected by the carbaryl application at either predator density. Carbay1 application increased the relative importance of predatory interactions in the food web at both predator densities with near significance level.	Chang et al 2005

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
Carbaryl (Sevin-4 oil) spray application at 840 g a.i./ha for spruce budworm suppression in Maine. Study area includes nine streams: 3 streams never exposed to carbaryl (i.e., untreated); 3 streams in areas treated with 840 g a.i./ha in June 1976 (i.e., 1-year streams); and 3 streams in areas treated with 840 g a.i./ha in year of the study and 1120 g a.i./ha previous year (i.e., 2-year streams). Concentrations of carbaryl in water not measured. The authors suggest (by analogy to other field studies with similar applications) that concentrations of carbaryl in water were probably in the range of 0.01 to 0.04 mg/L.	**Drift**: Drift numbers and diversity remained relatively stable in untreated streams and most sampled organism were alive; drift in 1-year streams increased up to 170 times 2 days after treatment and virtually all sampled organisms. Plecoptera (stoneflies), Ephemeroptera (mayflies), and Diptera (true flies which have only a single pair of wings) were common in samples; drift increased in 2/3 of 2-year streams, with diptera (true flies) accounting for >95% of sampled organisms, virtually all dead; in other 2-year stream, there was no measurable increase in drift. Furthermore, the number of taxa collected did not increase substantially in any of the 2-year streams. **Benthos**: Immediately after treatment, larger flies: Plecoptera (stoneflies), Ephemeroptera (mayflies) were found dead in the streams and Trichoptera (caddisflies) were distressed and *found leaving their cases*. At 30-60 days after treatment, benthos samples indicated significant decreases among stoneflies, mayflies and caddisflies, and stoneflies did not repopulate treated streams by 60 days post treatment. Stonefly populations in 2-year streams were low prior to treatment, compared with controls. Most flies and earthworms were unaffected by treatment.	Courtemanch and Gibbs 1980
Aerial application of Carbaryl (Sevin NOS) at 1.1 kg in 4.2 L water to control gypsy moth in Northampton County, PA on May 19, 21, 22, and 23. Study area included the watershed of Slateford Creek, which is a small, stony, cold-water stream nearly completely canopied by trees.	Drastic increase in drift at the time of spraying; average biomass of two samples taken on first day of spraying was 6 times greater than that of the average biomass for the previous 6 days; peak of drift reached 2 days after spraying was 160 times the normal average, which was followed by a rapid decrease to near-normal levels. Investigator speculates that this drop probably resulted from the mortality of drifters. Organism represented in the drift were predominately mayflies (Ephemeroptera) and stoneflies (Plecoptera).	Coutant 1964

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
8.4 kg/ha carbaryl (unspecified) applied via helicopter to plots in the Palix River sub-estuary in Willapa Bay, WA in 1992. Control site ~300 m from treated sites.	Sites were sampled from 2 days, 51 days, and 1 yr, and 2 yr after application to determine whether results observed in the small plots (see latter entry) were representative on a larger spatial scale. Only arthropods and mollusks were counted and identified to species.	Dumbauld et al 2001
5.6 kg/ha carbaryl (unspecified) applied with hand sprayer to plots in the Palix River sub-estuary and Cedar River sub-estuary in Willapa Bay, WA, in 1989. Control sites ~300 m from treated sites.	Benthic organisms sampled at 24 hr, 10 days, 1and 7 mo, and 1 yr after application. Most polychaetes, including the dominant species *Mediomastus californiensis* found at both sites, appeared unaffected by the application of carbaryl. Significant reduction in the number of ghost shrimps (*Neotrypaea californiensis*) and mud shrimps (*Upogebia pugettensis*) present on treated vs control plots 1 month after pesticide application. Densities of amphipods (*Eohaustorius estuarius*) at the Palix River site were reduced on the treated plots at 24 hr, and significantly reduced at 2 weeks, 1 and 3 months after application. No statistically significant effect of the pesticide was detected on the density of any mollusks until 3 mo after application, when the density of commensal bivalves (*Cryptomya californica*) and clams (*Macoma* sp.)at the Palix River site was significantly reduced on treated plots. Significant reduction remained at 1 yr after application. Significant reduction in oligochaetes 24 hr after application. Carbaryl concentration in sediments decreased rapidly, but was still detectable in the top 1 cm of sediment 2 wk after application. Difference in diversity between sites did not change with the application of carbaryl and the only significant change at a single location was at the Palix River site: 1 mo after application; species richness. $p < 0.01$ 1 yr after application; species diversity, $p < 0.02$.	Dumbauld et al 2001

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
Microcosm consisting of algae, midge larvae, snails, fish, and mosquito larvae in 3 liters of water. pH held at 4, 6, or 8. 120 µg of ^{14}C-carbaryl added to each system [nominal concentration of 0.04 mg/L of water].	1-naphthol was not detected at pH 8. Extensive degradation by all organisms. Greater ^{14}C-carbaryl concentrations in algae and snails than other organism.	Fisher and Lohner 1986
Aerial application to forest ponds in Maine at 0.840 kg/ha (0.75 lb/acre). No buffer – i.e., direct spray was likely. Pond areas ranged from 0.1 ha to 5.4 ha.	Observation up to 30 months. Almost complete elimination of amphipods (*Hyallela azteca* and *Crangonyx richmondensis*) with no recovery over 30 month period. Transient decrease in Ephemeroptera and Trichoptera. Reduction in Odonata for about one year. Maximum concentrations of 734 µg/L in surface water and 254µg/L in water column of a 1 ha pond and maximum concentrations of 246 µg/L in surface water and 5µg/L in water column of a 0.1 ha pond. Difference due to increased drift to the larger pond.	Gibbs et al. 1984
Two streams in Maine, one in spray area (Little Russell Stream, treated) and one up wind (Logan Brook, control). Application rate not specified.	Collected adult brook trout from each stream. AChE activity initially lower in treated stream but normal by 24 hours. No signs of frank toxicity. Increase in collected invertebrates in treated stream (probably a sign of toxicity).	Haines 1981
Artificial experimental ponds with and without *Chaoborus* larvae (predators) and with and without covering. Nominal concentration of 0.01 mg/L or 0.1 mg/L applied 10 times at two day intervals.	Carbaryl rapidly degraded with no measurable concentration by 24 hours after application. No impact on invertebrates (various Cladocera) at 0.01 mg/L with predators. At higher concentrations, changes in populations of species of Cladocera and Rotifera.	Hanzaato 1991a
Artificial experimental ponds with high or low densities of *Chaoborus* larvae (predators). Nominal concentration of 0.1 mg/L or 0.5 mg/L applied once at start of study.	Adverse effects on Cladocera at 0.1 mg/L. Adverse effects on all invertebrates at 0.5 mg/L. Rapid recovering *Chaoborus* but no recovery in Cladocera. This difference was attributed to *Chaoborus* predation on Cladocera rather than to carbaryl toxicity.	Hanazato and Yasuna 1990a
Artificial experimental ponds with mixed invertebrate populations. Nominal concentration of 0.5 mg/L applied three times at one week intervals.	Rapid and exponential dissipation/degradation. Transient increase in Chlorophyll *a* probably secondary to effects on grazers.. Substantial impact on Cladocera and Copepoda but not on Rotifera.	Hanazato and Yasuna 1990b

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
Mesocosm study. 0, 2, 5, 7, 10, 20, 50, 70, 100 or 200 μg/L carbaryl (commercial grade) were added to bags of East Twin Lake (OH) surface water with macrozooplankton from the entire water column. Bags were then suspended in the mid-epilimnion (2 m depth) of the lake for 4 days (May 25-29 1992).	On day 4, there was a significant negative exponential relationship between zooplankton biomass and dose. At 50 μg/L and higher, zooplankton biomass was reduced by roughly two fold relative to the control. At concentrations above 50 μg/L, cladocerans were reduced and copepods accounted for nearly all of the total zooplankton biomass. Overall, *Daphnia galeata* was the most sensitive, followed by other cladocerans. Calanoids and cyclopsids were the most tolerant. Concentration of carbaryl (μg/L) associated with a biomass reduction of $\geq$50%: *Daphnia galeata* = 5 *Bosmina longirostris* = 7 *Eubosmina coregoni* = 20 *Chydorus sphaericus* = 20 *Calanoid nauplii* =100 *Cyclopoid nauplii* =200 Cyclopoid copepodids >200 Calanoid copepdids >200 Carbaryl did not directly suppress algae; their biomass increased significantly with dose level. This coincided with the cladoceran decline, suggesting an algal response to reduced top-down control.	Havens 1994
Carbaryl (80W; Nufarm, Australia) was applied at 1, 10, or 100 ppb to artificial ponds (natural pond sediment, plankton, plants and damselfly (*Xanthocnemis zealandica*)) in 1996.	100 ppb (0.1 ppm) carbaryl (nominal concentration) significantly reduced emergence success in damselflies 10 days after application, whereas 1 and 10 ppb had no effect. Damselfly size (measured as average length of the front wings) and fluctuating asymmetry of the wings was unaffected by 10 ppb (data for 1 and 100 ppb not analyzed). Degradation rate of carbaryl was relatively constant for the first 5 weeks of the experiment but later rates increased considerably.	Hardersen et al 1999

Appendix 12: Aquatic Field and Microcosm Studies *(continued)*

Application	Observations	Reference
10 or 100μg/L carbaryl (unspecified) applied mesocosm ponds (groundwater, eutrophic lake bottom mud)	The dominant zooplankton species (control ponds), the large cladoceran *Daphnia galeata*, was replaced by medium cladocerans *Moina micrura* and *Diaphanosoma brachyurum* in the 10 μg/L carbaryl ponds. In the 100μg/L carbaryl ponds, all three species were eliminated, and the small cladoceran *Bosmina fatulis* increased and dominated the community exclusively. *B. fatulis* was eliminated at 500 μg/L. Difference in sensitivity of rotifers was observed at 100 μg/L; abundance of *K. valga* increased while the *Polyartha trigla* density decreased. *K. valga* withstood 500 μg/L but not 1000 μg/L .	Hanazato 1997 and Hanazato 1998b