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Strychnine

Human Health and Ecological Risk Assessment FINAL REPORT

Submitted to:

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ATTACHMENT

WorksheetMaker EXECL Workbook: SERA WS-052-17-03a: 0.5% and 1.8% Strychnine Hand
Baiting and 0.5% Burrow Builder Applications

ACRONYMS, ABBREVIATIONS, AND SYMBOLS

ACGIH	American Conference of Governmental Industrial Hygienists
AChE	acetylcholinesterase
AEL	adverse-effect level
a.i.	active ingredient
APHIS	Animal and Plant Health Inspection Service
ATSDR	Agency for Toxic Substances and Disease Registry
BCF	bioconcentration factor
bw	body weight
calc	calculated value
CBI	confidential business information
CD ₅₀	a dose causing convulsions in 50% of the animals
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
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
FQPA	Food Quality Protection Act
g	gram
GLP	Good Laboratory Practices
ha	hectare
HED	Health Effects Division (U.S. EPA/OPP)
HQ	hazard quotient
IARC	International Agency for Research on Cancer
IREED	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
lb	pound
LC ₅₀	lethal concentration, 50% kill

ACRONYMS, ABBREVIATIONS, AND SYMBOLS *(continued)*

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
MSMA	monosodium methanearsonate
MW	molecular weight
NAWQA	USGS National Water Quality Assessment
NCI	National Cancer Institute
NCOD	National Drinking Water Contaminant Occurrence Database
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
PHED	Pesticide Handlers Exposure Database
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
TIPA	Triisopropanolamine
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 (µg/cm ²)	11.21
pounds per gallon (lb/gal)	grams per liter (g/L)	119.8
square centimeters (cm ²)	square inches (in ²)	0.155
square centimeters (cm ²)	square meters (m ²)	0.0001
square meters (m ²)	square centimeters (cm ²)	10,000
yards	meters	0.9144

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

CONVERSION OF SCIENTIFIC NOTATION

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

EXECUTIVE SUMMARY

1
2 The human health risk assessment suggests that adverse effects in workers or members of the general public are
3 unlikely. Under normal and anticipated circumstances, the use of strychnine in below-ground applications for
4 the control of pocket gophers should pose minimal risks to workers and members of the general public.
5 Substantial reservations accompany the risk characterization for workers because of the lack of data on the
6 extent of worker exposures during applications of strychnine. Nonetheless, the exposure assessment for workers
7 is based on a set of conservative assumptions which should overestimate exposures. There are also uncertainties
8 in the dose-response assessment for workers. These uncertainties, however, focus on the reasonable supposition
9 that dermal exposures are likely to be less hazardous than oral exposures. Since the dose-response assessment is
10 based on oral toxicity, risks to workers are likely to be overestimated. The risk characterization for non-
11 accidental and expected exposures to members of the general public suggests that risks are negligible. One very
12 extreme accidental exposure scenario is of substantial concern— i.e. a child consumes bait accidentally
13 deposited on the ground surface. If such an event were to occur, the child could die, despite reasonably prompt
14 medical intervention. Thus, during below-ground applications of strychnine, extreme care should be exercised
15 to ensure that accidental spills are prevented, and, should they occur, that thorough remediation measures are
16 taken.

17
18 The ecological risk assessment does identify areas of concern. In the normal and anticipated below-ground
19 application of strychnine to control pocket gophers, adverse effects on fossorial rodents are inevitable. Adverse
20 effects on this group of organisms are amply demonstrated in multiple field studies. While not demonstrated in
21 field studies, adverse effects on mustelids and predatory snakes appear to be likely. At least for predatory
22 snakes, a probable case of a fatal exposure has been reported. Strychnine cannot be applied in grizzly bear
23 habitats or in the habitats of some species of fox or wolves without specific approval from the U.S. EPA. In the
24 absence of this limitation, adverse effects on grizzly bears through foraging on pocket gopher food caches are
25 plausible. Adverse effects on canid predators such as coyotes may be less likely but effects in canid predators
26 also appear to be plausible.

27
28 Many other aspects of the risk characterization for strychnine are accompanied by substantial uncertainties and
29 ambiguities. Almost all the uncertainty is associated with the nature of or limitations in the data available to
30 support the exposure assessments. Several field studies indicate that adverse effects on raptors are not likely. A
31 single field study reports reduced body weight in adult owls and equivocal effects on reproductive success that
32 might be related to the consumption of poisoned rodents after a below-ground application of strychnine. While
33 this concern is supported by toxicity data in sensitive species of birds, the association in the field observation is
34 weak. Incident data reported by the U.S. EPA indicate the possibility of adverse effects in raptors exposed to
35 strychnine; nevertheless, all of the reported incidents occurred prior to the restriction of strychnine to below-
36 ground applications. Thus, the probability of observing adverse effects in raptors associated with the below-
37 ground application of strychnine appears to be remote.

38
39 Accidental events or misapplications could lead to effects on a broader range of species. If a large amount of
40 strychnine is spilled onto the ground surface and not effectively and promptly remediated, adverse effects are
41 plausible in many species of birds and mammals. The probability of misapplication of strychnine is not clear;
42 however, this issue is likely to be a concern only with burrow builder applications.

1. INTRODUCTION

1 This document provides risk assessments for human health effects and ecological effects
2 to support an assessment of the environmental consequences of using strychnine in Forest
3 Service programs. Strychnine is a rodenticide used in Forest Service programs for animal
4 damage control. Pocket gophers (e.g., *Thomomys* spp. and *Geomys* spp.) are the only
5 labeled target species for currently registered formulations of strychnine. The strychnine
6 formulations covered in this risk assessment include formulations (i.e., baits)
7 incorporated in oats or milo grain (sorghum).
8

9
10 In addition to standard literature searches of TOXLINE and AGRICOLA, this risk
11 assessment considers the review of strychnine by WHO (IPCS 1989) as well as
12 strychnine reviews and risk assessments prepared by ACGIH (2001), the U.S. EPA
13 Office of Pesticide Programs (U.S. EPA/OPP 1996a,b) and the Office of Research and
14 Development (U.S. EPA/ORD 1987). The recent book on strychnine by Buckingham
15 (2008) was also consulted along with other more narrowly focused reviews in the open
16 literature (e.g., Baker et al. 1982; Colvin et al. 1988; Hayes 1982; Makarovsky et al.
17 2008; Rudd 1956). With few exceptions, full copies of the original open literature
18 citations identified in these reviews were obtained and information from secondary
19 sources was not used to develop the risk assessment. The exceptions—i.e., information
20 taken from secondary sources—are identified in the bibliography (Section 5).
21

22 Efficacy studies regarding the control of gophers or other species are central to the risk
23 assessment; however, studies that do not provide information on effects in nontarget
24 species are not discussed in detail (e.g., Apa et al. 1990; Brown et al. 1997; Deisch et al.
25 1990; Evans et al. 1990; Holbrook and Timm 1985; Khan et al. 1992; Kuhn and Peloquin
26 1974; Lee et al. 1995; Lewis and O'Brien 1986; Mutze 1989, 1998; Proulx 1998; Seyler
27 and Niemeyer 1974; Uresk et al. 1986; West 1962). Similarly, numerous publications
28 document suicide attempts with strychnine, some of which provide useful information
29 about the toxicity or pharmacokinetics of strychnine in humans and are discussed in
30 Section 3. Other studies focus on clinical aspects of strychnine poisoning (e.g.,
31 Radosavljevic et al. 2006; Savage et al. 1971); these studies are not covered in detail in
32 the current risk assessment.
33

34 The Reregistration Eligibility Decision (RED) for strychnine (U.S. EPA 1996a) is based
35 on unpublished strychnine studies submitted by registrants. In the preparation of the
36 current Forest Service risk assessment, the Freedom of Information Act request was
37 submitted to the EPA (HQ-RIN-01171-09) for a complete bibliography of all registrant-
38 submitted studies, consisting of 843 documents, some of which go back to the 1950s.
39 The EPA treats these studies as confidential business information (CBI); accordingly,
40 complete copies of the studies were not available for the current risk assessment. Even if
41 the studies were available, their comprehensive review is beyond the resources available
42 for the current risk assessment. As part of the FOIA, however, copies of Science
43 Chapters prepared by U.S. EPA/OPP were also requested and provided by U.S.
44 EPA/OPP. Science Chapters are support documents for the RED (U.S. EPA/OPP 1996a),
45 which include a more detailed review of relevant unpublished studies than is presented in

1 the RED. U.S. EPA/OPP kindly provided the Science Chapter prepared by the Health
2 Effects Division (U.S. EPA/OPP 1996c) and the Environmental Fate and Effects Division
3 (U.S. EPA/OPP 1996d).

4
5 In addition to the RED and the associated Science Chapters, the current Forest Service
6 risk assessment has also consulted the more recent risk assessment (U.S. EPA/OPP 2009)
7 on strychnine associated with potential risks to the California red-legged frog (*Rana*
8 *aurora draytonii*), the California tiger salamander (*Ambystoma californiense*), and the
9 San Joaquin kit fox (*Vulpes macrotis mutica*).

10
11 In addition to reviews published in the open literature, there is a substantial amount of
12 information on strychnine available on the Internet—e.g., nearly 1.4 million entries in a
13 simple Google search. For the most part, data obtained from the Internet are not used
14 unless the information is well documented. The most useful database found on the
15 Internet for this risk assessment is the ECOTOX database compiled and reviewed by the
16 U.S. EPA (U.S. EPA/ORD 2009). ECOTOX is also the main ecotoxicity database used
17 by the Pesticide Action Network (PAN at <http://www.panna.org/>). As with the reviews
18 cited above, the search of ECOTOX was used only to identify studies from the published
19 literature. All relevant open literature studies identified in ECOTOX were obtained and
20 reviewed as part of the current Forest Service risk assessment.

21
22 The human health and ecological risk assessments prepared for the USDA Forest Service
23 are not, nor are they intended to be, comprehensive summaries of all of the available
24 information. Nonetheless, this risk assessment reviews all studies identified in the open
25 literature that may be useful in assessing the consequences of using strychnine in Forest
26 Service programs. The Forest Service will update this and other similar risk assessments
27 on a periodic basis and welcomes input from the general public on the selection of studies
28 included in the risk assessment. This input is helpful, however, only if recommendations
29 for including additional studies specify why and/or how the new or not previously
30 included information would be likely to alter the conclusions reached in the risk
31 assessments.

32
33 Like other Forest Service risk assessments, this document has four chapters: the
34 introduction, program description, risk assessment for human health effects, and risk
35 assessment for ecological effects or effects on wildlife species. Each of the two risk
36 assessment chapters has four major sections, including an identification of the hazards
37 associated with strychnine, an assessment of potential exposure to the pesticide, an
38 assessment of the dose-response relationships, and a characterization of the risks
39 associated with plausible levels of exposure.

40
41 Although this is a technical support document and addresses some specialized technical
42 areas, an effort was made to ensure that the document can be understood by individuals
43 who do not have specialized training in the chemical and biological sciences. Certain
44 technical concepts, methods, and terms common to all parts of the risk assessment are
45 described in a separate document (SERA 2007a).

1 Almost no risk estimates presented in this document are given as single numbers.
2 Usually, risk is expressed as a central estimate and a range, which is sometimes quite
3 large. Because of the need to encompass many different types of exposure as well as the
4 need to express the uncertainties in the assessment, this risk assessment involves
5 numerous calculations. Relatively simple calculations are included in the body of the
6 document. More cumbersome calculations are presented in an EXCEL workbook,
7 consisting of sets of EXCEL worksheets, that is included as an attachment to this risk
8 assessment. The worksheets provide the detail for the estimates cited in the body of this
9 document. Documentation on the use of EXCEL workbooks is provided in SERA
10 (2009).
11

1

2

2. PROGRAM DESCRIPTION

3

2.1. OVERVIEW

4 Strychnine is a poison that has been used to control rats as well as other mammalian and
5 avian pests since the 17th century. Strychnine has also been used since the 16th century
6 and up to the mid-20th century as a presumed therapeutic agent for humans. Strychnine
7 has no current uses as a medicinal agent. As a pesticide, strychnine is banned in most
8 European countries and is registered in the United States only for below-ground
9 applications and only for the control of pocket gophers. Strychnine formulations consist
10 of strychnine mixtures with oats or sorghum. Most formulations consist of 0.5%
11 strychnine, the only exception being a 1.8% formulation which has a special needs label
12 for California and Nevada.
13

14

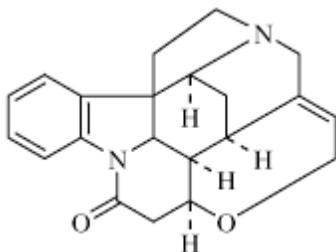
15 Subsurface applications of strychnine may be made by inserting the strychnine
16 formulations directly into gopher burrows or by constructing artificial burrows. Both
17 types of applications involve the use of specialized equipment and are made only by or
18 under the supervisions of licensed pesticide applicators. Application rates vary with the
19 density of the gopher populations. Labeled application rates for strychnine range from
20 0.005 to 0.018 lb a.i./acre. In general, the goal of strychnine applications is to reduce
21 gopher populations by at least 80%, which may require multiple applications.
22

23 The Forest Service use statistics for strychnine are unclear. Based on statistics from the
24 state of California, forestry uses of strychnine appear to be minor compared to total use.
25 Whether this pattern holds in other states or other Forest Service regions is unclear.
26 Strychnine may not be applied in geographical ranges for selected species (e.g., the
27 grizzly bear and the San Joaquin kit fox), unless special approval is obtained from the
28 U.S. EPA.

2.2. CHEMICAL DESCRIPTION AND COMMERCIAL FORMULATIONS

29 Structurally, strychnine is a complex molecule:
30

31



32

33 Typical structural nomenclature is not used for strychnine, and the CAS and IUPAC
34 name is simply *strychnidin-10-one*, with the *-one* designation referring to the ketone
35 moiety on the tenth carbon of the ring system. The physical and chemical properties of
36 strychnine are summarized in Table 1.
37

1 Strychnine is an alkaloid. The term *alkaloid* is a general designation for naturally
2 occurring compounds with complex (i.e., heterocyclic) ring systems that contain nitrogen.
3 As indicated above, strychnine is clearly an alkaloid. The term *strychnine alkaloid* is
4 commonly used in the literature on strychnine. While somewhat redundant, the term
5 *strychnine alkaloid* is useful in distinguishing strychnine from various strychnine salts,
6 such as strychnine sulfate and strychnine nitrate.

7
8 Strychnine is isolated commercially from the ground seeds of *Strychnos nux vomica*, an
9 evergreen tree with a natural range limited to Southeast Asia. The ground seeds are
10 commonly referred to as nux vomica. Strychnine may also be isolated from other species
11 of trees such as *Strychnos ignatii* and *Strychnos tieute*, all of which are native to the Far
12 East. Strychnine has been used as an herbal medicine by the Chinese, and the seeds of
13 *Strychnos Nux vomica* were used as a rat poison as early as the 16th or 17th century
14 (American Cancer Society 2008; Buckingham 2008; Goldfrank et al. 1981; Tomlin
15 2004). Strychnine has also been used as a therapeutic agent since the 16th century, and
16 this use continued into the 1960s (Yamarick et al. 1992). These uses resulted in a large
17 body of information on the effects of strychnine in humans (Section 3.1).

18
19 Strychnine alkaloid and strychnine sulfate formulations were registered in the United
20 States in 1947 by the USDA under the Federal Insecticide, Fungicide, and Rodenticide
21 Act (FIFRA). Since that time, registrations were issued for more than 350 formulations.
22 As of 1996, the year that the U.S. EPA reregistration process was completed, fewer than
23 50 registrations remained active, and formulations containing strychnine sulfate have
24 been cancelled (U.S. EPA/OPP 1996a). As summarized in Table 2, there are currently
25 only 28 active registrations for formulations containing strychnine alkaloid (PAN 2009).

26
27 Some past registrations for strychnine allowed for the control of several species of
28 rodents, predatory mammals, as well as some birds in both above-ground and below-
29 ground applications (Elliott and Avery 1991; Palmateer 1989; U.S. EPA/OPP 1996a;
30 West 1962). The U.S. EPA now limits the use of strychnine formulations exclusively for
31 the control of pocket gophers (U.S. EPA/OPP 1996a, p. 3). In addition, all above-ground
32 applications of strychnine were suspended in 1988, under a court order from the United
33 States District Court for Minnesota (Palmateer 1989). At the time the current Forest
34 Service risk assessment was prepared, only below-ground applications of strychnine are
35 permitted; accordingly, only those applications are considered in this risk assessment.
36 USDA/APHIS, one of the registrants for strychnine, has canceled all above ground uses
37 of strychnine (Stephens 2009). All forms of strychnine are banned in Britain, the
38 European Union, and Israel (Makarovsky et al. 2008).

39
40 As summarized in Table 3, Regions 5 and 6 of the Forest Service designated nine
41 strychnine formulations that are or may be in use. One of the formulations designated by
42 the Forest Service, Wilco Gopher Getter Restricted Use Bait, does not appear in the list
43 of active formulations provided in Table 2. Wilco Gopher Getter Restricted Use Bait has
44 a Special Needs Label which appears to limit applications to California and Nevada. A
45 label for this formulation was not found on the U.S. EPA label site

1 (<http://www.epa.gov/pesticides/pestlabels/>), and the label for this formulation was
2 obtained from the distributor's site, <http://wilcodistributors.com>.

3
4 The current Forest Service risk assessment is not limited to the formulations specified in
5 Table 3. The Forest Service may elect to use alternate formulations in the future. Thus,
6 the current risk assessment is intended to cover all formulations currently registered by
7 the U.S. EPA. All registered formulations are grain baits, specified either as oats or milo
8 grain. Other than grain, no inerts are identified in the EPA RED for the active
9 formulations of strychnine (U.S. EPA/OPP 1996a). Evans et al. (1990) identify
10 molasses, salt, glycerin, and *soda* (not otherwise specified) as inerts used in some grain
11 formulations.

12 **2.3. APPLICATION METHODS**

13 Subsurface applications of strychnine can be made by either hand baiting or by using a
14 mechanical burrow builder (Iowa State University 1992). One method of hand baiting
15 involves digging a hole into the gopher burrow and manually placing the bait in the
16 burrow. Typically the bait is placed in several locations in the burrow. Alternatively, a
17 bait dispensing probe may be used. As illustrated in Figure 1, the probe is a hollow tube
18 used to locate the burrow. Once the burrow is located, a device on the probe is used to
19 release a fixed amount of the bait into the burrow. A mechanical burrow builder, also
20 illustrated in Figure 1, is a device that attaches to a tractor which digs an artificial burrow
21 and places the bait into the burrow. A series of burrows are typically constructed at
22 intervals of 20-25 feet (Andelt and Case 1995; Iowa State University 1992; Oregon State
23 University 2009).

24 **2.4. MIXING AND APPLICATION RATES**

25 The strychnine formulations listed in Table 3 are pre-mixed. Thus, no mixing is required
26 by the applicator. Nonetheless, applicators will need to handle the pre-mixed bait in
27 either manual or mechanical applications. Worker exposures in handling and applying
28 strychnine formulations are considered further in Section 3.2.2 (Exposure Assessment for
29 Workers).

30
31 The amount of bait applied per acre depends on the density of the gopher population as
32 well as other site-specific factors. The product labels for all hand baiting formulations
33 indicate that 1 lb of formulation should be applied to 1-8 acres—i.e., application rates of
34 0.125-1.0 lb formulation/acre. For all of the 0.5% formulations, the corresponding
35 application rates for strychnine (a.i.) are 0.000625-0.005 lb a.i./acre. The Wilco Gopher
36 Getter Restricted Use Bait also recommends an application rate of 0.125-1.0 lb
37 formulation/acre. This formulation contains 1.8% a.i., and the application rate of 0.125-
38 1.0 lb formulation/acre corresponds to an application rate of 0.00225-0.018 lb a.i./acre.

39
40 As indicated in Table 3, the USDA/Animal and Plant Health Inspection Service (APHIS)
41 is also a registrant for strychnine, and two APHIS formulations labeled for mechanical
42 (*burrow builder*) applications—i.e., EPA Reg. Nos. 56228-11 and 56228-12—are labeled
43 for much higher application rates, relative to the other products summarized in Table 3.
44 The milo grain used for burrow builder applications (EPA Reg. No. 56228-11) has a

1 labeled rate of 1-2.5 lb formulation/acre, corresponding to 0.005-0.0125 lb a.i./acre. The
2 corresponding oat bait formulation (EPA Reg. No. 56228-12) has a somewhat lower
3 application rate of 1.0-2.0 lb formulation/acre, corresponding to 0.005-0.01 lb a.i./acre.
4

5 Typically, the goal of strychnine application is to reduce the gopher population by at least
6 80%. This goal often requires more than one application, and the application efficiency
7 is often checked only after the second application (Nolte and Wagner 2001).
8

9 The current Forest Service risk assessment considers the full range of labeled application
10 rates. The EXCEL workbook released with this risk assessment is based on a 0.5%
11 formulation applied at a rate of 1 lb formulation/acre or 0.005 lb a.i./acre. The
12 consequences of using other application rates as well as multiple applications are
13 discussed in the risk characterization for human health (Section 3.4) and ecological
14 effects (Section 4.4).

15 **2.5. USE STATISTICS**

16 Most Forest Service risk assessments attempt to characterize the use of a pesticide in
17 Forest Service programs relative to the use of the pesticide in agricultural applications.
18 The information on Forest Service use is typically taken from Forest Service pesticide
19 use reports (<http://www.fs.fed.us/foresthealth/pesticide/reports.shtml>), and information
20 on agricultural use is typically taken from use statistics compiled by the U.S. Geologic
21 Survey (<http://water.usgs.gov/nawqa/pnsp/usage/maps/>) and/or detailed pesticide use
22 statistics compiled by the state of California (<http://www.calepa.ca.gov/>). The USGS,
23 however, does not provide any use statistics for strychnine. Thus, comparisons are
24 limited to the reported use by the Forest Service, for which statistics are available up to
25 2004, use statistics from the state of California, as well as use statistics given in the RED
26 for strychnine (U.S. EPA/OPP 1996a).
27

28 Forest Service uses of strychnine from 2000 to 2004 are summarized in Table 4. The
29 Forest Service classification divides the United States into nine regions designated from
30 Region 1 (Northern) to Region 10 (Alaska). [Note: There is no Region 7 in the Forest
31 Service system.] Based on the data in Table 4, Figure 2 illustrates the relative use of
32 strychnine by weight in the various Forest Service regions. Between 2000 and 2004, the
33 greatest use of strychnine occurred in Region 1 (50% of all Forest Service use), followed
34 by Region 4 (36%) and then Region 6 (about 12.3%). These three regions account for
35 more than 98% of Forest Service use. Most of the remaining Forest Service use occurred
36 in Region 5 (1.7%). No uses of strychnine are reported in the East Coast (Regions 8 and
37 9) or in Southwest (Region 3), and very little use—i.e., one application of 0.75 lb in
38 2000—is reported in Region 2 (the Rocky Mountain Region).
39

40 As indicated Table 4, most Forest Service regions present use statistics in units of pounds
41 per acre. Region 1, however, also summarizes small applications (i.e., 0.1-0.6 lbs) made
42 from 2002 to 2004 in terms of bait stations. The term *bait station* typically designates
43 above-ground applications (e.g., Wolf 1962). It is unlikely, though not entirely clear, that
44 bait stations were used in Region 1, because strychnine was labeled only for below-
45 ground applications.

1
2 Another ambiguity in the report statistics involves Region 2 of the Forest Service for
3 which the use statistics appear to reflect pounds of formulation rather than pounds of
4 strychnine. The use of units in formulation rather than a.i. is suggested by the application
5 rate for Region 2 of 0.375 lb/acre. As indicated in Table 3, this application rate is
6 consistent with those for the strychnine formulations but is substantially higher than the
7 labeled application rates in terms of lb a.i./acre (i.e., 0.000625-0.018 lb a.i./acre). This
8 discrepancy has little impact on the use statistics because of the extremely low use of
9 strychnine in Region 2. Overall, the annual use of strychnine in Forest Service projects
10 from 2000 to 2004 is about 335 lbs a.i./year [$\approx 1677 \text{ lbs a.i.} \div 5 \text{ years} \approx 335.4 \text{ lbs}$].

11
12 By comparison, U.S. EPA/OPP (1996a) indicates that USDA/APHIS used about 1000-
13 1500 pounds of strychnine between 1989 and 1991, which corresponds to an annual use
14 of about 333-500 lbs a.i./year. These applications, however, were used to control not
15 only gophers but also ground squirrels, prairie dogs, and voles. Since strychnine is now
16 registered only for the control of pocket gophers, it is likely that the use of strychnine by
17 APHIS has diminished.

18
19 In California, a total of about 1050 lbs a.i. of strychnine was used during 2007, the most
20 recent year for which statistics are available (CDPR 2008). Most of the applications
21 made in California involved crops or flowers. Applications to timberland ($\approx 6.5 \text{ lbs}$) and
22 rangeland ($\approx 0.3 \text{ lbs}$) accounted for only about 0.65% of the total pounds of strychnine
23 applied [$6.8 \text{ lbs} \div 1050 \text{ lbs} \approx 0.006476$]. Based on an analysis of California use statistics
24 from 1999 to 2006, the use of strychnine in forests accounted for only about 0.65% of
25 total use [$79.63 \text{ lbs} \div 12199.46 \text{ lbs} \approx 0.0065$] (U.S. EPA/OPP 2009, Table 2.3, p. 23).

26
27 The available use data on strychnine do not support a direct assessment of its use by the
28 Forest Service, relative to other uses; nevertheless, it does appear that Forest Service use
29 would not be considered substantial, relative to agricultural uses based on the most recent
30 use statistics from California as well as use data from California from 1999 to 2006.
31 Whether this pattern will hold in other Forest Service regions, particularly regions in the
32 northwest, is unclear.

33 **2.6. RESTRICTIONS ON APPLICATION SITES**

34 In addition to restrictions on application methods (below ground only) and target species
35 (pocket gophers only), all product labels for strychnine listed in Table 3 indicate that the
36 formulations cannot be applied in geographical ranges for selected species unless
37 approval is obtained from the U.S. EPA. These limitations are not discussed in the RED
38 for strychnine (U.S. EPA/OPP 1996a) and appear to have been imposed after the RED
39 was issued.

40
41 As summarized in Table 5, all product labels listed in Table 3 indicate that the restrictions
42 apply to geographical ranges of the grizzly bear, the San Joaquin kit fox, the Morro Bay
43 kangaroo rat, and the grey wolf. Some product labels indicate that the restriction also
44 applies to the ranges of the Aleutian Canada goose, the salt marsh harvest mouse, and the

- 1 California condor. In any proposed application of strychnine, the product label should be
- 2 consulted to determine if any species restrictions apply to the proposed project.
- 3

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3. HUMAN HEALTH RISK ASSESSMENT

3.1. HAZARD IDENTIFICATION

3.1.1. Overview

The acute toxicity of strychnine and its mechanism of action are well-characterized. Strychnine is a neurotoxin that inhibits glycine, a neurotransmitter critical to the normal function of the nervous system in vertebrates. Strychnine is rapidly metabolized and detoxified by the liver. Strychnine is also well-absorbed and acts very rapidly, producing muscular hyperactivity, which can quickly lead to respiratory failure and death. Acute lethal doses in humans are as low as about 2 mg/kg bw, which is similar to reported lethal doses in rodents. In experimental studies with mammals, females appear to be more sensitive than males, and young animals appear to be more sensitive than mature animals to strychnine toxicity. Based on acute LD₅₀ values by various routes of administration, the differences in toxicity among males and females and among young and older animals, may reach a factor of 4.

As discussed further in the ecological risk assessment, lethal doses of around 2 mg/kg bw are reported for several species of mammalian wildlife. The minimum lethal dose in humans, however, is not well defined. Despite numerous cases of fatal strychnine poisoning, survival at doses as low 1.0 mg/kg bw appears to depend on rapid and aggressive medical care. Although strychnine is no longer used therapeutically, it had medicinal applications up until the 1970s. While extensive clinical trials of strychnine have not been conducted, it appears that doses ranging from about 0.02 to 0.1 mg/kg bw/day do not cause acute and overt toxic effects.

Although the acute toxicity of strychnine is well defined, the effects of longer-term exposures—i.e., subchronic and chronic—are poorly defined. Strychnine has not been well-assayed for several specific types of toxicities, including reproductive effects, immunotoxicity, endocrine disruption, and carcinogenicity. Nonetheless, U.S. EPA/OPP suggests that the human health risk assessment for strychnine should be based on acute toxicity, and although the supporting data are problematic in many ways, the weight-of-evidence supports this approach.

3.1.2. Mechanism of Action

The biochemical mechanism of action of strychnine is relatively well characterized. Strychnine interferes with or antagonizes glycine, an amino acid. One of the normal roles of glycine is to regulate nerve cell function. Nerve cells in the central nervous system that control muscle movement (motor neurons) generate electrical impulses by maintaining differences between intracellular and extracellular concentrations of positively charged ions (e.g., sodium, potassium, and calcium) and chloride, which is a negatively charged ion. The flow of these ions into and out of the nerve cells is regulated by ion channels. Another class of neurons, referred to as inhibitory neurons, release glycine. Glycine binds to receptors at chloride ion channels and increases the flow of chloride ions into motor neurons resulting in an inhibition of motor neuron activity.

1 Strychnine also binds to chloride channels and appears to compete with glycine, although
2 it is not clear that strychnine and glycine bind to the same receptors or to linked receptors
3 (Young and Snyder 1977). Unlike glycine, however, the binding of strychnine to the
4 chloride channels does not result in an increase in the permeability of chloride ion into
5 the motor neuron. Thus, strychnine effectively blocks the normal neuro-inhibitory
6 function of glycine (Banerjee et al. 1970; Bogdanov et al. 1994; Farroni and McCool
7 2004; Hardman and Limbird 1996; Hernandez et al. 1988; Makarovsky et al. 2008;
8 Perper 1985; Smith 1990; Renna et al. 2007; Rousseau et al. 2008; Vanderberg et al.
9 1992; Venard et al. 2008).

10
11 The net result of this biochemical interaction is hyperexcitability of the nervous system.
12 In other words, normal stimuli will result in an exaggerated muscular response which
13 leads to violent convulsions, the most common gross sign of toxicity associated with
14 strychnine poisoning (Boyd et al. 1983). The loss of muscular control may lead to
15 respiratory paralysis, and the proximal cause of death in many cases of strychnine
16 poisoning is classified as asphyxiation (ACGIH 2001). The duration between the
17 biochemical effects and gross toxic effects of strychnine is often very brief with gross
18 signs of toxicity apparent in less than 1 hour after exposure to acutely toxic doses (Baker
19 et al. 1982; CDC 1983; Craig 1955).

20
21 While the antagonism of glycine by strychnine in the central nervous system appears to
22 be the primary mechanism of toxicity, the interaction of glycine and strychnine at other
23 sites is not always competitive. For example, the injection of exogenous glycine into the
24 spinal cord of mice will potentate rather than antagonize strychnine-induced convulsions
25 in mice (Lewis and O'Brien 1986). Similarly, glycine has a protective effect on toxic
26 damage to proximal tubules of the kidney. Strychnine has the same protective effect and
27 does not interfere with the protective effect of glycine (Miller et al. 1994).

28 ***3.1.3. Pharmacokinetics and Metabolism***

29 Pharmacokinetics concerns the behavior of chemicals in the body, including their
30 absorption, distribution, alteration (metabolism), and elimination as well as the rates at
31 which these processes occur. This section of the risk assessment focuses on the available
32 information on the pharmacokinetic processes for strychnine, including a general
33 discussion of the uptake, distribution, metabolism, and elimination, with a focus on the
34 kinetics of absorption (Section 3.1.3.2) and excretion (Section 3.1.3.3).

35 ***3.1.3.1. General Considerations***

36 The pharmacokinetics of strychnine are relatively well characterized based on
37 information obtained from incidents involving human poisoning as well as experimental
38 studies in mammals.

39
40 Strychnine can be absorbed relatively fast from the gastrointestinal tract (Heiser et al.
41 1989; Makarovsky et al. 2008; Palatnick et al. 1997; Swissman and Jacoby 1964;
42 Yamarick et al 1992). The most relevant information for characterizing the rate of oral
43 absorption in humans comes from suicidal ingestions of strychnine in which serial
44 measurements of strychnine concentrations in plasma are available (Edmunds et al. 1986;

1 Heiser et al. 1989; Palatnick et al. 1997). The studies by Edmunds et al. (1986) and
2 Palatnick et al. (1997) show peak concentrations of strychnine in plasma within
3 approximately 2-4 hours after the ingestion of strychnine; however, these studies do not
4 provide a quantitative estimate of absorption rate from the gastrointestinal tract. The
5 study by Heiser et al. (1989) provides few measurements of strychnine in plasma but
6 gives an estimated first-order oral absorption rate of 2.68 hour⁻¹. The usefulness of this
7 estimate, however, is unclear because the patient was lavaged (i.e., an attempt was made
8 to wash out the contents of the stomach) shortly after treatment was initiated.

9
10 While strychnine appears to be rapidly absorbed, large amounts of strychnine are found
11 in the stomach following suicidal ingestion (Lloyd and Pedley 1953; Van der Copeman
12 1957); moreover, similar effects were observed in experimental mammals (Hatch and
13 Funnel 1968; Buck et al. 1972) and wildlife (Brown et al. 1996). As discussed further in
14 Section 4.2.2 (exposure assessment for mammals and birds), the stomachs of fatally
15 poisoned gophers contain a much greater concentration of strychnine, relative to other
16 parts of the carcasses. High concentrations of strychnine in the stomach of fatally
17 exposed mammals led to the suggestion that strychnine is poorly absorbed or not
18 absorbed from the stomach (e.g., Peoples 1970). A more reasonable explanation,
19 however, relates to the rapidity of both oral absorption and toxic action. As discussed in
20 Section 3.1.2.1, strychnine is a very fast acting poison. After ingestion of a large amount
21 of strychnine, lethal amounts are quickly absorbed from the gastrointestinal tract and the
22 animal dies before oral absorption is complete.

23
24 As is true for many toxic agents, the vehicle in which strychnine is administered may
25 affect the toxicity of the compound. While vehicle effects were not studied in mammals,
26 Hussain et al. (1993) report that strychnine in an aqueous solution is much more toxic to
27 birds than strychnine administered in millet, sorghum, or wheat. This study is discussed
28 further in Section 4.1.2.2. While somewhat speculative, the greater toxicity of strychnine
29 in water relative to strychnine in grain suggests that food or a full stomach may retard the
30 oral absorption of strychnine. There are no comparable mammalian studies in which
31 different vehicles were used with the same population of animals.

32
33 A retardation of the oral absorption rate of strychnine is important to the hazard
34 identification because strychnine is rapidly detoxified by the liver. Figure 3 provides an
35 overview of strychnine metabolism. The major *in vivo* metabolite of strychnine is the
36 21,22-epoxide which is further metabolized to two dihydroxy-derivatives. The role of the
37 liver in the metabolism of strychnine was first demonstrated by Priestly et al. (1931)
38 using a heart-lung-liver perfusion system in the dog. Subsequently, numerous studies
39 demonstrated that the liver plays a central role in the metabolism of strychnine (Kato et
40 al. 1962, 1968; Mishima et al. 1985; Makarovsky et al. 2008; Tanimoto et al. 1999;
41 Tsukamoto et al. 1964) and that the metabolism of strychnine leads to detoxification
42 (Bohlin et al. 1975; Davis and Yeh 1969; Iskander and Bohlin 1978). In comparative
43 studies in rats, only one metabolite (4-hydroxystrychnine with an LD₅₀ of about 0.56
44 mg/kg bw) approached the toxicity of strychnine (with an LD₅₀ of 0.47 mg/kg bw)
45 (Sandberg and Kristianson 1970). The nature of the strychnine metabolites suggests the
46 involvement of liver mixed-function oxidase. The role of liver mixed-function oxidase is

1 also indicated by the inhibition of strychnine metabolism by compounds (i.e., SKF-525A
2 and n-ocylamine) known specifically to inhibit mixed-function oxidase (Mishima et al.
3 1985; Kato et al. 1962,1968) as well as the enhancement of strychnine toxicity by
4 inhibitors of liver mixed-function oxidase (Adamson and Fouts 1959).

5
6 Liver mixed-function oxidase, also referred to as cytochrome P450, is inducible;
7 furthermore, substrates of mixed-function oxidase often induce (i.e., increase the quantity
8 of) these enzymes *in vivo* (e.g., Coon 2005; Goldstein et al. 1974; Lynch and Price 2007).
9 This phenomenon is important to the hazard identification for strychnine because the
10 induction of liver mixed-function oxidase often increases the ability of an animal to
11 tolerate higher doses of a toxic agent, so long as the agent is detoxified by the mixed-
12 function oxidase.

13
14 Despite the lack of experimental studies regarding the induction of liver mixed-function
15 oxidase by strychnine, indirect evidence suggests that strychnine will induce mixed-
16 function oxidase, resulting in strychnine tolerance. Lee et al. (1990) describe apparent
17 *acquired tolerance* in several pocket gophers during an efficacy study in which the
18 gophers were able to consume 1% strychnine treated bait with no signs of toxicity at
19 estimated doses of up to 275 mg/kg bw for periods of up to 28 days (Lee et al. 1990,
20 Table 1). One of the gophers, which tolerated daily doses of up to 57.2 mg/kg bw/day,
21 was taken off strychnine treated bait for 44 days. When re-exposed to strychnine treated
22 bait, this animal died after consuming only 7 mg/kg bw. Albeit circumstantial, this
23 pattern is consistent with the induction of mixed-function oxidase resulting in tolerance to
24 strychnine during the initial exposure and subsequent loss of tolerance attributable to the
25 return of mixed-function oxidase to lower and more normal levels prior to the second
26 period of exposure. The development of tolerance to strychnine may also be associated
27 with the initial reluctance of some organisms to consume large amounts of strychnine
28 treated bait (e.g., Nolte and Wagner 2001), with the sublethal exposures being sufficient
29 to induce liver mixed-function oxidase.

30 **3.1.3.2. Dermal Absorption**

31 Strychnine appears to be rapidly absorbed from the gastrointestinal tract (Section
32 3.1.2.1), and a human case report involving snorting strychnine, mistakenly thought to be
33 cocaine, suggests that strychnine may also be well absorbed from the lungs and nasal
34 passages (Boyd et al. 1983), as summarized in Appendix 1.

35
36 The dermal absorption of strychnine is not well studied. In an early review, Baker et al.
37 (1982) suggests that strychnine is not absorbed across the skin; however, the publication
38 does not support or provide sufficient documentation for this statement. U.S. EPA/OPP
39 (1996a,c) makes the assumption that strychnine is poorly absorbed by the skin; however,
40 as discussed further in Section 3.1.12, this assumption is based on an acute dermal
41 toxicity study in which exposure to 2000 mg/kg bw did not cause adverse effects in rats
42 (Cerven 1988e,f).

43
44 An incident involving dermal exposure of a woman to a liquid solution of strychnine
45 indicates that strychnine can be absorbed by the skin. As reported by Greene and

1 Meatherall (2001) and summarized in Appendix 1, the incident involved a woman who
2 spilled about 1 cup of a strychnine solution. Although the strychnine concentration of the
3 solution was not determined, Greene and Meatherall (2001) estimate that the solution
4 probably consisted of about 2% strychnine (i.e., 20,000 mg/L). The duration of contact
5 consisted of approximately 30 minutes, after which time the woman washed her hands.
6 The signs of systemic toxicity associated with this incident are discussed further in
7 Section 3.1.12. Dermal absorption was documented by measurements of concentrations
8 of strychnine in plasma (0.196 mg/L) and urine (6.85 mg/L) when the woman sought
9 medical attention 28 hours after exposure. While this incident provides a qualitative
10 indication of dermal absorption, the data presented by Greene and Meatherall (2001)
11 cannot be used to estimate a dermal absorption rate. Nonetheless, Greene and Meatherall
12 (2001) estimate that the woman absorbed about 600 mg of strychnine, based on the
13 measured plasma concentration at 28 hours after exposure as well as estimates of the
14 plasma half-life (i.e., 10 hours) and an apparent distribution volume of 13 L/kg. From the
15 assumption that distribution was complete by 4 hours after exposure, Greene and
16 Meatherall (2001) estimate that the peak plasma concentration was 0.786 mg/L.

17
18 The kinetic analysis offered by Greene and Meatherall (2001) is based on a number of
19 reasonable assumptions. As discussed further in Section 3.1.3.3, the plasma half-life of
20 10 hours and time to peak plasma concentration of 4 hours are consistent with plasma
21 concentrations reported in other episodes of human poisonings (Edmunds et al. 1986;
22 Heiser et al. 1989; Palatnick et al. 1997), and the apparent distribution volume is from the
23 analysis by Heiser et al. (1989). Nonetheless, Greene and Meatherall (2001) do not
24 derive a dermal absorption rate.

25
26 In the absence of experimental data on dermal absorption rates, Forest Service risk
27 assessments estimate first-order dermal absorption rates based on quantitative structure
28 activity relationships (QSAR), as documented in SERA (2007a). This method is based
29 on the analysis of dermal absorption rates for compounds with molecular weights ranging
30 from about 60 to 400 g/mole and log K_{ow} values ranging from about -2.8 to 7. Both of
31 these ranges encompass strychnine (i.e., a MW of about 334 g/mole and a log K_{ow} of 4)
32 (Table 1). Using this algorithm, the estimated first-order dermal absorption rates for
33 strychnine is 0.0035 (0.0014-0.0086) hour⁻¹. The rate calculations are detailed in
34 Worksheet B06 of the EXCEL workbook accompanying this risk assessment.

35
36 Forest Service risk assessments also use a QSAR algorithm developed by the EPA (U.S.
37 EPA 1992, 2007), when experimental data are not available to estimate a zero-order
38 dermal absorption rate (i.e., typically referred to as a K_p in units of cm/hour). This
39 method is based on the analysis of dermal absorption rates for compounds with molecular
40 weights ranging from about 32 to 764 g/mole and log K_{ow} values ranging from about
41 -2.25 to 5.4 (U.S. EPA 1992, Table 5-4). These ranges also encompass the
42 corresponding values for strychnine. As detailed in Worksheet B05 of the EXCEL
43 workbook which accompanies this risk assessment, the QSAR algorithm developed by
44 the EPA results in an estimated zero-order dermal absorption rate of 0.011 (0.0059-
45 0.021) cm/hour.

1 **3.1.3.3. Excretion**

2 Excretion half-lives can be used to infer the effect of longer-term exposures on body
3 burden, based on the *plateau principle* (e.g., Goldstein et al. 1974). The chemical
4 concentration in the body after a series of doses (X_{inf}) over an infinite period of time can
5 be estimated based on the body burden immediately after a single dose, X_0 , by the
6 relationship:

7

$$8 \quad \frac{X_{inf}}{X_0} = \frac{1}{1 - e^{-kt^*}}$$

9

10 where t^* is the interval between dosing and k is the first-order excretion rate.

11
12 Three reports include data regarding the clearance of strychnine from plasma following
13 suicidal ingestion: Heiser et al. (1989), Edmunds et al. (1986), and Palatnick et al. (1997).
14 All of these reports involve individuals who intentionally ingested large doses of
15 strychnine but received prompt medical attention, in which case, serial blood samples
16 were taken providing measurements of strychnine concentrations in the plasma. The
17 plasma half-lives reported in these cases range from 10 hours (Edmunds et al. 1986) to
18 15.9 hours (Palatnick et al. 1997). Heiser et al. (1989) do not report a plasma half-life,
19 but this report involves relatively few measurements of strychnine in the plasma. Based
20 on the graph of plasma concentrations provided in Heiser et al. (1989, Figure 2), the time
21 between the peak plasma concentration and one-half of the peak plasma concentration is
22 about 10 hours.

23
24 While the data on plasma half-lives provide a general indication that strychnine is not
25 likely to be accumulated, decreases in the concentration of a compound in plasma do not
26 necessarily reflect excretion of the compound—i.e., the compound could partition from
27 plasma to tissue rather than be excreted. The best data on body burdens of strychnine
28 comes from the study by Oguri et al. (1989) in which rats were administered strychnine
29 (^3H -) at a dose of 0.5 mg/kg bw by subcutaneous injection. Based on Figure 2 in Oguri et
30 al. (1989, p. 173), it appears that about 60% of the administered strychnine was excreted
31 in the feces and 30% was excreted in the urine within the first 24 hours after dosing. The
32 relatively minor role of the kidney in the excretion of strychnine was also noted in the
33 early kinetic studies in dogs and cats (Hatcher and Eggleston 1918).

34
35 Based on a standard first-order elimination model, the proportion (P_t) of a compound
36 remaining (i.e., not excreted) by a given time (t) is:

37

$$38 \quad P_t = e^{-kt}$$

39 where k is the first-order elimination rate in units of reciprocal time. Solving for k ,

40

$$41 \quad k = \frac{-\text{Ln}(P_t)}{t}$$

42

1 and using 0.1 as the proportion of the compound not eliminated in the study by Oguri et
2 al. (1989), the estimated first-order excretion rate (k) would be 2.3 days⁻¹, corresponding
3 to an elimination half-life of about 0.3 days or 8 hours. Substituting 2.3 days⁻¹ into the
4 equation for the plateau principle and using 1 day as the period between doses, the
5 maximum accumulation of strychnine in the body over a prolonged/infinite period of
6 exposure would be about 1.1 $[1 \div (1 - e^{-2.3 \times 1})]$.

7
8 The similarity between the whole-body elimination rate (\approx 8 hours) from the study in rats
9 and the plasma half-lives of about 10-16 hours in humans suggests that metabolism and
10 elimination are closely linked. That the plasma half-lives in humans are somewhat longer
11 than the whole-body half-life in rats should not be misconstrued. In general, plasma half-
12 lives should not be longer than whole-body half-lives in a system that follows first-order
13 kinetics. The plasma half-lives in humans could reflect a slower elimination rate relative
14 to rats but could also reflect the clinical condition of the individuals subsequent to the
15 ingestion of large amounts of strychnine as well as the effects of therapeutic measures
16 used in the treatment of those individuals.

17 **3.1.4. Acute Oral Toxicity**

18 **3.1.4.1. Effects in Humans**

19 As noted in Section 2, strychnine was used for centuries as a rodenticide and as a
20 therapeutic or medicinal agent. Consequently, the potential hazards of strychnine to
21 humans are well documented in cases of both accidental exposure and suicide attempts,
22 numerous reviews of poisoning incidents are published in the open literature (e.g.,
23 Blondell 1997, 2007; Decker et al. 1982; Eisemana and Petersen 2002; Hayes and
24 Vaughn 1977; Hernandez et al. 1988).

25
26 There are many documented cases of accidental exposures in children. Most of the
27 incidents involving the accidental exposure of young children are associated with the
28 accidental ingestion of strychnine tablets used medicinally (e.g., Craig 1955; Jackson et
29 al. 1971; Ross and Brown 1985; Stannard 1969; Swissman and Jacoby 1964). In the
30 open literature, there is only one incident in which a possible pesticide use of strychnine
31 was associated with poisoning in a child. In this incident, an 18-month old girl consumed
32 rice treated with strychnine (Savage et al. 1971, p. 30, Case 7). Savage et al. (1971) does
33 not describe the circumstances of the contamination, and it is not clear that the strychnine
34 treated rice was used as a pesticide. Nonetheless, this incident clearly did not involve
35 exposure to strychnine as a therapeutic agent.

36
37 Suicidal exposures to strychnine involve adults who intentionally consume strychnine,
38 and the source of strychnine can be either from medicinal tablets (e.g., Heiser et al 1989;
39 Salm 1952) or from rodenticides (Lambret et al. 1981; Palatnick et al. 1997; Perper
40 1985). Accidental exposures to pesticides are generally atypical in adults; nevertheless,
41 the literature on strychnine includes an accidental exposure scenario in which an adult
42 snorted strychnine powder believing that the powder was cocaine (Boyd et al. 1983;
43 O'Callaghan et al. 1982). Although the source of the strychnine powder is not clear, it is
44 unlikely that the powder came from strychnine rodenticide bait.

1 Generally, information on accidental and suicidal exposures is useful because it provides
2 lethal dose estimates; however, most of the accidental and suicidal incidents involving
3 strychnine do not include enough information to estimate the doses associated with the
4 exposure. The exceptions are detailed in Appendix 1 and summarized in Table 6. The
5 interpretation of these reports is further complicated by circumstances involving medical
6 treatment. With two exceptions (Lloyd and Pedley 1953; Perper 1985), the reports
7 summarized in Appendix 1 involve cases in which individuals received prompt medical
8 treatment at a hospital. Thus, even when doses can be estimated, the clinical outcomes
9 (i.e., survival or death) are of limited use in estimating a non-lethal dose, because it is
10 possible that the poisoned individuals would have died without effective medical care.

11
12 Table 6 is arranged in order of increasing dose. Not all studies include estimates of the
13 dose; nonetheless, these studies are considered in Table 6 because they report serum
14 concentrations of strychnine. The fatal doses range from about 1.4 to 80 mg/kg bw, and
15 the non-fatal doses range from 1 to 25 mg/kg bw. As noted above, the distinction
16 between fatal and non-fatal doses is not useful in terms of inherent risk because most of
17 the individuals received medical intervention.

18
19 Despite the relatively small sample size, the data indicate that peak plasma concentrations
20 of strychnine greater than 2.2 mg/L were fatal, despite prompt medical treatment. The
21 converse, however, is not true. Lloyd and Pedley (1953) report a relatively low plasma
22 concentration of 0.8 mg/L following a successful suicidal ingestion of strychnine. This
23 value, however, is not comparable to the other concentrations summarized in Table 6,
24 because the individual was found dead. Sgaragli and Mannaioni (1973) failed to detect
25 any strychnine in the blood of another poisoned individual. The reason for this failure is
26 not clear; however, the publication discusses apparent difficulties in the analytical
27 method.

28
29 The range of lethal doses summarized in Table 6 and detailed in Appendix 1 is
30 comparable to lethal doses reported in other reviews of strychnine—i.e., 16-120 mg
31 (Makarovsky et al. 2008) and 15-30 mg/kg bw (Boyd et al. 1983). Hayes (1982)
32 summarizes incidents from the older literature in which an individual survived a nominal
33 dose of about 13,000 mg (\approx 185 mg/kg bw). This individual vomited some of the dose
34 shortly after exposure and received medical attention. Thus, like the *non-fatal* exposures
35 summarized in Table 6, this report is not useful in estimating a non-hazardous dose in the
36 absence of medical intervention.

37
38 Boyd et al. (1983) state that ... *deaths have been reported from as little as 5 to 10 mg*; no
39 reference is provided for this statement. Moreover, the dose range is not associated with
40 specified body weights, and the statement cannot be confirmed. The lowest lethal dose
41 encountered in the literature is 16 mg from the report by Stannard (1969). As detailed in
42 Appendix 1, the estimated dose of 16 mg is associated with the death of a 1-year-old
43 child; however, the body weight of the child is not provided. Based on the recommended
44 average body weight of 11.4 kg for a 1-year-old infant (U.S. EPA/NCEA 2008, p. 8-2),
45 the estimated lethal dose for the child is about 1.4 mg/kg bw, which is very close to the
46 lowest reported lethal dose in an adult—i.e., 2.25-2.3 mg/kg bw (Salm 1952) as well as

1 the estimated range of potentially lethal doses of 1.1-1.8 mg/kg bw in U.S. EPA/OPP
2 (1996a, p. 13).

3
4 At the other end of the dose scale, the therapeutic uses of strychnine can be used to
5 suggest ranges of oral doses that do not result in overt toxic effects. As discussed at some
6 length by Buckingham (2008), strychnine was used medicinally for centuries. As
7 discussed in Section 3.1.2, strychnine's neurological effects lead to muscle contractions,
8 which at low doses can be viewed as an increase in muscle tone. Consequently,
9 strychnine was used to treat general lethargy, impotence, and even paralysis secondary to
10 a stroke (Hayes 1982). This use continued into the mid-20th century. In the case of the
11 poisoned infant documented by Stannard (1969), the child consumed pills containing
12 strychnine which were prescribed to the child's mother, who was pregnant at the time, as
13 part of an iron-containing *tonic*. In this case, the dose for the medication amounted to 1
14 mg strychnine per day, or about 0.017 mg/kg bw/day for a 60 kg woman. Higher doses
15 (i.e., 5-6 mg for females and 6-7 mg for males) were commonly used (Hayes 1982).
16 Based on standard body weights of 60 kg for a woman and 70 kg for a man, the upper
17 bound of these *therapeutic* doses correspond to about 0.1 mg/kg bw/day.

18
19 The therapeutic uses of strychnine at doses of about 0.02-0.1 mg/kg bw/day cannot be
20 interpreted as doses that are without harm or risk. As discussed further in Section 3.1.5,
21 long-term observations of patients undergoing strychnine therapy are limited.
22 Notwithstanding these limitations, the common use of strychnine at doses of 0.02-0.1
23 mg/kg bw/day clearly represents a body of human experience which suggests that these
24 dose levels are not likely to be associated with the rapid onset of overt acute toxicity.

25
26 The relationship of doses for the past uses of strychnine as a therapeutic agent—i.e.,
27 about 0.02-0.1 mg/kg bw—to the potentially lethal dose of about 1 mg/kg bw is not
28 unusual. In a survey of several toxic agents, the ratio of the LD₅₀ in mammals to the
29 short-term NOEC in mammals is about 10 for 20% of the compounds included in the
30 analysis and about 100 for 50% of the compounds included in the analysis (McNamara
31 1976). For strychnine, the proximity of the past therapeutic doses to the apparently lethal
32 doses may relate to the relatively rapid metabolism of strychnine by liver mixed-function
33 oxidase (Section 3.1.3). Metabolism by mixed-function oxidase is a saturable process.
34 Thus, if the dose is below the concentration that saturates liver metabolism,
35 concentrations in the blood may remain relatively low due to liver clearance. Once liver
36 metabolism is saturated at higher doses, the concentration in the blood may increase
37 substantially, dramatically increasing the severity of toxic effects.

38 ***3.1.4.2. Effects in Experimental Mammals***

39 In addition to human data on the acute oral toxicity of strychnine, there is a relatively
40 large body of information on the toxicity of strychnine to experimental and domestic
41 mammals as well as several species of mammalian wildlife. The acute oral toxicity
42 studies on mammalian exposure to strychnine are summarized in Appendix 2. Much of
43 this information is directly related to the use of strychnine as a rodenticide and its effects
44 on mammalian wildlife. These effects are discussed further in the ecological risk
45 assessment (Section 4.1.2.1). The following discussion focuses on studies in

1 experimental mammals. These studies are relevant to both the human health and
2 ecological risk assessment. Although this subsection is concerned primarily with oral
3 toxicity, studies involving injection/parenteral exposures are also considered because they
4 reflect differences in strychnine sensitivity among males and females and individuals of
5 different ages.

6
7 U.S. EPA/OPP (1996a,c) classifies strychnine as Category I (the most hazardous ranking)
8 for acute oral toxicity, based on standard LD₅₀ values in rats of 6.4 (5.8-71) mg/kg bw for
9 male rats and 2.2 (1.9-2.5) mg/kg bw for female rats. These LD₅₀ values are in the lower
10 bounds of lethal oral doses in humans—i.e., 1.4-80 mg/kg bw (Table 6). The LD₅₀ for
11 female rats is about a factor of 3 below the LD₅₀ for male rats [$6.4 \div 2.2 \approx 2.91$], and the
12 confidence limits for male and female rats do not overlap. In other words, based on this
13 study, female rats appear to be significantly more sensitive than male rats to strychnine.
14 As discussed further in the following subsection, this pattern is consistently observed in
15 rat studies. Differences in strychnine sensitivity among male and female mice are less
16 well documented and appear to be less pronounced. Differences in strychnine sensitivity
17 based on age follow a similar trend: younger rats are substantially more sensitive than
18 older rats, and similar but less pronounced differences in sensitivity are apparent in mice.

19 ***3.1.4.2.1. Sex Difference in Sensitivity***

20 The increased sensitivity of females, relative to males, noted in the oral study cited by
21 U.S. EPA/OPP (1996a,c) is also found in studies using parenteral dosing. The early
22 study by Poe et al. (1936) using intraperitoneal injections of strychnine notes that female
23 rats, ranging in age from 6 weeks to about 6 months, were about 2-4 times more sensitive
24 to the lethal effects of strychnine, compared with male rats of the same age, as discussed
25 below in greater detail.

26
27 Kato et al. (1962) report similar differences in the sensitivity of male and female rats to
28 strychnine. On subcutaneous injection, Kato et al. (1962) noted that female rats were
29 more sensitive than male rats by factors of about 2.2-2.9, based on comparisons of both
30 LD₅₀ values as well as doses associated with convulsions in 50% of the rats (CD₅₀
31 values). Similar results were obtained following intraperitoneal injections (Kato et al.
32 1962, Table 1). No differences in strychnine sensitivity among male and female rats,
33 however, were noted following intravenous injection (left femoral vein) or following the
34 intraperitoneal injection of strychnine in a 0.1 mM solution of SKF 525A. According to
35 the investigators, the failure to note differences on intravenous injection or in
36 intraperitoneal injections of SKF 525A (an inhibitor of mixed function oxidase activity)
37 suggest that there are no inherent differences in the sensitivity of the neuro-receptors
38 between male and female rats but that male rats metabolized and detoxified strychnine
39 more rapidly than did female rats. This supposition was confirmed by Kato et al. (1962)
40 in studies on the metabolism of strychnine by liver microsomal preparations and liver
41 slices. In both cases, the metabolic activity of liver preparations from normal male rats
42 was greater than that of female rats by factors of about 2-2.5, very similar to the
43 differences in the magnitude of the LD₅₀ and CD₅₀ values for male and female rats. In a
44 final set of *in vitro* studies, Kato et al. (1962) also demonstrated that differences in the

1 metabolic rates between male and female liver preparations were eliminated by castrating
2 the male rats.

3
4 Davis and Yeh (1969) also used intraperitoneal dosing in rats. As discussed further
5 below (Section 3.1.4.2.2), this study was focused on differences in sensitivity between
6 young and old rats. Nonetheless, Davis and Yeh (1969) provide a brief note indicating
7 that no differences between males and females rats were noted in 3- and 4-week-old age
8 groups but that ...*significant sex difference beyond 4 weeks...* was noted. The nature and
9 magnitude of the difference, however, is not specified.

10
11 Lamanna and Hart (1958) conducted a study in which strychnine was administered by
12 intraperitoneal injection to male and female mice of different sizes—i.e., approximately
13 10, 18, and 25 grams. The ages of the mice are not reported; however, the authors
14 indicate that the size differences reflected the different ages of the mice. In this study,
15 differences in sensitivity to strychnine based on gender were not remarkable. The LD₅₀
16 values in the 10-gram weight group indicate that females were less sensitive than males
17 by a factor of about 1.08 [$15.1 \mu\text{g} \div 14 \mu\text{g} \approx 1.0786$]. For the other size groups, females
18 were more sensitive than males; however, the differences in sensitivity were modest in
19 the 18-gram weight group—i.e., a factor of about 1.03 [$31 \mu\text{g} \div 30 \mu\text{g} \approx 1.0333\dots$]. The
20 greatest difference between male and female mice was noted in the 25-gram weight
21 group—i.e., a factor of about 1.14 [$48.0 \mu\text{g} \div 41.9 \mu\text{g} \approx 1.1456$]. None of these
22 differences is as substantial as the differences observed in rats. Based on an examination
23 of the confidence intervals for the LD₅₀ values (Lamanna and Hart 1958, Table 1, p. 310),
24 the sensitivity differences between male and female mice were significant only in the
25 assays of the 25-gram weight group. The minimal differences in sex specificity in the
26 smaller and younger groups of animals are similar to the observations in rats by Davis
27 and Yeh (1969), discussed in the above paragraph.

28
29 The human data do not reflect clear gender-related differences in sensitivity to strychnine
30 (Section 3.1.4.1). In humans, the two lowest fatal doses are recorded for an adult female
31 (Salm 1952) and a 1-year-old girl (Stannard 1969). As discussed in Section 3.1.4.1,
32 however, the distinction between fatal and non-fatal exposures, summarized in Table 6, is
33 of limited use in assessing sensitivity patterns, because most of these exposures appear to
34 involve potentially lethal exposures, some of which were successfully treated with
35 medical intervention.

36 ***3.1.4.2.2. Age Difference in Sensitivity***

37 In addition to gender-related differences in strychnine sensitivity, age-related differences
38 are reported in several rat studies. Poe et al. (1936), as discussed above, observed that
39 young male rats appear to be somewhat more sensitive than older male rats to
40 intraperitoneal injections of strychnine, citing LD₅₀ values of 1.4 mg/kg for 6-week-old
41 rats, 1.9 mg/kg for 10-week-old rats, and 2.3 mg/kg for 18-week as well as 6- to 8-month-
42 old rats. For female rats the reported LD₅₀ values are: 0.9 mg/kg for 6-week-old rats, 1.1
43 mg/kg bw for 18-week-old rats, and ≈ 1.4 mg/kg for 6- to 8-month-old rats. Notably, the
44 range of age-related differences in sensitivity—i.e., a factor of about 1.6 for males and
45 females based on comparisons between 6-week-old and 6-month-old animals—is less

1 than the range of gender-related differences—i.e., factors of about 2-2.5, as discussed
2 above.

3
4 Davis and Yeh (1969) also assayed differences in the susceptibility of 3-, 4-, 5-week-old
5 and 6-month-old rats. As discussed in Section 3.1.4.2.1, the groups of 3- and 4-week-old
6 rats included males and females; whereas, the groups of 5-week-old and 6-month-old rats
7 included only males. This focus of the study was to estimate strychnine doses associated
8 with convulsions, rather than lethality; consequently, the results of the CD₅₀ values—i.e.,
9 estimates of doses causing convulsions in 50% of the test animals—are presented only in
10 graphical form (Davis and Yeh 1969, unnumbered figure on p. 1292). Based on visual
11 estimates of the CD₅₀ values from this figure, 5-week-old rats were more sensitive than
12 6-month-old rats by about a factor of 1.8—i.e., $3 \text{ mg/kg bw} \div 1.7 \text{ mg/kg bw} \approx 1.76$ —very
13 similar to the factor of 1.6 in 6-week versus 6-month-old rats discussed above (Poe et al.
14 1936). In a comparison of 3-week-old animals to 6-month-old animals, the younger
15 animals appear to be more sensitive than the older animals by a factor of 4 [$3 \text{ mg/kg bw} \div$
16 0.75 mg/kg bw]. Furthermore, this factor of 4, based on age difference, is identical to the
17 upper bound of gender-based differences in rat sensitivity to strychnine (Section
18 3.1.4.2.1).

19
20 Davis and Yeh (1969) speculate that the differences in sensitivity between younger and
21 older rats are associated with differences in metabolic rates. As in the study by Kato et
22 al. (1962), Davis and Yeh (1969) tested this supposition by conducting a parallel series of
23 bioassays in rats pretreated with SKF 525A. Pretreatment with this inhibitor of mixed-
24 function oxidase enhanced the toxicity of strychnine to rats in all age groups; however,
25 the magnitude of the increase was proportional to age, suggesting that as rats age, their
26 tolerance to strychnine increases as a result of their increased ability to metabolize
27 strychnine.

28
29 A more complex pattern of sensitivity is apparent in very young rats. A study by Kubova
30 and Mares (1995) examined the effects of strychnine on neonatal rats (3-days-old)
31 relative to young rats (up to 25-days-old). The neonatal rats were not more sensitive than
32 25-day old rats. In fact, it appears that the rats' sensitivity to strychnine increases from
33 Day 3 to Day 18 and then declines. The basis for this difference in sensitivity is not
34 clear.

35
36 As discussed above, Lamanna and Hart (1968) estimated LD₅₀ values for exposure to
37 strychnine via intraperitoneal injection in male and female mice of differing body sizes
38 ranging from 10 grams (i.e., the youngest mice) to about 25 grams (the oldest mice).
39 Lamanna and Hart (1968, Table 1, p. 310) report the LD₅₀ values in units of mg/animal.
40 When these values are converted to units of mg/kg bw, the smaller and younger mice
41 appear to be more sensitive than the larger and older mice by a factor of 1.3 for males
42 [$1.85 \text{ mg/kg bw} \div 1.4 \text{ mg/kg bw}$] and a factor of 1.16 for females [$1.75 \text{ mg/kg bw} \div$
43 1.51]. As with the gender-related differences in sensitivity, the age-related differences in
44 mouse sensitivity are qualitatively similar to but less pronounced than the pattern
45 observed in rats.

1 **3.1.5. Subchronic or Chronic Systemic Toxic Effects**

2 Although the EPA typically requires chronic toxicity studies in both rats and mice for
3 pesticide registration (e.g., <http://www.epa.gov/opptsfrs/home/guidelin.htm>) there do not
4 appear to be any chronic toxicity studies on strychnine. Moreover, the U.S. EPA's Office
5 of Pesticide Programs determined that chronic toxicity data on strychnine are not
6 required:

7
8 *The human health assessment for strychnine is based on the acute*
9 *toxicity for the technical and is described below. Because of the*
10 *high acute toxicity via the oral and ocular routes, subchronic and*
11 *chronic data were not required.*

12 – U.S. EPA/OPP 1996a, p. 13

13
14 In the above quotation, the term *technical* refers to technical grade strychnine. The
15 concern noted above for the ocular route of exposure is discussed further in Section
16 3.1.11.3.

17
18 Though not explicitly stated in U.S. EPA/OPP (1996a), it appears that the EPA assumes
19 that repeated exposure to strychnine doses that are not acutely toxic will not result in
20 longer-term toxic effects. As discussed further in Section 3.1.5.1 below, available
21 multiple dose studies in mammals are of limited use in evaluating this assumption.
22 Consequently, information on kinetics, mechanism of action, and the available
23 subchronic toxicity studies in birds are considered in this risk assessment (Section
24 3.1.5.2). This atypical approach is necessary because the assumption that longer-term
25 exposure to acutely nontoxic doses of strychnine will not result in adverse effects is
26 central to the risk characterization for both workers and members of the general public.

27 ***Section 3.1.5.1. Multiple Doses in Mammals***

28 The strychnine studies involving multiple doses in experimental mammals, which can be
29 used to evaluate the assumption that chronic toxicity is not of concern are extremely
30 limited; moreover, the design of the available studies would generally preclude using
31 them quantitatively in a risk assessment.

32
33 Of the available studies involving multiple doses of strychnine, the 28-day gavage study
34 by Seidl and Zbinden (1982) is closest to a standard toxicity study. As discussed in
35 Section 3.3 (Dose-Response Assessment), the EPA Office of Research and Development
36 (but not U.S. EPA/OPP) uses this study to derive a chronic RfD on strychnine.
37 According to the investigators, the study was designed specifically to assess the safety of
38 strychnine in clinical use with a particular focus on whether longer-term exposures to
39 strychnine result in toxic effects that are not anticipated from shorter-term studies—i.e.,
40 the basic hypothesis discussed above. Thus, despite its limitations, the study is discussed
41 in some detail.

42
43 Seidl and Zbinden (1982) used single-dose gavage administration of strychnine to
44 estimate the *maximally tolerated single doses* in male and female rats—i.e., a single dose
45 that did not cause overt signs of toxicity. Based on preliminary single dose studies, Seidl

1 and Zbinden (1982) used doses of estimated the *maximally tolerated single doses* as
2 2.5 mg/kg bw for female rats and 8 mg/kg bw for male rats. It should be noted that these
3 doses are not NOAELs because deaths were observed in all of the single dose studies.
4 The precise experimental design used to determine these *maximally tolerated single*
5 *doses* is not described in the publication.

6
7 After determining the *maximally tolerated single doses*, Seidl and Zbinden (1982) gave
8 groups of 12 female rats repeated daily doses of 2.5 mg/kg bw and groups of 12 male rats
9 repeated daily doses of 5 and 10 mg/kg bw for 28 days. All doses were administered as a
10 2000 mg/L solution of strychnine in distilled water. Groups of 12 male and 12 female
11 rats were dosed only with distilled water at volumes of 1.25-5 mL/kg.

12
13 Seidl and Zbinden (1982) report that one female rat in the 2.5 mg/kg bw/day dose group
14 died on Day 19; in the 5 mg/kg bw/day dose group, one male rat died on Day 5; and in
15 the 10 mg/kg bw/day dose group, five of twelve male rats died between Day 3 and 27.
16 All deaths occurred between 0.5 and 6 hours after dosing. No deaths occurred in the
17 control groups. Signs of toxicity are described briefly as follows: *10 to 20 minutes after*
18 *each treatment the animals showed increased muscle tone or a slight tremor, which*
19 *subsided gradually during the following 60 minutes.* The publication does not explicitly
20 state whether these signs of toxicity occurred only in fatally ill animals or in all or most
21 of the dosed animals. It appears, however, that these signs of toxicity apply to the
22 animals that did not die. The publication goes on to note that fatally exposed animals ...
23 *exhibited symptoms of acute strychnine intoxication with tonic muscle contractions and*
24 *respiratory paralysis.* In surviving animals, no changes in body weight, food
25 consumption, urinalysis, ophthalmological exams, behavioral response (rotating rod test),
26 organ weights, or histopathology were observed.

27
28 Within the context of the design of the study to assess the longer-term use of strychnine
29 as a therapeutic agent, Seidl and Zbinden (1982) offer the following conclusion:

30
31 *The present study, in which maximally tolerated doses*
32 *administered for a month, gave no evidence of tissue damage or*
33 *functional organ disorders. While this finding is encouraging, it is*
34 *important to underline that in our study only relatively low doses*
35 *(approximately 10 times the therapeutic dose) could be given due*
36 *to the dose-limiting pharmacological effects. Therefore, the*
37 *experiment is of limited usefulness and clinicians must still be*
38 *advised to monitor their patients not only for signs of acute*
39 *strychnine intoxication, but also for potential long term adverse*
40 *effects.*

41 – Seidl and Zbinden (1982), pp. 270-271

42
43 Within the context of the assumption that acutely sub-toxic doses of strychnine will not
44 result in chronic effects with long-term exposures, the key consideration in the study by
45 Seidl and Zbinden (1982) is the identification of the *maximum tolerated dose*. Seidl and
46 Zbinden (1982) appear to have selected a *maximum nonlethal* dose rather than the

1 *maximum nontoxic* dose. As discussed above, it appears that surviving animals
2 evidenced signs of neurotoxicity. Thus, this study does not directly contradict the
3 assumption that acutely nontoxic doses (as opposed to nonlethal doses) administered over
4 prolonged periods will be nontoxic.

5
6 As discussed in Section 3.1.3.1, Lee et al. (1990) conducted 28-day feeding studies in
7 gophers, the target species. Although these were dietary, rather than gavage studies, the
8 publication estimates the amount of contaminated bait consumed by the gophers. This
9 study, however, is not relevant for assessing chronic toxicity because it involved four
10 gophers that apparently developed an acquired tolerance to strychnine, probably through
11 the induction of detoxifying enzymes.

12
13 The very early study by Hale (1906) is focused specifically on attempting to induce
14 strychnine tolerance in dogs and guinea pigs. The basic design of the experiments
15 involved subcutaneous dosing of single animals at varying intervals using progressively
16 higher doses. As with the study by Seidl and Zbinden (1982), however, the lowest doses
17 used by Hale (1909) were associated with sublethal signs of toxicity, which were
18 generally characterized as increased reflexes or, in some cases, convulsions. Thus, the
19 study by Hale (1906) is not useful in assessing hazards associated with longer-term
20 exposures to acutely non-toxic doses.

21
22 Anthony et al. (1984) conducted a very small study involving repeated oral doses in
23 mink. This study employed a group of five mink that survived single dose exposures to
24 strychnine at least 6 days prior to the 5-day study. The single dose studies are
25 summarized in Appendix 2 and discussed further in Section 4.1.2.1. Five surviving mink
26 were dosed at 0.84 mg/kg bw/day in corn oil for 5 consecutive days. One mink died, but
27 the time to death is not provided in the study. Another mink survived but evidenced
28 hypersensitivity to sound and light for 4-6 hours after exposure. The remaining three
29 mink evidenced no signs of toxicity. While this is a repeated dose study that is
30 characterized by Anthony et al. (1984) as *chronic*, the duration of the study is very short
31 and would be more typically classified as acute. Again, this study is not useful in
32 assessing the longer-term consequences of repeated exposures to acutely non-toxic doses.

33
34 Other repeated dosing studies involve human exposures. As discussed in Section 3.1.4,
35 strychnine has been used as a therapeutic agent at doses of about 0.02-0.1 mg/kg bw. In
36 what appears to be a very preliminary assessment of human tolerance to strychnine, Hale
37 (1909) describes the administration of daily oral doses of 7.5 mg of strychnine sulfate to a
38 160 pound (≈ 72.6 kg) man for 8 consecutive days. Using the conversion factor of 0.7732
39 from Table 1, a dose of 7.5 mg strychnine sulfate corresponds to about 5.8 mg of
40 strychnine [$0.7732 \times 7.5 \text{ mg} = 5.799 \text{ mg}$ strychnine alkaloid]. Thus, the daily dose was
41 about 0.08 mg/kg bw [$5.8 \text{ mg} \div 72.6 \text{ kg} = 0.07988 \text{ mg/g bw}$]. This experiment was
42 focused on urinary excretion, which was assayed only qualitatively. Hale (1909) does
43 not comment on any signs of toxicity in this individual. Nonetheless, the major focus of
44 the Hale (1909) study was on the toxicity of strychnine and it seems reasonable to
45 suggest that no signs of toxicity were observed. The dose of 0.08 mg/kg bw/day is near
46 the upper bound of reported therapeutic doses.

1
2 There are several reports (Ch'ien et al. 1978; Gitzelmann et al. 1977a,b; Gitzelmann et al.
3 1978) on the therapeutic use of strychnine to treat nonketotic hyperglycinemia, a
4 congenital condition in which glycine is present at atypically high concentrations leading
5 to a variety of neurologically related disease conditions. Doses below 0.2 mg/kg bw
6 administered to a young child with this condition were not associated with signs of
7 strychnine toxicity (Ch'ien et al. 1978). Similarly, a total dose of 0.3 mg/kg bw did not
8 induce adverse effects in another young child (Gitzelmann et al. 1977b). In the case of a
9 6-month-old child, strychnine nitrate was administered at doses of 0.3-1.1 mg/kg bw/day
10 for 18 months with no adverse effects characteristic of strychnine exposure (Gitzelmann
11 et al. 1978). Using the conversion factor of 0.8414 from Table 1, these doses are
12 equivalent to 0.25~0.92 mg/kg bw of strychnine alkaloid. Similar doses over shorter
13 periods of exposure have been used in children up to 10 years old with no reported
14 adverse effects (Gitzelmann et al. 1978). Both of these patients, however, were also
15 given anticonvulsants. Another complication in the interpretation of these studies
16 involves dose titration. As detailed in Gitzelmann et al. (1977a), varying the strychnine
17 dose in one patient did lead to signs of strychnine toxicity when the dose was increased
18 from 0.33 to 0.4 mg/kg. Eventually, however, the patient was able to tolerate doses of up
19 to 0.9 mg/kg strychnine nitrate (equivalent to about 0.75 mg/kg strychnine alkaloid).

20
21 Because these reports involve individuals with an excess of glycine, the individuals may
22 have been less sensitive to strychnine than individuals without nonketotic
23 hyperglycinemia. Thus, the usefulness of these reports to assess the potential chronic
24 effects of strychnine exposure in the general population may be limited. Nonetheless, the
25 increasing doses of strychnine—i.e., 0.25~0.92 mg/kg bw—used by Gitzelmann et al.
26 (1978) are similar in exposure design to the increasing strychnine doses that Hale (1906)
27 administered to dogs, with one important exception: Gitzelmann et al. (1978) used a
28 series of increasing *nontoxic* doses while Hale (1906) used a series of increasing *toxic* but
29 *nonlethal* doses. Consequently, the failure of Gitzelmann et al. (1978) to note toxicity on
30 longer-term exposures to acutely *nontoxic* doses does provide limited support to the
31 approach taken by U.S. EPA/OPP (1996a) in focusing only on acute toxic effects. While
32 the signs of strychnine toxicity noted in Gitzelmann et al. (1977) appear to be associated
33 with dose titration rather than a cumulative effect, this cannot be stated with certainty.

34 **3.1.5.2. Other Information**

35 As discussed in Section 3.1.3.3, the available information in both experimental mammals
36 and humans indicate that longer-term exposures to strychnine will not lead to a
37 substantial accumulation of strychnine in the body. Specifically, based on the plateau
38 principle, chronic exposure to strychnine at a fixed daily dose is likely to result in peak
39 body burdens of strychnine that are only a factor of 1.1 higher than peak body burdens
40 following a single exposure.

41
42 The lack of strychnine accumulation in the body as a result of exposure is consistent with
43 the assumption that the duration of exposure will not lead to an increase in the severity of
44 effects. Nonetheless, the severity of effects could increase if a toxic agent damages the
45 organism at a rate exceeding the capacity of the organism to repair the damage. In other

1 words, both pharmacokinetics and toxicodynamics need to be considered. For
2 strychnine, the mechanism of action does not suggest a potential for cumulative damage.
3 As discussed in Section 3.1.2, the primary mechanism of action is the inhibition of
4 glycine at chloride ion channel receptors. It seems reasonable to assert that this inhibition
5 will be related to the concentration of strychnine at the receptor site and that this
6 concentration will be related to the concentration of strychnine in plasma. Once
7 strychnine is cleared from plasma, normal nerve function will occur. This appears to be
8 the basis for therapy in cases of strychnine poisoning (Section 3.1.4.1). Thus, for
9 strychnine, the lack of accumulation with longer-term exposures is consistent with the
10 assumption that acutely nontoxic doses of strychnine will not be associated with adverse
11 effects on longer-term exposures.

12
13 One last independent line of evidence involves the information on the short-term and
14 longer-term toxicity of strychnine in birds. Toxicity data on birds are not normally used
15 in the hazard identification for human health effects. Nonetheless, it is important to note
16 that EPA's human health risk assessment (U.S. EPA/OPP 1996c) and ecological risk
17 assessment (U.S. EPA/OPP 1996d) are conducted by two separate groups within U.S.
18 EPA/OPP, the Health Effects Division (HED) and the Ecological Fate and Effects
19 Division (EFED). While HED made the assumption that chronic toxicity data are not
20 required for strychnine, EFED required both acute and reproductive toxicity studies in
21 birds. The latter studies are used to assess chronic risks in birds.

22
23 As discussed further in Section 4.1.2.2 (hazard identification for birds) and detailed in
24 Appendix 4 (toxicity studies in birds), acute, subacute, and reproductive toxicity studies
25 were conducted with both mallard ducks and quail.

26
27 The acute and subacute dietary studies both yielded LC_{50} values for quail and mallards.
28 In terms of comparing toxicities, LC_{50} values are preferable to NOEC and LOEC values
29 because LC_{50} values incorporate all information from the experiment. The acute and
30 subacute dietary studies were both conducted at the same facility by the same individual.
31 The acute dietary studies in quail and mallards are summarized in U.S. EPA/OPP (1996d)
32 and are attributed to Pedersen (1989). These are 5-day dietary exposures with a 3-day
33 recovery period. The subchronic (28-day) dietary studies were published by Sterner et al.
34 (1998). In quail, the 5-day dietary LC_{50} is 212 ppm, and the 28-day dietary LC_{50} is 679.8
35 ppm—i.e., a factor of 3.2 higher than the 5-day dietary LC_{50} . For mallards, the 5-day
36 dietary LC_{50} is 3536 ppm and the 28-day dietary LC_{50} is 4973.6 ppm—i.e., a factor of 1.4
37 higher than the 5-day dietary LC_{50} .

38
39 The reproduction studies in quail and mallards were published by Pedersen et al. (2000),
40 summarized in U.S. EPA/OPP (1996d), and cited as a registrant submission—i.e.,
41 Pedersen 1993. The reproduction studies do not involve estimates of LC_{50} values.
42 Another complication with these studies is that Pedersen et al. (2000) classify the 33.2
43 ppm group in the mallard study as a NOEC; whereas, the U.S. EPA/OPP (1996d)
44 classifies the 33.2 ppm group in the mallard study as a LOEC. This difference in
45 classification appears to be based on the finding of reduced testes weight in one male
46 duck from the parental (F_0) group. This effect is considered incidental by the study

1 authors (Pedersen et al. 2000, p. 533); nonetheless, in U.S. EPA/OPP (1996d, p. 5) this
2 finding is considered a treatment-related effect even though a decrease in testes size was
3 not noted at higher doses. Regardless of the interpretation of the testes weight, no
4 mortality or overt signs of toxicity in mallards were noted in the 33.2 ppm exposure
5 group, which corresponded to a daily dose of about 2.3 mg/kg bw. This chronic dose is
6 very close to single dose gavage LD₅₀ values for mallards—i.e., 2.27-2.83 mg/kg bw
7 (Hudson et al. 1984). For quail, both Pedersen et al. (2000) and U.S. EPA/OPP (1996d)
8 cite the dietary exposure of 1113.6 ppm and an NOEC, equivalent to about 95.7 mg/kg
9 bw/day. A single dose gavage LD₅₀ is not available in bobwhite quail, but Hudson et al.
10 (1984) report a gavage LD₅₀ of 24.7 mg/kg bw in Japanese quail.

11
12 All of the above comparisons involving the acute, subchronic, and reproductive studies in
13 birds support the assumption that longer-term exposures to acutely nontoxic doses of
14 strychnine are unlikely to cause adverse effects. As discussed further in Section 4.1.2.2.3
15 and illustrated in Figure 14, the reproduction study in mallards (Pedersen et al. 2000) is
16 the only study that suggests a potential for increasing toxicity with an increasing duration
17 of exposure. In this reproduction study, the dietary concentration of 68.9 ppm is
18 classified as an LOEC based on signs of neurotoxicity in some adult birds. In the 28-day
19 subchronic study in mallards (Sterner et al. 1998), however, no signs of neurotoxicity
20 were noted at a dietary concentration of 91.8 ppm.

21 ***3.1.6. Effects on Nervous System***

22 The hazard identification for the neurotoxicity of strychnine is self-evident. As detailed
23 in Section 3.1.2, strychnine is a direct neurotoxin and the mechanism of neurotoxicity is
24 well characterized and extensively documented. As detailed in Section 3.1.4, exposures
25 to acutely toxic doses of strychnine result in signs of neurotoxicity ranging from
26 hyperactivity to convulsions, respiratory failure, and death. The potential neurotoxic
27 action of chronic exposures to acutely sub-toxic doses of strychnine, however, cannot be
28 assessed (Section 3.1.5).

29 ***3.1.7. Effects on Immune System***

30 There are various methods for assessing the effects of chemical exposure on immune
31 responses, including assays of antibody-antigen reactions, changes in the activity of
32 specific types of lymphoid cells, and assessments of changes in the susceptibility of
33 exposed animals to resist infection from pathogens or proliferation of tumors.
34 Nevertheless, the body of literature on strychnine does not include studies which focus on
35 the immunological effects of strychnine exposure.

36
37 Specific studies regarding the effects of pesticides on immune function are not required
38 for pesticide registration. Accordingly, the U.S. EPA human health risk assessment of
39 strychnine (U.S. EPA/OPP 1966c) does not address the potential effects of strychnine
40 exposure on immune function, and aside from noting that data are not available, neither
41 does the WHO review (IPCS 1989).

42
43 In the only study regarding dermal effects in humans exposed to strychnine,
44 hypersensitivity of the legs is noted (Greene and Meatherall 2001). This study is

1 discussed further in Section 3.1.11.1. The underlying mechanism for the hypersensitivity
2 is not clear but it appears to involve a neurological effect, characteristic of strychnine,
3 rather than an immunological effect.

4 **3.1.8. Effects on Endocrine System**

5 Mechanistic studies on estrogen, androgen, or thyroid hormone systems (i.e., assessments
6 on hormone availability, hormone receptor binding, or post-receptor processing) are used
7 most often to assess the direct effects of chemicals on endocrine function. Also, changes
8 in the structure of major endocrine glands (i.e., the adrenal, hypothalamus, pancreas,
9 parathyroid, pituitary, thyroid, ovary, and testis) may be indicative of effects on the
10 endocrine system. Disruption of the endocrine system during development may give rise
11 to effects on the reproductive system that are expressed only after maturation.
12 Consequently, multigeneration exposure is recommended for the toxicological
13 assessment of suspected endocrine disruptors. The endocrine system is also important in
14 normal growth and development, and changes in growth may be indicative of endocrine
15 disruption.

16
17 In the 28-day oral toxicity study in which rats were exposed to neurotoxic doses of
18 strychnine, Seidl and Zbinden (1982) report there were no histopathological changes in
19 the adrenals, pancreas, pituitary gland, thyroid gland, or testes. This is the only available
20 information regarding the potential effects of strychnine exposure on endocrine function.
21 As noted in Section 3.1.9, there are no multigeneration reproduction studies involving
22 exposure to strychnine. This endpoint is not addressed by U.S. EPA/OPP (1996a,b;
23 1998a), and the WHO review on strychnine (IPCS 1989) only mentions that these data
24 are lacking.

25 **3.1.9. Reproductive and Developmental Effects**

26 Typically, U.S. EPA/OPP requires both developmental studies to assess the potential of a
27 pesticide to cause birth defects or other adverse effects on the fetus or very young
28 animals and reproduction studies to determine whether exposing one or more generations
29 of the test animal to a pesticide will interfere with normal reproductive processes.
30

31 Neither developmental nor reproductive toxicity studies in mammals are discussed in the
32 EPA risk assessments on strychnine (U.S. EPA/OPP 1996a,c). While not specifically
33 noted in U.S. EPA/OPP (1996a, Appendix B), these studies appear to have been waived
34 in conjunction with the decision by U.S. EPA/OPP to consider only acute endpoints in
35 their assessment of strychnine. This decision is discussed in some detail in Section 3.1.5
36 of the current Forest Service risk assessment. There are, however, registrant-submitted
37 reproduction studies in birds, some of which note adverse effects in some species
38 (Section 4.1.2.2).
39

40 Neither multigeneration studies nor reproductive toxicity studies in mammals were found
41 in the open literature on strychnine; however, there are two developmental studies
42 (Bovet-Nitti and Bovet 1959; Garcia-Alcocer et al. 2005).
43

1 The early study by Bovet-Nitti and Bovet (1959) provides little experimental detail. A
2 group of eight pregnant rats were given a single intramuscular dose of strychnine at 0.5
3 mg/kg bw on Day 4 of pregnancy. No effects were noted in six of the eight animals or
4 their offspring; however, all the offspring of one rat died. The time of death is specified
5 only as at birth or within 24 hours of birth. In the other rat, gestation was *terminated*.
6 The termination is described only as a ...*failure to implant, degeneration of blastocyst, or*
7 *hormonal disturbance* (Bovet-Nitti and Bovet 1959, Table 1, last footnote). The study
8 results specific to strychnine are not further discussed in the publication.

9
10 The more recent study by Garcia-Alcocer et al. (2005) is similar to a standard
11 developmental study. Groups of five pregnant rats were given a single gavage dose of
12 2.5, 5.0, or 8.0 mg/kg strychnine on Day 8 of gestation. Two of the five rats in the high
13 dose group had seizures and were discarded. Although there is no tabular summary of
14 the data, the study notes a dose-related increase in the number of abnormal embryos (see
15 Figure 3B in publication). Most of the abnormalities were characterized as neural tube
16 defects. It is not clear if the dose-response relationship is based on the total number of
17 abnormal offspring per dose group or the number of abnormal offspring per litter.

18 **3.1.10. Carcinogenicity and Mutagenicity**

19 Bioassays for carcinogenicity involve chronic exposures that encompass a substantial
20 proportion of an animal's lifespan. As noted in Section 3.1.5, no information is available
21 on the chronic toxicity of strychnine.

22
23 Carcinogenicity is often associated with the ability of a chemical to cause genetic
24 damage. The only assay of strychnine for genetic damage is the *in vitro* study by
25 Hoffmann et al. (1987a,b) using two strains of *Salmonella typhimurium*. Concentrations
26 of 1.5-6 mM (\approx 500-2000 mg/L) induced a concentration dependant increase in genetic
27 duplications in one of the two strains. As noted in Section 3.1.4, strychnine
28 concentrations in plasma that exceed approximately 2.2 mg/L appear to be lethal in
29 humans even with aggressive medical intervention. Given the very high concentrations
30 of strychnine used in the *in vitro* assay by Hoffmann et al. (1987a,b), the direct relevance
31 of this study to an *in vivo* cancer assessment of strychnine appears to be marginal.

32 **3.1.11. Irritation and Sensitization (Effects on the Skin and Eyes)**

33 **3.1.11.1. Skin Irritation**

34 One standard study regarding potential dermal irritation in rabbits after exposure to
35 technical grade strychnine was submitted to U.S. EPA/OPP (Cerven 1988a,b). The study
36 found no dermal irritation or signs of toxicity, and U.S. EPA/OPP (1996a,c) classifies
37 strychnine as Category IV—the lowest category for dermal irritancy in the EPA ranking
38 scheme. The low ranking for dermal irritation is consistent with the report from Greene
39 and Meatherall (2001) in which there was no evidence of dermal irritation in a woman
40 who had direct dermal contact with a solution of strychnine.

1 **3.1.11.2. Skin Sensitization**

2 The open literature on strychnine does not include skin sensitization studies; moreover,
3 no such studies were submitted to the EPA (U.S. EPA/OPP 1998a,c). Although skin
4 sensitization studies in guinea pigs are typically required by U.S. EPA/OPP for pesticide
5 registration, the EPA human health risk assessment conducted in support of the
6 reregistration of strychnine notes that no skin sensitization study was submitted but that
7 such a study is required (U.S. EPA/OPP 1998c, p. 3). This requirement, however, is not
8 listed in the RED for strychnine (U.S. EPA/OPP 1998a, Appendix B); consequently, it is
9 not clear whether the EPA waived the requirement for a skin sensitization study for
10 strychnine.

11 **3.1.11.3. Ocular Effects**

12 As with dermal irritation and other acute endpoints, U.S. EPA/OPP has standard test
13 requirements for eye irritation and a classification scheme for eye irritation which ranges
14 from Category I (most irritating) to Category IV (least irritating). One standard study on
15 ocular effects (Cerven 1988c,d) was submitted to U.S. EPA/OPP. In this study, technical
16 grade strychnine was inserted in one eye of each of six rabbits. Four of the six animals
17 died, and slight irritation (Category III) was noted in the two surviving animals. While
18 the eye irritancy was not severe, the mortality in four of the six treated animals led to the
19 classification of strychnine as a Category I eye irritant. The dose involved in this study
20 was about 52 mg/kg bw. As discussed further in Section 4.1.2.1, a dose of 52 mg/kg bw
21 is substantially above the acutely lethal dose in mammals; furthermore, mortality in the
22 eye irritation study appears to reflect rapid absorption of strychnine through the eye.

23 **3.1.12. Systemic Toxic Effects from Dermal Exposure**

24 As noted in Section 3.1.3.2 (Dermal Absorption), U.S. EPA/OPP (1996a,c) concludes
25 that strychnine is poorly absorbed from the skin, based on the dermal toxicity study in
26 rats in which neither mortality nor signs of toxicity were noted at a limit dose of 2000
27 mg/kg bw (Cerven 1988e,f). Accordingly, U.S. EPA/OPP (1996a) classifies the acute
28 dermal toxicity of strychnine as Category III, the second lowest ranking in the EPA
29 classification system. U.S. EPA/OPP (1996a, p. 12) does indicate that a 21-day dermal
30 toxicity study should be conducted to confirm this classification.

31
32 Concern for the dermal toxicity of strychnine is enhanced substantially by the Greene and
33 Meatherall (2001) case report. As discussed in Section 3.1.3.2 and summarized in
34 Appendix 1, Greene and Meatherall (2001) report an incident in which a woman was
35 dermally exposed to a solution ($\approx 2\%$ or 20,000 mg/L) of strychnine. While not
36 specifically noted in Greene and Meatherall (2001), this concentration substantially
37 exceeds the solubility of strychnine in water (143 mg/L in Table 1). Thus, it seems
38 plausible to suggest that the strychnine was in some type of organic solvent or aqueous
39 suspension. Exposure was limited to the palm of one hand, and the duration of exposure
40 is given as 30 minutes. The woman remained asymptomatic for about 12 hours. At this
41 time, the woman experienced shaking and spasms of the arms and legs which developed
42 further to muscular pain and hypersensitivity to touch. All of these effects are symptoms
43 of systemic toxicity consistent with the effects of strychnine. The latency period is
44 atypical. As noted in Section 3.1.3.1, strychnine is generally considered to be a fast

1 acting poison. The longer latency period, however, is consistent with the slower
2 anticipated rate of dermal absorption, relative to other routes of exposure. The longer
3 latency might also have been due to the nature of the solvent or liquid suspension that
4 contained the strychnine.

5 ***3.1.13. Inhalation Exposure***

6 No studies are available on the acute inhalation toxicity of strychnine. The EPA human
7 health risk assessment conducted in support of the reregistration of strychnine notes that
8 an acute inhalation study is required (U.S. EPA/OPP 1998c, p. 3). In the RED for
9 strychnine, however, EPA/OPP (1998a, p. 12) explicitly notes that the requirement for an
10 inhalation study was waived but that strychnine is classified as Toxicity Category I
11 *...based on the high toxicity by other routes of exposure*. Given the lack of plausible
12 inhalation exposures to strychnine in the normal use of this compound as a rodenticide,
13 this approach to the inhalation hazards of strychnine is reasonable.

14 ***3.1.14. Inerts and Adjuvants***

15 Inerts and adjuvants are not a substantial concern for strychnine. As discussed in
16 Section 2.2, strychnine is formulated in grain, either oats or sorghum. Additives used in
17 strychnine formulations are essentially food stuffs intended to make the formulation more
18 palatable to pocket gophers—e.g., molasses, salt, glycerin, and soda (Evans et al. 1990).
19 Given the high toxicity of strychnine and the clear hazards that exposure to strychnine
20 can present, there is no basis for asserting that inerts or adjuvants that might be added to
21 strychnine formulations are likely to present significant or substantial hazards, relative to
22 the toxicity of strychnine itself.

23 ***3.1.15. Impurities and Metabolites***

24 As discussed in Section 3.1.3.1, the metabolites of strychnine appear to be less toxic than
25 strychnine itself (Bohlin et al. 1975; Davis and Yeh 1969; Iskander and Bohlin 1978;
26 Sandberg and Kristianson 1970).

27
28 Technical grade strychnine undoubtedly contains some impurities. To some extent,
29 concern for impurities in technical grade strychnine is reduced by the fact that the
30 existing toxicity studies on strychnine were conducted with the technical grade product
31 itself or the technical grade product in formulation. Thus, if toxic impurities are present
32 in the technical grade product, they are likely to be encompassed by the available toxicity
33 studies on the technical grade product.

34
35 As with inerts and adjuvants, there is little doubt that the biological activity of the
36 impurities in and metabolites of technical grade strychnine do not pose a substantial risk,
37 relative to the toxicity of strychnine itself.

38 ***3.1.16. Toxicological Interactions***

39 As discussed in Section 3.1.3.1, strychnine is metabolized and detoxified by mixed-
40 function oxidase, also known as the cytochrome P450 enzyme system. As discussed in
41 Section 3.1.4.1, information is available indicating that compounds that inhibit mixed-

1 function oxidase (e.g., SKF-525A and n-ocylamine) will enhance the toxicity of
2 strychnine.

3
4 The cytochrome P450 enzyme system consists of many different specific enzymes
5 (referred to as isozymes) involved in the metabolism of many naturally occurring and
6 man-made chemicals (Coon 2005; Lynch and Price 2007). It is likely that co-
7 administration of chemicals which are metabolized by the same P450 isozyme(s)
8 involved in the metabolism of strychnine would enhance the toxicity of strychnine by
9 competing with strychnine for metabolism. In other words, if strychnine is administered
10 along with another compound that is metabolized by the same P450 isozyme, the
11 presence of the second compound could decrease the rate of strychnine metabolism and
12 thus prolong the toxic effect of strychnine.

13
14 Another characteristic of the cytochrome P450 enzyme system is that isozymes are often
15 induced by the substrates that they can metabolize. The induction of P450 enzymes by
16 strychnine is suggested by the *acquired tolerance* to strychnine in several pocket gophers
17 and the loss of tolerance when exposure to strychnine was discontinued (Section 3.1.3.1).
18 Kato et al. (1963) demonstrated that pre-treatment of rats and guinea pigs with
19 phenobarbital, a classic inducer of P450, will increase the metabolism of strychnine. It
20 seems reasonable to suggest that pre-exposures to chemicals that induce the isozyme(s)
21 responsible for the metabolism of strychnine could reduce the toxicity of strychnine by
22 enhancing detoxification.

23
24 Finally, many chemicals can damage the liver resulting in a diminished capacity of the
25 liver to metabolize and hence detoxify strychnine. Consequently, pre-exposure and
26 perhaps simultaneous exposure to such compounds could enhance the toxicity of
27 strychnine. These suppositions are speculative but only modestly so. While little
28 information is available on the interactions of strychnine with other chemicals, the
29 patterns in chemical interactions relating to the cytochrome P450 enzyme system are well
30 documented and well understood (e.g., Yang 1994). Nonetheless, the nature of the
31 toxicological interaction will depend on the doses and timing of exposures.
32 Consequently, the interactions that might be expected under certain circumstance are
33 difficult to predict.

34

1 **3.2. EXPOSURE ASSESSMENT**

2 **3.2.1. Overview**

3 Details of the exposure assessments for workers and members of the general public are
4 provided in the EXCEL workbook that accompanies this risk assessment. These
5 workbooks contain sets of worksheets on strychnine that provide details for each
6 exposure scenario discussed in this risk assessment. In addition, the workbooks include
7 summary worksheets for worker exposures (Worksheet E01) and exposures to members
8 of the general public (Worksheet E02). The documentation for these worksheets is
9 provided in SERA (2009a).

10
11 U.S. EPA/OPP (1996a,c) declines to quantify exposures for workers because no directly
12 relevant data are available on below-ground hand baiting or burrow builder applications
13 of strychnine. The current Forest Service risk assessment, on the other hand, develops
14 worker exposure rates for hand baiting, based on the U.S. EPA Pesticide Handler's
15 Exposure Database (PHED Task Force 1995). While worker exposure rates for burrow
16 builder applications cannot be developed based on the available data, it is reasonable to
17 assert that burrow builder applications are likely to involve lesser worker exposure rates
18 in units of mg/kg bw per lb a.i./handled. Thus, the rates for hand baiting are applied to
19 burrow builder applications. Because burrow builder applications entail a worker
20 handling greater amounts of strychnine per day than workers involved in hand baiting,
21 the estimated exposures for workers involved in burrow builder applications—i.e., about
22 0.006 (0.0003 to 0.015 mg/kg bw)—are substantially greater than those for workers
23 involved in hand baiting—i.e., about 0.0003 (0.00007 to 0.001 mg/kg bw). Accidental
24 exposures focus on contaminated gloves.

25
26 The proper use of gloves has a major impact on potential worker exposures. The U.S.
27 EPA/OPP (1996a, p. 15) requires the use of *chemical resistant gloves*. The product
28 labels identified in the conduct of this risk assessment, however, specify waterproof
29 gloves is more than 3 pounds of bait are handled. Otherwise, only cotton gloves are
30 required. Thus, there is some uncertainty in which types of gloves would be worn during
31 applications of strychnine treated baits. Consequently, three contaminated glove
32 scenarios are given for three different periods of exposure—i.e., 1 minute, 1 hour, and 1
33 workday. The workday duration is not typical in Forest Service risk assessments and is
34 intended to reflect the potentials for either the improper use of gloves or the use of gloves
35 that might not offer adequate protection.

36
37 Because proper worker hygiene is an important part of the label instructions for
38 strychnine applications, a separate accidental exposure scenario is given for workers who
39 do not follow label directions in terms of washing shortly after strychnine exposures are
40 completed. The accidental exposure scenario of greatest concern involves workers
41 wearing contaminated gloves for the entire day. This exposure scenario, which is
42 equivalent to workers involved in hand baiting without using gloves, leads to estimated
43 exposures of 0.15 (0.08 to 0.3) mg/kg bw.
44

1 For members of the general public, most exposures to strychnine associated with below-
2 ground applications are likely to be insignificant. Based on an extremely conservative
3 assessment of possible concentrations of strychnine in surface water resulting from
4 below-ground applications, the maximum dose is estimated to be 0.005 (0.002 to 0.01)
5 mg/kg bw. The upper bound of this exposure could occur either as the result of an
6 accidental spill or as the result of an atypical loss of strychnine treated bait from a below-
7 ground application in a treated field to an adjacent stream. Although uncommon,
8 contamination of stream water associated with below-ground applications of strychnine is
9 documented in Forest Service monitoring studies. Except for these cases of uncommonly
10 high concentrations of strychnine in stream water, exposure levels of strychnine are likely
11 to be below 0.00002 mg/kg bw for the general public.

12
13 One extreme accidental exposure scenario is developed for a young child who might
14 consume bait accidentally deposited on the surface of the ground, which is unanticipated
15 and has not been observed in below-ground applications of strychnine. Nonetheless, this
16 unprecedented exposure scenario leads to estimated doses of about 3 (2 to 4) mg/kg bw.

17 **3.2.2. Workers**

18 **3.2.2.1. General Exposures**

19 **3.2.2.1.1. Hand Baiting**

20 As described in SERA (2007a), worker exposure rates in Forest Service risk assessments
21 are expressed in units of mg of absorbed dose per kilogram of body weight per pound of
22 chemical handled. Based on analyses of several different pesticides using a variety of
23 application methods, default exposure rates are normally estimated for three different
24 types of applications: directed foliar (backpack), boom spray (hydraulic ground spray),
25 and aerial. A summary of these exposure rates is given in Table 7. Because these
26 exposure rates are based on biomonitoring studies, they represent composites of all routes
27 of exposure. None of these exposure rates, however, are directly applicable to hand
28 baiting or burrow builder applications of strychnine, as discussed in Section 2.2.

29
30 As also discussed in SERA (2007a), the U.S. EPA's Office of Pesticide Programs
31 employs a deposition based approach using data from the Pesticide Handler's Exposure
32 Database (PHED Task Force 1995). In this type of model, the exposure dose is estimated
33 from air concentrations and skin deposition monitoring data. These estimates can be used
34 to calculate the absorbed dose when estimates are available on absorption rates for
35 inhalation and dermal exposure. As summarized in Table 8, standard exposure rates for
36 37 application methods have been developed (Keigwin 1998). These application rates
37 involve three different types of dermal exposures—no clothing, a single layer of clothing
38 with no gloves, and a single layer of clothing with gloves—as well as estimates of
39 inhalation exposure. Note that Scenario 17 in Table 8 applies to *Granular bait dispersed*
40 *by hand*, however, the bait used in this scenario is an insecticide, not a rodenticide. The
41 Pesticide Handlers Exposure Database (PHED) contains data on insecticides, fungicides,
42 herbicides, fumigants, and plant growth regulators but does not contain any data on
43 rodenticide applications (PHED 1995).

1 In the absence of worker exposure studies on bait applications of strychnine, the EPA
2 (EPA/OPP 1996a,c) declined to provide a quantitative exposure assessment for workers:

3
4 *The Agency recognizes four primary exposure scenarios for*
5 *strychnine: (1) mixing and applying bait formulations; (2) mixing*
6 *and applying paste formulations; (3) mixing/loading for burrow*
7 *building applications; and, (4) applying baits using burrow builder*
8 *equipment. However, due to the absence of exposure data which*
9 *would be adequate for the Agency to estimate exposures for these*
10 *four scenarios, a quantified exposure assessment could not be*
11 *conducted.*

12
13 *While EPA does not have, nor is it requiring, appropriate data for*
14 *reliable exposure estimates from the use of strychnine products,*
15 *the Agency believes the minimal poisoning incident information*
16 *suggests there are exposures. ... Also, through this document,*
17 *labeling is being required to include the use of personal protective*
18 *equipment (chemical resistant gloves, protective eyewear, and a*
19 *dust mask).*

20 U.S. EPA/OPP (1996a, p. 15)

21
22 The meaning of the above statement concerning *poisoning incident information*
23 suggesting that *there are exposures* is not clear. U.S. EPA/OPP (1996a, p. 12-13)
24 discusses poisoning incidents, and the EPA discussion is consistent with the discussion of
25 human poisoning incidents in Section 3.1.4.1 and Appendix 1 of the current Forest
26 Service risk assessment. No reports of human poisonings associated with the application
27 of strychnine in gopher control or other rodenticide uses were encountered in the
28 strychnine literature. Nonetheless, the statement that worker exposures to strychnine will
29 occur during baiting applications of strychnine is self-evident.

30
31 In the absence of information on worker exposures associated with applications of
32 strychnine or other similar rodenticides, the decision rendered in U.S. EPA/OPP
33 (1996a,c) not to quantify worker exposure is clearly justified. Nonetheless, if exposures
34 cannot be quantified, risks cannot be quantified, and the failure to quantify risks limits the
35 purpose of the risk assessment. As an exploratory effort, a worker exposure assessment
36 can be based on a conservative weight-of-evidence approach using both standard Forest
37 Service worker exposure rates as well as worker exposure rates from the Pesticide
38 Exposure Handlers Database (PHED).

39
40 As summarized in Table 7, the highest worker exposure rate used in Forest Service risk
41 assessments is for backpack applications—i.e., 0.003 (0.0003 to 0.01) mg/kg bw per lb
42 a.i. handled. The backpack application exposure rates are based on studies of directed
43 foliar applications of liquid formulations of herbicides in which inadvertent exposures
44 may occur over a large proportion of the body of the worker. While these exposure rates
45 are not obviously relevant to applications of granular formulations, the Forest Service
46 risk assessment on hexazinone (SERA 2005, Section 3.2.2.1) analyzes a worker exposure

1 study of belly grinder applications of a granular formulation of hexazinone and derives an
2 absorbed dose rate of 0.0033 (0.0016 to 0.0068) mg/kg bw per lb a.i. handled, strikingly
3 similar to the exposure rates for backpack applications of liquid formulations of
4 pesticides. Belly grinder applications, like backpack applications, involve procedures in
5 which exposures may occur over a substantial proportion of the workers body. In plain
6 language, backpack and belly grinder applications can be messy. Intuitively, it seems
7 reasonable to suggest that worker exposure rates associated with these types of
8 applications are likely to be greater than exposures of workers to strychnine during hand
9 baiting of gopher holes.

10
11 As summarized in Table 8, standard exposure rates from the Pesticide Handlers Exposure
12 Database (PHED) are developed for backpack applications of liquid formulations
13 (Scenario 34) and belly grinder applications of granular formulations (Scenario 30). Note
14 that the PHED rates are given in units of mg pesticide per lb a.i. handled rather than
15 mg/kg body weight per lb a.i. handled, which are used in Forest Service worker exposure
16 rates. Also unlike Forest Service exposure rates, the standard PHED rates are given as
17 single values (i.e., point estimates) rather than a range of values. Notwithstanding these
18 differences, the similarity of the exposure rates for backpack and belly grinder
19 applications, discussed above, is apparent in the PHED rates as well. The PHED rates for
20 belly grinder applications are higher than those for backpack applications by a factor of
21 about 4 based on total dermal exposure and a factor of about 2 based on inhalation
22 exposure. Given the variability in the backpack rates based on absorbed dose—i.e.,
23 0.0003-0.01 mg/kg bw per lb a.i. handled or a factor of about 33—the PHED rates for
24 belly grinder and backpack applications are not substantially different.

25
26 In contrast, the PHED exposure rates for *Granular bait dispersed by hand* are extremely
27 high—i.e., 71 mg/lb a.i. handled for total dermal exposure with gloves and 0.47 mg/lb a.i.
28 handled for inhalation exposure. Relative to the PHED rates for backpack and belly
29 grinder applications, the rate for granular bait is a factor of about 8- 28 higher based on
30 dermal exposure and about 8-16 higher based on inhalation exposure. Relative to all of
31 the standard PHED scenarios summarized in Table 8, the rates for granular bait
32 applications are the second highest based on dermal exposures (with gloves) and the fifth
33 highest based on inhalation exposures. Thus, while the exposure rates given in the PHED
34 scenarios for granular baits dispersed by hand may not be directly applicable to hand
35 applications of strychnine to gopher dens, these rates are among the highest exposure
36 rates in the PHED scenarios and may serve as a plausible but conservative basis for
37 estimating worker exposures during hand baiting of gopher dens.

38
39 The algorithm for implementing the PHED exposure rates for *Granular bait dispersed by*
40 *hand* are given in Worksheet C01a of the EXCEL workbook that accompanies this risk
41 assessment.

42
43 Note that worksheet C01a is based on the use of a 0.5% bait formulation. As discussed in
44 Section 2 and summarized in Table 3, 0.5% formulations of strychnine are the
45 formulations to be used most commonly in Forest Service programs. One formulation,
46 Wilco Gopher Getter Restricted Use Bait, contains 1.8% strychnine. If a worker were to

1 apply the 1.8% formulation in the same manner as the 0.5% formulation, the amount of
2 strychnine would be greater by a factor of 3.6 [$1.8\% \div 0.5\%$]. This use of a 1.8%
3 formulation would linearly increase the estimated exposure and consequent risk. A
4 separate worksheet for the use of a 1.8% formulation is not used. Instead, the increased
5 exposure is addressed quantitatively in Worksheet E02, as discussed further in the risk
6 characterization for workers (Section 3.4.2).

7
8 Because the PHED exposure rates are given as mg a.i./lb a.i. handled, an estimate is
9 needed of the amount of bait that a worker will handle in 1 day. For hand baiting gopher
10 burrows, the amount of bait a worker will handle appears to be highly variable. The
11 Forest Service estimates that workers may apply between 1 and 15 pounds of bait
12 (Prudhomme 2010). The lower end of the range is very close to the estimate from the
13 field study by Fagerstone et al. (1980), in which two crews took 6 days to apply
14 strychnine treated bait at a rate of 1 kg/ha to two sites with a surface area of 8 hectares
15 each. Thus, a total of 16 kg of formulation was handled over a 6-day period by two
16 crews, which is equivalent to about 3 lbs per day per crew [$16 \text{ kg} \times 2.2 \text{ lb/kg} \div (6 \text{ days} \times$
17 $2 \text{ crews}) \approx 2.933$]. Fagerstone et al. (1980) does not specify the number of individuals in
18 each crew. Making the conservative assumption of two individuals per crew, each
19 individual handled about 1.5 lbs formulation/day.

20
21 Substantially higher amounts of strychnine use are reported in the study by Wood (1965)
22 on hand baiting of rodent dens. This report indicates that 100 pounds of bait was applied
23 in 28 man-hours. This is equivalent to about 3.6 pounds of bait per hour. Assuming a 7-
24 (6- to 8-hour) day for application, the amount handled per hour is about 25.2 (21.6 to
25 28.8) pounds of formulation per day. Notably, however, the Wood (1965) study involved
26 den applications for the control of kangaroo rats. From the description of the application
27 method by Wood (1965)—i.e., manually placing one teaspoon of strychnine into the top
28 of each rat den—it seems likely that the amounts of strychnine handled in this study
29 would be somewhat higher than the amounts that might be handled in the apparently
30 more labor intensive hand baiting of gopher burrows.

31
32 For the current Forest Service risk assessment, the assumption is made that a worker
33 involved in hand baiting gopher dens will handle 8 (1 to 15) pounds per day. The lower
34 and upper bounds are based on the estimates from Prudhomme (2010), and the central
35 estimate is taken as the arithmetic mean of the range. These amounts are entered into
36 Worksheet A01 and are multiplied by the proportion of strychnine in the formulation—
37 e.g., 0.005 for a 0.5% formulation a worker will handle 0.04 (0.005 to 0.075) lbs a.i./day.
38 These values are included by link to Worksheet C01a in the area labeled **Amnt**. The
39 consequences of workers handling greater or lesser amounts of formulation or using a
40 more concentrated formulation are discussed in the risk characterization for workers
41 (Section 3.4.2).

42
43 The amount deposited on the skin of worker is based on the PHED dermal exposure rate
44 of 71 mg a.i./lb a.i. handled—i.e., dermal rates with the use of chemically resistant
45 gloves. As noted above, U.S. EPA/OPP (1996a, p. 15) requires the use of chemically
46 resistant gloves. The 71 mg/lb is the dermal exposure rate and not the absorbed dose rate.

1 In Worksheets C01a, the absorbed dermal dose is calculated using the first-order dermal
2 absorption rates, as discussed in Section 3.1.3.2.

3
4 Note that an 8-hour exposure period is considered. This period is used under the
5 assumption that workers will shower at the end of the work day to effectively remove any
6 residual exposure to strychnine dust from the bait grain. Nonetheless, the RED for
7 strychnine (U.S. EPA/OPP 1996a, p. 33) as well as all product labels for strychnine
8 contains the following language:

9
10 *Users should remove clothing immediately if pesticide gets*
11 *inside. Then wash thoroughly and put on clean clothing.*

12
13 *Users should remove PPE immediately after handling this*
14 *product. Wash the outside of gloves before removing. As*
15 *soon as possible, wash thoroughly and change into clean*
16 *clothing.*

17
18 Poor personal hygiene—i.e., failure to wash thoroughly—is considered further as an
19 accidental exposure scenario in the following subsection.

20
21 The inhalation exposure rate of 0.47 mg/lb handled is used without adjustment. This is
22 standard practice in EPA exposure assessments using PHED in which 100% absorption is
23 considered for the inhalation route. Notably, in Worksheet C01a, the dermal absorbed
24 dose accounts for about 60-90% of the total absorbed dose. This is consistent with
25 general observations on the predominance of dermal exposure for workers applying
26 pesticides (e.g., Ecobichon 1998; van Hemmen 1992) as well as observations on the
27 significance of dermal exposures in granular applications of hexazinone discussed above
28 (SERA 2005).

29
30 As noted above, the standard worker exposure rate for backpack applications of liquid
31 formulations is 0.003 (0.0003 to 0.01) mg/kg bw per lb a.i. handled. For comparison, the
32 worker exposure rate derived in Worksheets C01a is equivalent to 0.034 (0.018 to 0.074)
33 mg/kg bw/day per lb a.i. handled. Thus, the worker exposure rate derived for bait
34 applications relative to backpack applications is about a factor of 10 higher based on the
35 central estimates and a factor of about 7 higher based on the upper bounds. In the
36 absence of any more directly relevant data on worker exposures during hand baiting with
37 strychnine, it seems plausible that the worker exposure rates of 0.034 (0.018 to 0.074)
38 mg/kg bw/day per lb a.i. handled derived from the PHED exposure estimates for granular
39 hand baiting are conservative—i.e., the rates are likely to overestimate exposures.

40
41 Note that the PHED-based worker exposure rates of 0.034 (0.018 to 0.074) mg/kg bw/day
42 per lb a.i. handled is given to 2 significant digits rather than the typical approach used in
43 Forest Service risk assessments in which worker exposure rates are expressed with only
44 one significant digit – e.g., is 0.003 (0.0003 to 0.01) mg/kg bw per lb a.i. handled as
45 discussed above. The use of two significant digits for the exposure rates based on PHED
46 is not intended to reflect a greater level of accuracy in the PHED rates. The two digit

1 level of significance simply reflects the convention typically used by the U.S. EPA/OPP
2 in which exposure rates are expressed using two significant digits (e.g., Keigwin 1998).

3 **3.2.2.1.2. Burrow Builder Applications**

4 As discussed in Section 2.3 and illustrated in Figure 1, strychnine may also be applied
5 using a mechanical burrow builder (Andelt and Case 1995; Case and Jasch 1994; Iowa
6 State University 1992; Oregon State University 2009; Virchow et al. 2003). Because
7 burrow builders are tractor-towed devices, the nature of worker exposure as well as the
8 amount of strychnine that a worker might handle could differ substantially from hand
9 baiting.

10
11 Burrow builder applications will typically involve the use of greater amounts of bait by
12 an individual applicator than will hand baiting. The most detailed description of a
13 burrow builder application is given by Hegdal and Gatz (1976). In this field study, three
14 burrow builders were used to treat 662 hectares (about 1636 acres) over an 8-day period
15 for 14 hours per day. Thus, the average hourly treatment rate was about 5 acres per hour
16 [$1636 \text{ acres} \div (3 \text{ burrow builders} \times 8 \text{ days} \times 14 \text{ hours/day}) \approx 4.86 \text{ acres/hour}$]. Thus, based
17 on a typical 7- (6- to 8-) hour workday, an applicator could treat about 35 (30-40) acres
18 per day. At a typical application rate of 1 lb formulation per acre, an individual worker
19 would handle 35 (30-40) pounds per day.

20
21 The applicability of the worker exposure rates derived for hand baiting to burrow builder
22 applications is questionable. During the loading process, in which the bait formulation is
23 placed into a large container attached to the top of the burrow builder apparatus, it is
24 plausible that a worker may be subject to greater inhalation exposure than would occur
25 during hand baiting. The product labels, however, require a worker to wear a dust
26 filtering respirator when loading more than 3 lbs. of formulation into a mechanical device
27 such as a burrow builder. As discussed by Keigwin (1998), the use of a dust/mist
28 respirator should reduce inhalation exposures by a factor of 80%. During the application
29 process, the worker will be on a tractor above the level of the burrow builder and will pull
30 the burrow builder device from the rear of the tractor. Consequently, it seems reasonable
31 to suppose that the worker exposure rate using a burrow builder will be less than that of a
32 worker involved in hand-baiting. This supposition is supported by the PHED estimates
33 for solid broadcast spreaders with open cabins (Scenario 15 in Table 8), which are far less
34 than the exposure rates associated with granular bait dispersed by hand (Scenario 17 in
35 Table 8).

36
37 Unlike the case with hand baiting, however, PHED does not provide exposure estimates
38 that can be clearly related to mechanical bait applications. As discussed in the previous
39 subsection, the PHED exposure estimates for hand baiting are substantially higher than
40 exposure estimates for other manual granular applications (i.e., Scenarios 15, 16, 30, and
41 31). Consequently, it is not clear that using exposure rates from PHED for other
42 mechanical granular applications is sufficiently protective. Thus, for burrow builder
43 applications, the current Forest Service risk assessment uses worker exposure rates which
44 are identical to those used for hand baiting.
45

1 In the EXCEL workbook that accompanies this risk assessment, a custom worksheet,
2 C01a-BB, is included for burrow builder applications. This worksheet is identical to
3 C01a for hand baiting, except that the amount of formulation handled is taken as 35 (30
4 to 40) pounds per day based on the study by Hegdal and Gatz (1976). Thus, the amount
5 handled by a worker is entered manually into Worksheet C01a-BB as 0.175 (0.15 to 0.2)
6 lbs a.i. /day.

7 **3.2.2.2. Accidental Exposures**

8 Two types of accidental exposure scenarios are considered: contamination of gloves with
9 strychnine and the failure to follow prudent personal hygiene practices after completing
10 applications of strychnine. Although the latter type of exposure may be better viewed as
11 a misapplication rather than an accidental event, it is considered in this section on
12 accidental exposures because the failure to follow proper hygiene practices is a
13 substantial deviation from label instructions. In other words, failure to follow prudent
14 personal hygiene practices is not an expected event.

15
16 Contaminated glove scenarios are typically included in Forest Service risk assessments
17 involving liquid formulations (SERA 2007a). For granular formulations, no standard
18 methods for estimating exposure are available. Nonetheless, dust from strychnine treated
19 bait on the surface of the skin might be regarded as analogous to exposure to a neat
20 (undiluted) solution. For such exposures, the EPA recommends using the solubility of
21 the compound in water as an approximation of the chemical concentration on the surface
22 of the skin. The apparent rationale for this approach is that the amount of the chemical
23 on the surface of the skin will saturate the pore water of the skin, and the factor limiting
24 the chemical concentration in pore water will be the water solubility of the chemical. As
25 indicated in Table 1, the water solubility of strychnine is 143 mg/L (Tomlin 2001), which
26 is equivalent to 0.143 mg/ml. Thus, accidental exposures to gloves contaminated with
27 strychnine dust are considered equivalent to dermal exposures to a saturated aqueous
28 solution of strychnine.

29
30 The contaminated glove scenario encompasses three exposure periods: 1 minute
31 (Worksheet C02a), 1 hour (Worksheet C02b) and 8 hours (Worksheet C02c). The first
32 two duration periods are standard in Forest Service risk assessments. The 8-hour period
33 of exposure is included to illustrate the consequences of a worker applying strychnine
34 over the course of a day with grossly contaminated gloves—i.e., equivalent to handling
35 strychnine without using gloves. Because the concentration of strychnine is considered
36 constant—i.e., at the water solubility—zero-order kinetics are used with the estimates of
37 dermal permeability (K_p in cm/hr) as discussed in Section 3.1.3.2.

38
39 The other type of quasi-accidental exposure involves the failure of the worker to wash
40 after applications of strychnine are complete. As noted in Section 3.2.2.1, the product
41 labels for strychnine instruct workers *...to wash thoroughly and change into clean*
42 *clothing* as soon as possible after completing applications. For general or expected
43 exposures in Section 3.2.2.1 and Worksheet C01a, the exposure duration is assumed to be
44 8 hours. If a worker does not change into clean clothing and wash, the functional
45 exposure period could be longer. Worksheet C01b implements this scenario by assuming

1 a functional exposure period of 24 hours. This may be grossly conservative because the
2 underlying scenario involves the worker not only failing to wash but also not changing
3 clothes for a 16-hour period post application.
4

5 On the other hand, concern may be expressed for the efficacy for washing. As discussed
6 in SERA (2007a), dermal absorption is a complex process in which the binding of
7 chemicals to various constituents of the skin can result in both lag periods as well as
8 reservoir effects. This is clearly illustrated in the study by Greene and Meatherall (2001)
9 in which the individual washed in a very short period of time after dermal contact but did
10 not develop symptoms for several hours. As noted in Section 3.1.12, however, this
11 exposure involved a liquid solution of strychnine. Based on the reported concentration of
12 strychnine in the solution ($\approx 2\%$), it seems likely that the solution consisted of an organic
13 solvent. Thus, it is reasonable to suppose that the strychnine penetrated into the skin and
14 that most of the strychnine was not effectively removed by washing. For bait
15 formulations, however, the skin of the worker will be contaminated with dust that
16 contains strychnine. While some residual skin contamination may remain after washing,
17 most of the strychnine will be on the surface of the skin in the form of dust, and it seems
18 likely that washing will effectively remove most of the strychnine and substantially
19 diminish exposure.

20 **3.2.3. General Public**

21 **3.2.3.1. General Considerations**

22 **3.2.3.1.1. Likelihood and Magnitude of Exposure**

23 Because strychnine is limited to underground applications only, the likelihood of any
24 significant exposures to members of the general public is remote. U.S. EPA/OPP
25 (1996a,c) proposes no quantitative exposure assessments for members of the general
26 public in terms of dietary exposures or exposures associated with contaminated drinking
27 water. In addition, the EPA ecological risk assessment (U.S. EPA/OPP 1996d)
28 specifically notes:

29
30 *With the present below-ground use pattern, strychnine is not likely*
31 *to reach ground or surface water. The material is incorporated*
32 *into baits, which are largely, if not exclusively, applied as a below-*
33 *ground spot treatment to specific burrows occupied by pocket*
34 *gophers, and not as a broadcast or general treatment.*

35
36 *For these reasons, the Agency's concerns are minimal, in that soil*
37 *and ground or surface water do not seem likely to be materially*
38 *affected by below-ground use of strychnine.*

39 – U.S. EPA/OPP 1996a, p. 8

40 **3.2.3.1.2. Summary of Assessments**

41 Notwithstanding the above statement concerning the implausibility of significant
42 strychnine exposures to members of the general public, Forest Service risk assessments
43 routinely include accidental exposure scenarios as well as a general set of extremely

1 conservative non-accidental exposure scenarios. With some exceptions, these scenarios
2 are used in the current Forest Service risk assessment. Three sets of standard exposures
3 which are not considered for strychnine involve the consumption of contaminated
4 vegetation, dermal contact with contaminated vegetation, and direct spray scenarios.

5
6 As discussed further below (Section 3.2.3.6), strychnine is not applied to vegetation and
7 does not appear to translocate from soil to vegetation. Thus, scenarios for the
8 consumption of or dermal contact with contaminated vegetation are not relevant.

9 Similarly, strychnine is not broadcast. While some bizarre scenarios might be
10 constructed for dermal contact with the bait, they would not be instructive or of
11 substantial use in this risk assessment. Section designations for these excluded scenarios
12 are given below as a matter of convenience for individuals who regularly use many
13 different Forest Service risk assessments—i.e., the section designations in all Forest
14 Service risk assessments are consistent or nearly so.

15
16 Despite the low potential for strychnine contamination of surface water based on Gleams-
17 Driver modeling, Forest Service monitoring data indicate that surface water
18 contamination is possible. Thus, all standard exposure scenarios, both accidental and
19 non-accidental, involving exposures to contaminated water are considered. One exposure
20 scenario not usually considered in Forest Service risk assessment involves the direct
21 consumption of bait by a small child. This is an admittedly extreme exposure scenario
22 developed as a replacement for the equally extreme scenario concerning the direct spray
23 of a naked child, included in most Forest Service risk assessments.

24
25 The exposure scenarios developed for the general public are summarized in Worksheet
26 E03 of the EXCEL workbook that accompanies this risk assessment. As with the worker
27 exposure scenarios, details about the assumptions and calculations used in these
28 assessments are given in a series of worksheets, D01 to D08b, in this EXCEL workbook.

29 ***3.2.3.2. Consumption of Bait by a Child***

30 This scenario concerns the accidental consumption of strychnine treated bait by a child,
31 and is included in the current risk assessment as a replacement for the equally extreme
32 scenario that takes into account the direct spray of a young child with a pesticide solution
33 (SERA 2007a, Section 3.2.3.2). The scenario concerning the accidental consumption of
34 strychnine treated bait by a child is detailed in Worksheet D01 and is quite simple. The
35 scenario assumes that a young child ingests a mouthful of strychnine treated bait. The
36 amount of bait consumed is taken as 8.2 (5.5 to 10.9) grams, based on the estimated
37 volume of a mouthful for a young (13.5 kg) child—i.e., 8.2 (5.5 to 10.9) mL (Ratnapalan
38 et al. 2003). Obviously, the estimated bait consumption is somewhat arbitrary. Volumes
39 of half of a mouthful, two mouthfuls, or any number of other amounts could be used.
40 The scenario is intended to illustrate the consequences of a child consuming a substantial
41 but plausible amount of bait.

42
43 The probability of this scenario is low, given that strychnine gopher bait is applied below
44 ground. As described in Section 3.2.2.1.1, each burrow hole is baited with about 3.7
45 grams of formulation. Thus, the mouthful of bait used in this scenario would be

1 equivalent to the amount used to bait approximately 2-3 burrow holes. Nonetheless,
2 burrow builder applications of strychnine may result in inadvertent surface contamination
3 due to burrow collapse or incidental spills above ground during burrow builder
4 applications (Hegdal and Gatz 1976; Smallwood 1999; USDA/APHIS 1994). Other
5 types of accidental soil surface contamination during hand baiting are possible. In the
6 event of accidental or incidental soil surface contamination, it is reasonable to assume
7 that a young child might consume treated bait. For instance, Savage et al. (1971) report
8 the consumption of toxic amounts of contaminated rice by a young child.

9 ***3.2.3.3. Dermal Exposure from Contaminated Vegetation***

10 Scenarios involving dermal contact with contaminated vegetation are based on data from
11 applications to vegetation. These scenarios are not relevant to subsurface applications of
12 strychnine.

13 ***3.2.3.4. Contaminated Water***

14 ***3.2.3.4.1. Accidental Spill***

15 The accidental spill scenario is presented for the acute consumption of contaminated
16 water after an accidental spill into a small pond (0.25 acres in surface area and 1 meter
17 deep). This scenario is dominated by arbitrary variability, and the specific assumptions
18 used will generally overestimate exposure. The actual concentrations in the water would
19 depend heavily on the amount of compound spilled, the size of the water body into which
20 it is spilled, the time at which water consumption occurs relative to the time of the spill,
21 and the amount of contaminated water consumed. Because this scenario is based on the
22 assumption that exposure occurs shortly after the spill, no dissipation or degradation is
23 considered.

24
25 All Forest Service risk assessments consider some type of accidental spill scenarios. For
26 applications involving a solution of either a granular or liquid formulation, the accidental
27 spill scenarios are generally based on spills of a field solution, specifically 100 (20-200)
28 gallons of the pesticide after dilution to the concentration recommended for application.
29 This scenario is obviously not relevant to strychnine. For granular formulations that are
30 not pre-mixed prior to application, the typical assumption is that 40 (16-80) pounds of the
31 active ingredient are spilled into the small pond. For both the liquid and granular
32 applications, the amounts spilled are intended to represent a batch of material that might
33 be assembled in a single place and subsequently spilled into a small body of water.
34 While these assumptions may be reasonable for most herbicides and some insecticides
35 which are applied to relatively large areas, these amounts do not seem plausible for
36 strychnine.

37
38 Most strychnine applications will involve a 0.5% formulation. Thus, a spill of 40 (16-80)
39 pounds of the active ingredient would involve 8000 (3200-16,000) pounds of a
40 formulation—i.e., 2 tons with a range from 1.6 to 8 tons. For hand baiting, this amount is
41 clearly inappropriate. As discussed in Section 3.2.2.1.1, hand baiting gopher burrows is
42 labor intensive; consequently, an individual worker is expected to apply only about 1.5
43 (0.75-3) lbs of formulation per day. For burrow builder applications, a single worker

1 could apply approximately 35 (30-40) pounds of formulation per day, as discussed in
2 Section 3.2.2.1.2. Although these amounts are greater than the amounts likely to be
3 applied by a single worker involved in hand baiting, they are much less than the 8000
4 (3200- 16,000) pounds of formulation required for a spill of 40 (16-80) pounds of the
5 active ingredient.
6

7 In the current Forest Service risk assessment on strychnine, an accidental spill is based on
8 30 (20-40) pounds of a 0.5% formulation, which corresponds to 0.15 (0.1-0.2) pounds of
9 strychnine. The amount of spilled formulation is within the range of amounts that
10 correspond to a load of a burrow builder. The specific amounts, however, are also
11 influenced by monitoring data provided by the Forest Service. As discussed further in
12 Section 3.2.3.4.5, the Forest Service reported two instances in which strychnine was
13 detected in water at concentrations ranging from 13 to 23 ppb after strychnine
14 applications of approximately 0.33 lb a.i./acre. For a 0.5% formulation, this corresponds
15 to an application rate of about 0.00165 lb a.i./acre. At an application rate of 1 lb
16 formulation per acre (0.005 lb a.i./acre), the expected corresponding concentrations in
17 water would be about 40-70 ppb.
18

19 As detailed in Worksheet D05 of the EXCEL workbooks that accompany this risk
20 assessment and are summarized in Table 9, the accidental spill scenario described above
21 leads to surface water concentrations of about 68 (45 to 91) ppb. Thus, this accidental
22 spill scenario is used in the current risk assessment to encompass both plausible
23 accidental spills as well as strychnine concentrations in water, albeit atypically, after
24 below-ground applications of strychnine treated baits.

25 ***3.2.3.4.2. Accidental Direct Spray/drift for a Pond or Stream***

26 Forest Service risk assessments concerned with broadcast applications of pesticides
27 typically include estimates of surface water contamination associated with drift of the
28 pesticide into small ponds and small streams (SERA 2007a, Section 3.2.3.4). These types
29 of estimates are not appropriate for below-ground applications of strychnine and are not
30 included in this current Forest Service risk assessment of strychnine.

31 ***3.2.3.4.3. GLEAMS Modeling***

32 As noted in Section 3.2.3.1.1, U.S. EPA/OPP (1996a,c,d) did not conduct exposure
33 assessments for strychnine concentrations in surface water because below-ground
34 applications of strychnine do not appear to present a substantial risk for surface water or
35 ground water contamination. This is a reasonable supposition; however, Forest Service
36 monitoring data (Section 3.2.3.4.5) report detectable concentrations of strychnine in
37 stream water (i.e., about 13-23 ppb) after below-ground applications of strychnine.
38 Consequently, standard Gleams-Driver modeling was conducted for strychnine to explore
39 the plausibility that the monitored concentrations of strychnine were associated with
40 normal transport processes—i.e., runoff, sediment loss, and loss due to percolation.
41

1 Gleams-Driver is a program developed for the Forest Service to estimate expected peak
2 and longer-term pesticide concentrations in surface water—i.e., ponds, lakes, or streams.
3 Gleams-Driver serves as a preprocessor and postprocessor for GLEAMS (Knisel and
4 Davis 2000). GLEAMS is a field scale model developed by the USDA/ARS and has
5 been used for many years in Forest Service and other USDA risk assessments
6 (SERA 2007b).

7
8 Table 10 summarizes the chemical-specific values used in GLEAMS. The notes to
9 Table 10 indicate the sources of the chemical-specific values used in the GLEAMS
10 modeling effort, most of which are based on the physical and chemical properties and the
11 environmental fate data on strychnine summarized in Table 1.

12
13 GLEAMS and, hence, Gleams-Driver are not designed to model below-ground
14 applications of bait. GLEAMS does have an input parameter for depth of
15 incorporation—i.e., the depth in which the chemical is incorporated into soil during the
16 application process—as well as soil injection. Deeper incorporation or injection depths
17 will reduce the amount of the chemical available for loss due to runoff or sediment
18 transport. In below-ground applications of strychnine, however, the chemical is not
19 incorporated or injected into the soil; instead, it is placed beneath the soil surface in the
20 burrow. Exploratory Gleams-Driver simulations indicate that incorporation depths of 8-
21 10 inches result in extremely low strychnine concentrations in surface water—i.e., far
22 below the 13-23 ppb concentrations reported by the Forest Service. Consequently, as an
23 extremely conservative approach to estimate upper bound concentrations, all Gleams-
24 Driver simulations were conducted as surface simulations with a minimal depth of
25 incorporation (i.e., 1 cm). The sole intent of this approach was to estimate worst-case
26 concentrations.

27
28 The locations selected for modeling include a total of nine sites, as summarized in
29 Table 11. As discussed in SERA (2007b), these locations are standard sites for the
30 application of Gleams-Driver in Forest Service risk assessments and are intended to
31 represent combinations of precipitation (dry, average, and wet) and temperature (hot,
32 temperate, and cool). For each site, Gleams-Driver was used to simulate 100 applications
33 of strychnine at a unit application rate of 1 lb/acre, and each of the simulations was
34 followed for a period of more than 1½ years post application.

35
36 Details of the results for the Gleams-Driver runs are provided in Appendix 6. A
37 summary of the results for the Gleams-Driver runs are presented in Table 9, along with a
38 summary of the spill scenarios discussed in Section 3.2.3.4.2, other modeling efforts, and
39 monitoring data, discussed further in the following subsections. Note that two sets of
40 values are displayed. The upper set of values in plain (non-bold) type face are the water
41 contamination rates (WCRs) expressed in units of ppb ($\mu\text{g a.i./L}$) at a unit application rate
42 of 1 lb a.i./acre. These WCR values are identical to the concentrations given in Appendix
43 6 and reflect the Gleams-Driver modeling which was conducted at an application rate of
44 1 lb a.i./acre. As discussed in SERA (2007a), Gleams-Driver modeling is typically
45 conducted at an application rate of 1 lb a.i./acre to avoid a loss of numerical precision,
46 because GLEAMS outputs pesticide loss using fixed floating point numbers. Below the

1 WCR values are the corresponding concentrations in surface water expected at an
2 application rate of 1 lb formulation per acre. For a 0.5% formulation, this is equivalent to
3 an application rate of 0.005 lb a.i./acre.
4

5 Note that the peak water contamination rate (WCR) is 25.2 ppb. At an application rate of
6 0.005 lb a.i./acre, the expected peak concentration of strychnine in surface water is 0.071
7 ppb. As discussed further in Section 3.2.3.4.5, this concentration is below the maximum
8 monitored concentration of 23 ppb (Podsiadlo 1998) by a factor of over 300 [$23 \text{ ppb} \div$
9 $0.071 \text{ ppb} \approx 323.9$].

10 **3.2.3.4.4. Other Modeling Efforts**

11 Because of the discrepancies between the Gleams-Driver modeling and the monitoring
12 data from the Forest Service (Podsiadlo 1998), additional modeling was conducted using
13 three surface water models developed by the U.S. EPA: GENEEC (U.S. EPA/OPP
14 2001a), FIRST (U.S. EPA/OPP 2001b), and PRZM/EXAMS (Burns 2006).
15

16 GENEEC is an acronym for Generic Estimated Environmental Concentrations.
17 GENEEC is a very simple (Tier 1) screening model used to estimate plausible upper
18 bound concentrations of pesticides in surface water in a standard farm pond. FIRST is
19 also a screening level model used to estimate concentrations of a pesticide in a standard
20 or index reservoir.
21

22 PRZM/EXAMS is a more sophisticated (Tier 2) model system in which the Pesticide
23 Root Zone Model (PRZM) is linked with the Exposure Analysis Modeling System
24 (EXAMS). PRZM is analogous to GLEAMS in that PRZM is a field scale model which
25 estimates the transport of pesticides in the root zone. The EXAMS model uses the output
26 from PRZM to model the fate of a chemical in a water body, based on standard
27 environmental fate processes—e.g., sorption, hydrolysis, biodegradation, and dispersion.
28 PRZM-EXAMS was run using the EXPRESS interface, Version 1.03.02 (Burns 2006),
29 which is available at <http://www.epa.gov/ceampubl/swater/express/index.html>. The
30 EXPRESS interface accommodates modeling a farm pond and an index reservoir, both of
31 which were modeled for strychnine applications.
32

33 As with GLEAMS and Gleams-Driver, none of the EPA models is designed for below-
34 ground applications to burrows. Consequently, all models were applied assuming surface
35 applications.
36

37 The model inputs used with GENEEC, FIRST, and PRZM-EXAMS were generally
38 identical to those used in the Gleams-Driver modeling (Table 10). GENEEC, FIRST, and
39 PRZM-EXAMS are not designed to accept variable inputs such as those used in the
40 Gleams-Driver modeling for half-lives in aquatic sediment and soil as well as estimates
41 of K_{oc} and K_d . For these parameters, only the central estimates given in Table 10 were
42 used. The EPA models also require inputs not used directly in Gleams-Driver—e.g., the
43 fractional area treated and estimates of photolysis. Thus, EPA default model inputs were
44 used for the fractional area, and photolysis was assumed to be negligible. PRZM-
45 EXAMS requires a large number of site-specific inputs. In the EXPRESS interface, these

1 inputs are encapsulated in model scenarios—i.e., the site specific inputs for a set of
2 specific locations for which EPA has developed site parameters and meteorological
3 inputs. For the current modeling, the Oregon Christmas Tree scenario was selected
4 because this is the only scenario which approximates a forest rather than an agricultural
5 site.

6
7 The results from the EPA models are summarized in Table 9. All of the EPA modeling
8 was done using a unit application rate of 1 lb a.i./acre, and the results are consistent with
9 the Gleams-Driver modeling. The peak concentrations estimated from the Tier 1 models
10 were about 6.5 ppb (GENEEC) and about 19 ppb (FIRST). These concentrations are
11 somewhat higher than the upper bound values from PRZM-EXAMS—i.e., about 5.7 ppb
12 for the index reservoir and 2.1 ppb for the farm pond. This pattern is foreseeable, given
13 that the intent of the Tier 1 models is to provide conservative estimates of concentrations
14 that are likely to overestimate actual concentrations.

15
16 By comparison, the Gleams-Driver modeling resulted in the highest estimates of
17 strychnine concentrations in water—i.e., up to 25.2 ppb at an application rate of 1 lb
18 a.i./acre. Again, this result is to be expected. The concentrations in Table 9 for the
19 Gleams-Driver modeling represent a total of 18 different sets of 100 year simulations
20 based on nine sets of climate data (combinations of dry, moderate, and wet rainfall
21 patterns and warm, temperate, and cool temperatures) in three types of soils (clay, loam,
22 and sand). In addition, the Gleams-Driver data used for strychnine incorporated
23 variability in the estimates of several of the environmental fate parameters for strychnine,
24 as specified in Table 9.

25 **3.2.3.4.5. Monitoring Data**

26 As indicated in U.S. EPA/OPP (2009), monitoring studies on strychnine in water are not
27 published in the open literature on strychnine.

28
29 As summarized in an unpublished report by Podsiadlo (1998), the Forest Service
30 conducted several below-ground applications of strychnine between 1996 and 1997 in
31 areas with various types of streams. The stream descriptions given by Podsiadlo (no
32 date) follow the Class I to Class III categorizations. Class I streams designate streams
33 which contain fish breeding populations for at least part of the year. Class II streams are
34 generally used to designate smaller streams which do not contain fish breeding
35 populations but support communities of other aquatic vertebrates or aquatic invertebrates.
36 Class III streams are smaller, intermittent streams which do not support fish populations.

37
38 Prior to applications in 1996, all streams in the treatment areas were assayed for
39 strychnine to determine the possible presence of strychnine from previous years of
40 application. Following applications, monitoring for strychnine in streams was conducted
41 with a limit of detection of 10 ppb ($\mu\text{g/L}$). While not specifically noted in the summary
42 by Podsiadlo (no date), additional records provided by the Forest Service indicate that 42
43 sites, with a total area of 667 acres, were treated with a total of 468 lbs of bait, at an
44 average application rate of about 0.7 lb/acre.

45

1 Strychnine was not detected in any of the larger (Class I or Class II streams) for which
2 100-foot buffers were used—i.e., no strychnine was applied within 100 feet of the
3 streams. For applications near the smaller Class III streams, a 50-foot buffer was used.
4 Strychnine was detected in two Class III streams. In one stream, strychnine was detected
5 at 13 ppb. This stream was below a 48-acre area that had been treated with 15.4 lbs of
6 bait (0.32 lb/acre). In the other stream, strychnine was detected at 23 ppb. This stream
7 was below three areas totaling 14 acres which had been treated with a total of 4.8 lbs of
8 bait (0.34 lb/acre).

9
10 As discussed in the two previous subsections and summarized in Table 9, the maximum
11 anticipated concentration of strychnine in stream water after broadcast surface
12 applications is 25.2 ppb per lb a.i. applied per acre. For a 0.5% formulation applied at a
13 rate of about 0.33 lb formulation per acre, the expected peak concentration in stream
14 water would be about 0.04 ppb [0.33 lb formulation/acre x 0.005 x 25.2 ppb per lb a.i. =
15 0.04148]. This expected peak concentration is below the monitored concentrations of 13
16 and 23 ppb by factors of about 325 and 575, respectively.

17
18 In discussing the two detections of strychnine, Podsiadlo (no date) notes that no further
19 detections of strychnine were found in stream water through 2001. The discrepancies
20 between the expected and monitored strychnine concentrations at the two sites suggest
21 that these concentrations were associated with an event other than normal processes of
22 runoff loss, sediment loss, and percolation.

23
24 For example, GLEAMS provides outputs of chemical concentrations in runoff water—
25 i.e., chemical concentrations water which is running directly off the field. As indicated in
26 Table 5 of Appendix 5 (Gleams-Driver simulations), the highest peak concentration in
27 stream water is modeled for a site with high rainfall and low temperature. The upper
28 bound and central estimates of strychnine in runoff water for this site are illustrated in
29 Figure 4 for a surface application of strychnine at 1 lb a.i./acre. The upper bound of the
30 peak concentration is about 0.092 mg/L, equivalent to 92 µg/L or 92 ppb. Thus, at an
31 application rate of 0.33 lb formulation/acre (equivalent to about 0.00165 a.i./acre for a
32 0.5% formulation), the estimated peak concentration in runoff water is about 0.5 ppb. In
33 other words, the concentrations of strychnine in the sites reported by Podsiadlo (no
34 date)—i.e., 13 and 23 ppb—are higher than the maximum expected concentrations of
35 strychnine in runoff water by factors of about 26-46.

36
37 Flow rates for the streams from the sites covered in the Podsiadlo (no date) report are not
38 available. The report notes, however, that heavy rains occurred following the
39 applications of strychnine at the sites associated with detections of strychnine in streams.
40 Based on the Gleams-Driver modeling, average and maximum flow rates for the stream
41 with the maximum modeled concentration of strychnine are about 2-4 million L/day. The
42 amount of formulation applied to the site with the 13 ppb detection was 15.4 lbs, which is
43 equivalent to about 0.077 lb a.i. for a 0.5% formulation, which is in turn equivalent to
44 about 35,000 mg [0.077 lb x 453,600 mg/lb = 34,972.2 mg]. If 35,000 mg of a chemical
45 is released over the course of a day into a stream flowing at a rate of 2-4 million L/day,
46 the concentrations in the stream would be about 8.75-17.5 ppb [35,000 mg ÷ 2,000,000 to

1 4,000,000 L = 0.00875 to 0.0175 mg/L]. These concentrations are in the range of the 13
2 ppb detection.

3
4 It is not reasonable, however, to assume that all applied strychnine would run off to a
5 stream over the course of a single day. Nonetheless, transient water concentrations
6 similar to those reported in the Forest Service monitoring might occur during the course
7 of 1 day if a much smaller fraction of the applied strychnine was discharged to the
8 stream. For example, if 2% of a 35,000 mg application of strychnine were washed into a
9 stream with a flow rate of 2 million L/day in a brief period of time (e.g., 30 minutes), the
10 strychnine concentration in the stream over that period would be about 17 ppb [$0.02 \times$
11 $35,000 \text{ mg} \div (0.5 \text{ hr} \times 2,000,000 \text{ L}/24 \text{ h}) \approx 0.0168 \text{ mg/L}$]. In the absence of additional
12 information, it is possible to infer that the monitoring data reported by Podsiadlo (no
13 date) are associated with such an atypical event.

14 **3.2.3.4.6. Concentrations in Water Used for Risk Assessment**

15 Table 11 summarizes the surface water concentrations of strychnine used in this risk
16 assessment. The concentrations are specified as water contamination rates (WCRs)—i.e.,
17 the concentrations in water expected at a normalized application rate of 1 lb a.i./acre,
18 converted to units of ppm or mg/L per lb a.i./acre. In Table 9, units of exposure are
19 expressed as ppb or $\mu\text{g/L}$, as a matter of convenience. In Table 11, however, ppb is
20 converted to ppm because ppm and mg/L are the units of measure used in the EXCEL
21 workbook for contaminated water exposure scenarios in both the human health and
22 ecological risk assessments. The water contamination rates are entered in Worksheet
23 B04 in each of the EXCEL workbooks that accompany this risk assessment. The values
24 in Worksheet B04 are linked to the appropriate scenario-specific worksheets in the
25 EXCEL workbooks.

26
27 The surface water concentrations summarized in Table 11 are based on Gleams-Driver
28 simulations as well as estimates from the models developed by the U.S. EPA (Table 9).
29 The central estimate of the peak water contamination rate for strychnine is 0.002 per lb
30 a.i./acre, based on the central estimate from the stream modeling using Gleams-Driver
31 (1.82 ppb) rounded to 2 ppb. The lower bound of the peak water contamination rate is
32 0.0007 mg/L per lb a.i./acre, which is the approximate lower bound of the
33 PRZM/EXAMS simulations of the farm pond (0.684 ppb in Table 9) and the lower bound
34 from Gleams-Driver for stream concentrations in wet and warm locations with loam soils
35 (0.7 ppb in Appendix 6, Table 5). The upper bound of the peak water contamination rate
36 is taken as 0.025 mg/L per lb a.i./acre, based on the upper bound of the concentration of
37 strychnine in streams modeled using Gleams-Driver—i.e., 25.2 ppb, as summarized in
38 Table 9 and detailed in Appendix 6 (Table 5).

39
40 The longer-term values for the water contamination rates (WCRs) are taken from the
41 results of the EPA models discussed in Section 3.2.3.4.4. This approach is taken because
42 the EPA models estimate higher long-term concentrations, relative to Gleams-Driver.
43 The upper bound of the longer-term WRC is taken at 0.0028 mg/L, based on the
44 estimated annual average concentration from the FIRST model—i.e., 2.8 ppb at an
45 application of 1 lb/acre. The central estimate and lower bound of the longer-term WCR

1 values are 0.001 and 0.0007 mg/L, respectively, based on the results of the
2 PRZM/EXAMS model for the index reservoir—i.e., the central estimate of 0.975 ppb, or
3 about 1 ppb, and the upper bound of 0.712 ppb at an application rate of 1 lb/acre.
4

5 Notably, the lower bound longer-term WCR, 0.0007 mg/L, is identical to the lower
6 bound of the acute WCR. Similarly, the central estimate of acute WCR, 0.002 mg/L, is
7 only modestly higher than the central estimate of the longer-term WCR, 0.001 mg/L.
8 These similarities between the acute and longer-term WCR values reflect the use of the
9 most conservative models, which are different for peak concentrations (Gleams-Driver)
10 and longer-term concentrations (the EPA models).
11

12 All of the estimates of the WCR values for strychnine in surface water are admittedly
13 problematic. As detailed in Sections 3.2.3.4.3 and 3.2.3.4.4, all of the modeled estimates
14 are based on surface applications of strychnine. In other words, the models assume that
15 technical grade strychnine is applied by broadcast application. This, of course, will not
16 be the case in Forest Service programs. Strychnine will be applied as grain bait to below-
17 ground burrows. Given that the strychnine is formulated as bait which is applied below
18 ground, the expected surface water concentrations are likely to be negligible, and this is
19 basically the position taken by U.S. EPA/OPP (Section 3.2.3.1.1). This position has
20 merit, and arguably the WCR values given in Table 11 may grossly overestimate surface
21 water concentrations of strychnine from below-ground applications.
22

23 On the other hand, as discussed in Section 3.2.3.4.5, the Forest Service has monitoring
24 data indicating that strychnine concentrations were 13-23 ppb at some locations after
25 below-ground applications of about 0.33 lb formulation/acre. Assuming a 0.5%
26 formulation results in an application rate of 0.00165 lb a.i./acre, and the strychnine
27 concentrations of 13-23 ppb monitored by the Forest Service correspond to water
28 contamination rates of about 8-14 mg/L per lb a.i./acre [0.013 to 23 mg/L \div 0.00165 lb
29 a.i./acre \approx 7.879 to 13.939 mg/L per lb a.i./acre].
30

31 The unresolved discrepancies between the monitoring data and the modeling may reflect
32 site-specific factors such as the depth of the soil layer, the porosity of the soil, and
33 macropore flow. As discussed in Section 3.2.3.4.5, the concentrations monitored by the
34 Forest Service are not predictable, based on the most extreme estimates from several very
35 conservative surface water models. In addition, detectable concentrations of strychnine
36 were noted at only two of 40 sites in the 1996 applications; moreover, in subsequent
37 years there have been no reports of detectable concentrations of strychnine in surface
38 water, which supports the notion that these monitored concentrations are clearly atypical.
39

40 As discussed above, the WCR values used in the current Forest Service risk assessment
41 are not adjusted to account for the atypically high concentrations noted in the Forest
42 Service monitoring report. Instead, as discussed in Section 3.2.3.4.1, the accidental spill
43 scenario is structured so that the estimated surface water concentrations associated with
44 the accidental spill encompass the Forest Service monitoring report. This is not to
45 suggest that the concentrations of 13 and 23 ppb noted in the Forest Service report
46 (Podsiadlo no date) are associated with any apparent accidental event or misapplication.

1 While these concentrations are atypical, the concentrations cannot be regarded as
2 accidental. Thus, in the current Forest Service risk assessment on strychnine, the
3 accidental spill scenario is also used to encompass unusual (but not accidental) events
4 that result in atypically high concentrations of strychnine in surface water, as discussed
5 further in the risk characterization for both human health (Section 3.4) and ecological
6 effects (Section 4.4).

7 **3.2.3.5. Oral Exposure from Contaminated Fish**

8 This risk assessment includes three sets of exposure scenarios for the consumption of
9 contaminated fish, and each set includes separate estimates for the general population and
10 subsistence populations. These exposure scenarios consist of one set for acute exposures
11 following an accidental spill (Worksheets D03a and D03b), another set for acute
12 exposures based on expected peak concentrations (Worksheets D06a and D06b), and the
13 third set for chronic exposures based on estimates of longer-term concentrations in water
14 (Worksheets D08a and D08b). The two worksheets in each of these three sets are
15 intended to account for different rates of wild-caught fish consumption in both general
16 and subsistence populations. Details of exposure scenarios involving the consumption of
17 contaminated fish are provided in Section 3.2.3.5 of SERA (2007a).

18
19 The concentration of strychnine in water following an accidental spill is based on the
20 accidental spill scenario detailed in Section 3.2.3.4.1. As noted in the previous
21 subsection, the current risk assessment on strychnine is atypical in that the accidental spill
22 scenario is also used to assess risks associated with rare (but non-accidental) events in
23 which unusually high concentrations of strychnine have been noted in surface water after
24 below-ground applications of strychnine.

25
26 The concentration of the pesticide in fish (C_F) is taken as the product of the concentration
27 of the chemical in water (C_W) and the bioconcentration factor (BCF):

$$28 \quad C_{Fish_{mg/kg}} = C_{W_{mg/L}} \times BCF_{L/kg}$$

29
30
31 Bioconcentration is measured as the ratio of the concentration in the organism to the
32 concentration in the water. For example, if the concentration in the organism is 5 mg/kg
33 and the concentration in the water is 1 mg/L, the BCF is 5 L/kg [5 mg/kg ÷ 1 mg/L]. As
34 with most absorption processes, bioconcentration depends initially on the duration of
35 exposure but eventually reaches steady state.

36
37 The open literature on strychnine does not include detailed bioconcentration studies.
38 Furthermore, the EPA waived the standard requirement for a bioconcentration study in
39 fish, because there is no expectation that below ground applications of strychnine will
40 lead to substantial concentrations of pesticide in surface water (U.S. EPA/OPP
41 1996d, p. 8)

42
43 As with dermal absorption rates (Section 3.1.3.2), various algorithms are available for
44 estimating the BCF based on the structure and physical properties of a chemical. One
45 such program, EPI Suite, was developed by the EPA (Meylan and Howard 2007). As

1 summarized in Table 1, the BCF for strychnine, as estimated by EPI Suite, is 8.718.
2 HSDB (2010) provides a somewhat lower estimate of 2. For the current risk assessment,
3 the EPI Suite estimate is rounded to 8.7 and used for all exposure scenarios involving the
4 consumption of contaminated fish.

5 ***3.2.3.6. Dermal Exposure from Swimming in Contaminated Water***

6 To assess the potential risks associated with swimming in contaminated water, an
7 exposure assessment is developed for a young woman swimming in surface water for 1
8 hour (Worksheet D04).

9
10 Conceptually and computationally, this exposure scenario is virtually identical to the
11 contaminated gloves scenario used for workers (Section 3.2.2.2)—i.e., a portion of the
12 body is immersed in an aqueous solution of the compound at a fixed concentration for a
13 fixed period of time. The major differences in the two scenarios involve the pesticide
14 concentration in water and the exposed surface area of the body. For the worker wearing
15 contaminated gloves, the assumption is made that both hands are exposed. For the
16 swimmer, the assumption is made that the entire surface area of the body is exposed to
17 the expected peak concentrations in ambient water (Table 11). Also, like the exposure
18 scenario involving contaminated gloves, the swimming scenario is conservative in that it
19 assumes zero-order absorption directly from the water to the systemic circulation. While
20 the swimmer will not be immersed for 1 hour, the entire body surface is used both as a
21 conservative approximation and to consider intermittent episodes during which the whole
22 body might be immersed or at least wet.

23
24 The 1-hour period of exposure is somewhat, but not completely, arbitrary, given that
25 longer periods of exposure are plausible. Nonetheless, the 1-hour period is intended as a
26 unit exposure estimate. In other words, the exposure and consequently the risk will
27 increase or decrease linearly with the duration of exposure, as indicated in Worksheet
28 D04. Thus, a 2-hour exposure would lead to a hazard quotient that is twice as high as
29 that associated with an exposure period of 1 hour. In cases in which this or other similar
30 exposures approach a level of concern, further consideration is given to the duration of
31 exposure in the risk characterization (Section 3.4). For strychnine, the levels of exposure
32 are far below a level of concern.

33 ***3.2.3.6. Oral Exposure from Contaminated Vegetation***

34 Most Forest Service risk assessments as well as risk assessments conducted by the U.S.
35 EPA/OPP typically estimate concentrations of a pesticide in terrestrial vegetation
36 following foliar applications based on empirical relationships developed by Fletcher et al.
37 (1994) between application rates and residues in various types of vegetation. For
38 subsurface applications, however, this type of exposure assessment is not appropriate.

39
40 Because strychnine is applied to the ground, concern could be expressed for
41 concentrations in edible vegetation based on the translocation of strychnine from the
42 ground into the edible portions of a plant. The translocation of strychnine from
43 subsurface applications of bait into alfalfa and apple trees was assayed by Smith (1982).
44 No evidence of strychnine translocation was noted. This finding is consistent with

1 general relationships noted by Bromilow et al. (1990) which suggest that compounds
2 with K_{ow} values of 10,000 (the K_{ow} for strychnine) or greater will not translocate in
3 xylem. Thus, no exposure assessments for the consumption of contaminated vegetation
4 are included in this risk assessment of strychnine.

5
6
7

1 3.3. DOSE-RESPONSE ASSESSMENT

2 3.3.1. Overview

3 The dose-response assessment for strychnine is somewhat unusual. The U.S. EPA Office
4 of Research and Development (U.S. EPA/ORD) derived a chronic RfD for strychnine;
5 however, the RfD is based on a study that typically would not serve as the basis for a
6 chronic RfD—i.e., the duration of the study is not chronic, the study involves very few
7 animals, it is not a well-documented study, and the study does not identify a NOAEL. In
8 addition, the chronic RfD derived by U.S. EPA/ORD does not consider the substantial
9 amount of data on human toxicity.

10
11 The U.S. EPA Office of Pesticide Programs (U.S. EPA/OPP) did not derive an acute or
12 chronic RfD for strychnine, suggesting that there is no need for a chronic RfD because
13 strychnine is not likely to cause cumulative toxicity. The position taken by U.S.
14 EPA/OPP appears to be reasonable and is supported by the American Conference of
15 Governmental Industrial Hygienists (ACGIH). In the absence of an acute RfD or an
16 acceptable chronic RfD, the current Forest Service risk assessment bases both surrogate
17 acute and chronic RfDs on the threshold limit value (TLV) recommended by ACGIH,
18 which has been in effect for more than 50 years. This TLV is equivalent to a dose of 0.02
19 mg/kg bw and is intended to be protective in both acute and longer-term exposures. This
20 TLV is based on human data and is consistent with the information available on the
21 mechanism of action and pharmacokinetics of strychnine.

22
23 Because some of the exposure scenarios for humans exceed the surrogate RfD of 0.02
24 mg/kg bw, dose-severity relationships are considered. These relationships are based
25 exclusively on human data. While any exposure above 0.02 mg/kg bw is regarded as
26 unacceptable, there is little reason to assert that doses of up to 0.1 mg/kg bw will be
27 associated with overt signs of toxicity. Oral doses as low as 1 mg/kg bw, however, are
28 likely to be toxic and could be lethal. Some individuals have survived after consuming
29 much higher oral doses but only with prompt medical care. Oral doses in excess of about
30 25 mg/kg bw are likely to be lethal even with prompt medical care. Dermal exposures
31 appear to be less hazardous; however, this supposition is based dermal absorption rates as
32 well as rates of detoxification and is supported by only a single case report.

33 3.3.2. Acute RfD

34 Acute RfDs are generally intended to represent exposures that are not likely to be harmful
35 so long as the exposure occurs for only a brief period. U.S. EPA/OPP often derives acute
36 RfDs based on developmental studies in which a chemical is administered to a pregnant
37 mammal (typically a rat) for several days during gestation. This approach is typically
38 used because adverse effects observed during such exposures may often be associated
39 with a single dose.

40
41 As noted in Section 3.1.5 and discussed further in the following subsection on the chronic
42 RfD, U.S. EPA/OPP (1996a,c) determined that subchronic and chronic toxicity data are
43 not required and that the human health risk assessment of strychnine should be based on

1 acute toxicity. Nevertheless, U.S. EPA/OPP (1996a,c) does not derive an acute RfD for
2 strychnine, which is troublesome because, in the absence of an acute RfD, risks
3 associated with strychnine exposures cannot be characterized quantitatively.

4
5 Generally, Forest Service risk assessments do not derive RfDs, and, instead, adopt acute
6 and chronic RfDs derived by the EPA. In the absence of an RfD derived by U.S.
7 EPA/OPP, attempts are made to identify comparable values from other offices within
8 EPA and other organizations such as the American Conference of Governmental
9 Industrial Hygienists (ACGIH), World Health Organization (WHO), the Centers for
10 Disease Control (CDC), or the Agency for Toxic Substances and Disease Registry
11 (ATSDR).

12
13 Other than the marginal chronic RfD for strychnine discussed in Section 3.3.3, the only
14 health criterion for strychnine is the TLV of 0.15 mg/m³ (ACGIH 2001). This
15 concentration is intended to represent an inhalation exposure (time-weighted) that is not
16 expected to be toxic over short-term or longer-term occupational exposures. While the
17 TLV is given as an inhalation exposure, it is based on an estimated oral dose of 0.02
18 mg/kg bw/day. This TLV has been in effect since 1957. Up to 1985, ACGIH
19 recommended a short-term exposure limit of 0.45 mg/m³, corresponding to an oral dose
20 of 0.06 mg/kg bw/day. This short-term TLV was withdrawn in 1987 (ACGIH 2001).

21
22 As discussed in Section 3.1.4.1, strychnine doses ranging from 0.02 to 0.1 mg/kg bw/day
23 have been used therapeutically for members of the general public (Hayes 1982; Stannard
24 1969). Aside from the use of strychnine at higher doses in individuals with nonketotic
25 hyperglycinemia (Section 3.1.5.1) and a very brief report by Hale (1909) there are no
26 systematic studies regarding the safety of strychnine as a therapeutic agent in the
27 available literature. Nonetheless, the TLV of 0.15 mg/m³ (0.02 mg/kg bw) does appear to
28 be conservative given that it is based on the lower bound of the range of therapeutic
29 doses.

30
31 For the current Forest Service risk assessment on strychnine, the dose of 0.02 mg/kg
32 bw/day is adopted from the TLV of 0.15 mg/m³, and 0.02 mg/kg bw/day is used as a
33 surrogate acute RfD.

34 **3.3.3. Chronic RfD**

35 The U.S. EPA Office of Research and Development (U.S. EPA/ORD) has developed and
36 maintains a database of RfDs, the Integrated Risk Information System or IRIS
37 (<http://www.epa.gov/iris/>). This effort is distinct from the RfDs developed by the U.S.
38 EPA's Office of Pesticide Programs (U.S. EPA/OPP).

39
40 The IRIS database presents a chronic RfD for strychnine of 0.0003 mg/kg bw/day (U.S.
41 EPA/ORD 1987). As noted in Section 3.1.5.1, this RfD is based on the study by Seidl
42 and Zbinden (1982) in which groups of 12 female rats were given repeated daily doses of
43 2.5 mg/kg bw and groups of 12 male rats were given repeated daily doses of 5 or 10
44 mg/kg bw for 28-days. A NOAEL was not identified. U.S. EPA/ORD (1987) selected
45 the lowest dose tested—2.5 mg/kg bw/day—as a LOAEL/FEL (Frank Effect Level). As

1 discussed in Section 3.1.5.1, one of the rats in this does group died. U.S. EPA/ORD
2 (1987) states that *...no symptoms were exhibited by survivors*. While the EPA discussion
3 does not elaborate on this point, U.S. EPA/ORD (1987) appears to mean that no longer-
4 term signs of toxicity were observed in surviving animals. As noted in Section 3.1.5.1,
5 the paper by Seidl and Zbinden (1982) is not explicit in describing the effects observed in
6 animals shortly after dosing; nonetheless, it appears that signs of acute strychnine toxicity
7 were observed in all exposure groups of animals.

8
9 Because the 2.5 mg/kg bw/day dose is viewed as a LOAEL/FEL, an uncertainty factor of
10 10,000 was used to derive the RfD. The uncertainty factor is a multiple of factors of 10
11 for less than chronic to chronic exposure, animal to human extrapolation, differences in
12 sensitivity in human populations, and the adjustment of a LOAEL/FEL to a NOAEL.
13 U.S. EPA/ORD (1987) expresses reservations with the derivation of this RfD: *In view of*
14 *this concern [the use of a LOAEL/FEL] and the limitations in the database, the derived*
15 *RfD should be viewed as an interim estimate*.

16
17 As discussed in Section 3.1.5, U.S. EPA/OPP (1996a,c) does not consider a chronic RfD
18 or chronic toxicity studies requirements for strychnine, because chronic effects after
19 prolonged exposures to acutely nontoxic doses of strychnine are not likely to occur.
20 Citing the early kinetic study by Hatcher and Eggleston (1918), ACGIH (2001)
21 essentially concurs, indicating that *...there is no evidence of cumulative toxicity*. Note
22 that the term *cumulative toxicity* refers to an increased severity or magnitude of the
23 response to a given daily dose as the duration of exposure increases.

24
25 Unless there is a compelling reason to do otherwise, Forest Service risk assessments
26 adopt RfDs derived by U.S. EPA and generally adopt the most conservative RfD. Thus,
27 the typical approach in a Forest Service risk assessment would be to adopt the 0.0003
28 mg/kg bw/day chronic RfD derived by U.S. EPA/ORD (1987). For strychnine, however,
29 this RfD is not used. The RfD is rejected on the basis that U.S. EPA/ORD (1987) did not
30 consider the substantial data regarding the effects of strychnine exposure in humans and
31 did not consider data on the dose-duration relationships for strychnine. As discussed in
32 some detail in Section 3.1.5 (Subchronic and Chronic Toxicity), the available information
33 on the pharmacokinetics and mechanism of action of strychnine support the
34 interpretations offered by U.S. EPA/OPP (1996a,c) and ACGIH (2001). In addition, the
35 multiple dose studies in both mammals and birds generally support the supposition that
36 serious chronic effects are not likely to occur in longer-term exposures to acutely
37 nontoxic doses of strychnine.

38
39 The current Forest Service risk assessment adopts the general conclusions of U.S.
40 EPA/OPP (1996a,b) and the approach taken by ACGIH (2001). The 0.02 mg/kg bw/day
41 dose which forms the basis of TLV derived by ACGIH (2001) is used both as the
42 surrogate acute RfD and surrogate chronic RfD.

43 **3.3.4. Dose-Severity Relationships**

44 Forest Service risk assessments often attempt to define dose-severity relationships in
45 order to more fully interpret the plausible consequences of exceeding the RfD. Dose-

1 severity relationships are generally based on comparisons of human data to data on
2 experimental animals or systematic patterns in toxicity among various species.
3 Strychnine is somewhat exceptional in that the dose-severity relationships can be based
4 on the substantial information regarding strychnine toxicity to humans (Section 3.1.4.1).

5
6 The proposed dose-severity relationships for strychnine are summarized in Table 12. By
7 definition, no adverse effects are anticipated at or below the surrogate RfD of 0.02 mg/kg
8 bw/day. As discussed in the two previous subsections, this surrogate RfD is applied to
9 both acute and chronic exposures. Given the human experience with strychnine and
10 given that the basis for the surrogate RfD—i.e., the ACGIH TLV—has been in effect for
11 more than half a century, confidence in this toxicity benchmark is reasonably high.

12
13 The next two higher doses in Table 12—i.e., 0.06 and 0.1 mg/kg bw—correspond to HQs
14 of 2 and 5, respectively. These doses are based on the former short-term TLV and the
15 former therapeutic doses for strychnine. The short-term TLV was withdrawn by ACGIH
16 (2001), and strychnine is not currently used as a therapeutic agent. Thus, these doses are
17 not proposed as acceptable levels of exposure. Nonetheless, these doses constitute
18 exposures that were considered acceptable, and there is no indication that these doses
19 would be associated with overt signs of toxicity in humans.

20
21 Doses at or above about 1 mg/kg bw (corresponding to an HQ of 50) may be lethal. As
22 summarized in Table 6, the lowest documented lethal dose in humans is about 1.4 mg/kg
23 bw (Stannard 1967), and a dose of 1 mg/kg bw has been associated with signs of toxicity
24 that were sufficiently severe to warrant medical attention (Boyd et al. 1983).

25 Intermediate doses ranging from 0.2 to greater than 1 mg/kg bw have been used to treat
26 individuals with nonketotic hyperglycinemia. As discussed in Section 3.1.5.1, however,
27 these individuals suffer from an excess of glycine. Consequently, individuals with
28 nonketotic hyperglycinemia may be less sensitive than members of the general
29 population to strychnine.

30
31 Oral exposures to doses greater than 1 mg/kg bw (i.e., HQs >50) should be regarded as
32 potentially lethal, and oral doses of about 25 mg/kg bw are likely to be lethal even in
33 instances in which the individual receives prompt medical care. This assessment,
34 however, may not apply to dermal exposures. The single incident reported by Greene
35 and Meatherall (2001) suggests that dermal exposures are less hazardous than oral
36 exposures. In the incident documented by Greene and Meatherall (2001), a dermal dose
37 of about 10 mg/kg bw was associated with signs of strychnine toxicity but the onset of
38 toxicity was much less rapid than in cases of oral exposure, and the signs of toxicity were
39 not as severe as those that would be expected after comparable oral doses of strychnine.
40 These differences between oral and dermal toxicity appear to reflect the slower
41 absorption of strychnine by the dermal route, relative to the oral route. With slower
42 dermal absorption, the rapid metabolism of strychnine by the liver would tend to diminish
43 the severity of the toxic effects. Nonetheless, this interpretation is based on only a single
44 case report. As discussed further in the risk characterization, some accidental dermal
45 exposures to strychnine lead to HQs at about the level of concern (HQ=1), and the single

1 case report by Greene and Meatherall (2001) does not substantially reduce concern for
2 such exposures.
3

1 3.4. RISK CHARACTERIZATION

2 3.4.1. Overview

3 Under normal and anticipated circumstances, the use of strychnine in below-ground
4 applications for the control of pocket gophers should pose minimal risks to workers and
5 members of the general public.

6
7 Substantial reservations accompany the risk characterization for workers because of the
8 lack of data on the extent of worker exposures during applications of strychnine.
9 Nonetheless, the exposure assessment for workers is based on a set of conservative
10 assumptions which should overestimate exposures. There are also uncertainties in the
11 dose-response assessment for workers. These uncertainties, however, focus on the
12 reasonable supposition that dermal exposures are likely to be less hazardous than oral
13 exposures. Since the dose-response assessment is based on oral toxicity, risks to workers
14 are likely to be overestimated.

15
16 The upper bound hazard quotients for workers involved in the normal and proper
17 application of strychnine are below the level of concern by a factor of about 3 for hand
18 baiting with a 0.5% formulation of strychnine (HQ=0.3) and reach but do not exceed the
19 level of concern for hand baiting with a 1.8% formulation (HQ=1). Accidental dermal
20 exposure scenarios for workers lead to HQs of up to 14. Because strychnine appears to
21 less toxic via dermal exposures and because the HQ is based on an oral toxicity value, it
22 is not clear that the high accidental HQs will lead to observable signs of strychnine
23 toxicity in workers.

24
25 The risk characterization for non-accidental and expected exposures to members of the
26 general public suggests that risks are negligible. The only reservation about the risk
27 characterization involves reports of monitoring data from the Forest Service which
28 indicate that below-ground applications of strychnine may sometimes, albeit rarely, lead
29 to peak concentrations in surface water which rival those expected from an accidental
30 spill or gross misapplication of the pesticide. The data from these monitoring reports
31 cannot be explained. Nonetheless, even in the event of an accidental spill, the HQs are
32 below the level of concern—i.e., the highest HQ associated with contaminated surface
33 water following an accidental spill is 0.5.

34
35 One very extreme accidental exposure scenario, in which a child consumes bait
36 accidentally deposited on the ground surface, is of substantial concern. If such an event
37 were to occur, the child could die, even if the child received reasonably prompt medical
38 care. Thus, during below-ground applications of strychnine, extreme care should be
39 exercised to ensure that accidental spills are prevented, and, if they occur, that thorough
40 remediation measures are taken.

41 3.4.2. Workers

42 As summarized in Worksheet E02, none of the general exposures for workers exceed the
43 level of concern (HQ=1). Note that two sets of HQs are given for hand baiting, one set

1 for the use of a 0.5% formulation—i.e., HQs = 0.07 (0.005 to 0.3)—and another set for
2 the use of a 1.8% formulation—i.e., HQs = 0.2 (0.02 to 1). As discussed in Section
3 3.2.2.1.1, the exposure assessment for hand baiting, most formulations registered for
4 hand baiting consist of a 0.5% formulation of strychnine, but one formulation, Wilco
5 Gopher Getter Restricted Use Bait, consists of the 1.8% formulation. The HQs for hand
6 baiting are linearly related to the concentration of strychnine in the bait. Thus, the HQs
7 for hand baiting using a 1.8% formulation are calculated in Worksheet E02 and the HQs
8 for using a 0.5% formulation multiplied by a factor of 3.6—i.e., $1.8\% \div 0.5\%$.

9
10 Only one set of HQs is given for burrow builder applications—i.e., HQs = 0.3 (0.1 to
11 0.7), and these HQs are based on the use of a 0.5% formulation. Formulations that
12 contain 1.8% strychnine are not registered for burrow builder applications.

13
14 Uncertainties in the HQs for general exposures are due primarily to uncertainties in the
15 exposure assessment. As discussed in Section 3.2.2.1, there are no worker exposure
16 studies involving hand baiting with strychnine, and the EPA declined to conduct a
17 quantitative exposure assessment (U.S. EPA/OPP 1996a,c); hence, there is no
18 quantitative risk characterization for workers involved in strychnine hand baiting for
19 gopher control. The worker exposure assessments for hand baiting given in the current
20 Forest Service risk assessment are based on worker exposure rates from PHED which
21 involve hand baiting using granular insecticide bait. While the use of the PHED
22 exposure rates appears to provide a conservative exposure assessment for workers
23 involved in hand baiting with strychnine formulations for gopher control, the lack of a
24 study on worker exposures to strychnine is a source of uncertainty. Worker exposure
25 rates for burrow builder applications cannot be estimated, and the worker exposure rates
26 for hand baiting are applied to burrow builder applications. Again, this appears to be a
27 conservative assumption but, in the absence of data on worker exposures to strychnine
28 during burrow builder applications, the exposure assessment is tenuous.

29
30 The accidental exposure scenarios for workers lead to HQs that exceed the level of
31 concern, which is not uncommon in risk assessments of pesticides. Greatest concern is
32 associated with the failure to use chemically-resistant gloves effectively. The accidental
33 exposure scenario involving contaminated gloves worn over the course of an entire day
34 leads to HQs of 8 (4 to 14). These HQs are obviously unacceptable and would represent
35 a gross mishandling of strychnine.

36
37 Uncertainties in the risk characterization for the accidental worker exposure scenarios are
38 less dependent on the exposure assessment than on the dose-response assessment. All of
39 the contaminated glove scenarios involve dermal exposure. As discussed in Section 3.3.4
40 and summarized in Table 12, HQs range from 4 to 14, and signs of toxicity might be
41 expected based on information from cases of human poisoning. Nonetheless, the
42 accidental HQs are based on the surrogate RfD of 0.02 mg/kg bw which is, in turn, based
43 on oral rather than dermal exposures. As noted in Section 3.1.12, U.S. EPA/OPP (1996a)
44 does not have substantial concern for the dermal toxicity of strychnine based on the
45 results of an acute dermal toxicity study in rats in which no adverse effects were noted at
46 a dose of 2000 mg/kg bw (Cerven 1988e,f).

1
2 The current Forest Service risk assessment takes a somewhat more conservative approach
3 based on estimates of dermal absorption rates for strychnine (Section 3.1.3.2) as well as
4 the case report by Greene and Meatherall (2001) in which an individual was adversely
5 affected by dermal exposure to strychnine. Nonetheless, Greene and Meatherall (2001)
6 note that their report is the only instance of dermal toxicity in humans in the literature on
7 strychnine. In addition and as discussed in Section 3.3.4, estimates of the dermal dose
8 from this case report clearly suggest that the dermal toxicity of strychnine is less than the
9 oral toxicity of strychnine. This relationship is consistent with the slow rate of dermal
10 absorption relative to oral absorption and the rapid rate of strychnine detoxification by
11 the liver.

12
13 On balance, the risk characterization for workers suggests that workers involved in the
14 application of strychnine for gopher control will not be subject to exposures that exceed
15 the level of concern so long as reasonable worker protection measures, as dictated on the
16 product labels, are taken. The failure to follow label directions could lead to exposures
17 that exceed the level of concern by factors of up to about 14. Nonetheless, it is not clear
18 that these excursions above the surrogate RfD would lead to observable signs of
19 strychnine toxicity in workers. This conclusion is consistent with the lack of reported
20 incidents of occupational poisonings from strychnine.

21 **3.4.3. General Public**

22 The risk characterization for members of the general public is simple and unambiguous.
23 If strychnine is properly used in below-ground baiting for gopher control, exposures and
24 risks to members of the general public are negligible. The highest non-accidental HQ is
25 0.0007, the upper bound for a child consuming surface water. This HQ is below the level
26 of concern by a factor of more than 1400.

27
28 As discussed in Section 3.2.3.4.5, monitoring data from the Forest Service indicate that
29 strychnine concentrations in surface water may reach up to about 25 ppb ($\mu\text{g/L}$) in
30 streams in areas where strychnine is used in below-ground applications. This appears to
31 be a rare event, and these concentrations cannot be explained by normal processes of
32 pesticide loss even under the assumption that strychnine is applied to the soil surface.
33 The accidental spill scenario used in the current Forest Service risk assessment leads to
34 water concentrations ranging from about 45 to 90 ppb, and these concentrations
35 somewhat exceed the peak concentration monitored by the Forest Service. As detailed in
36 Worksheet E04, the upper bound HQ for the accidental scenarios involving the
37 consumption of contaminated water is 0.5, below the level of concern by a factor of 2.
38 Thus, even in the event of an atypical contamination of surface water, there is no
39 indication that exposures to members of the general public consuming surface water will
40 exceed the level of concern (HQ=1).

41
42 The accidental exposure scenario involving a child who consumes bait accidentally
43 spilled onto the surface of the soil is, of course, of substantial concern. The HQs for this
44 extreme accidental exposure scenario are 152 (102 to 202). These HQs correspond to
45 doses of about 2- 4 mg/kg bw. The lowest documented lethal dose for strychnine is 1.4

1 mg/kg bw, and this dose was associated with the death of a child who consumed pills
2 containing strychnine. The child died, despite reasonably prompt medical treatment
3 (Stannard 1969). This scenario requires little interpretation. If a child were to consume a
4 substantial amount of strychnine treated bait, the child might die. This accidental
5 scenario is based on the consumption of 0.5% bait; however, the risk characterization
6 would be essentially the same for any bait containing a higher concentration of
7 strychnine.

8 ***3.4.4. Sensitive Subgroups***

9 As discussed in Section 3.1.3.3, strychnine is detoxified by the liver, specifically by liver
10 mixed-function oxidase. Consequently, individuals with impaired liver function may be
11 at greater risk than other members of the population. Differences in liver function may
12 also be associated with differences in sensitivity between males and females as well as
13 younger and older individuals. As discussed in Section 3.1.4.2.1, studies in rats indicate
14 that females seem to be more sensitive than males to strychnine by factors of about 2-2.5
15 (based on LD₅₀ values), and these differences are associated with higher rates of
16 strychnine metabolism in males, relative to females. As discussed in Section 3.1.4.2.2,
17 young rats appear to be somewhat more sensitive than mature rats to strychnine, and
18 these differences have also been linked to slower rates of strychnine metabolism in the
19 liver of younger rats, relative to mature rats. It is not clear whether the gender- and age-
20 related differences in sensitivity to strychnine observed in rats are relevant to human
21 exposure. The two lowest fatal doses of strychnine in humans both occurred in females
22 (Salm 1952; Stannard 1969); however, the interpretation of the case reports on fatal and
23 non-fatal exposures to strychnine is confounded by differences in medical treatment
24 following intoxication.

25
26 Another atypical subgroup in the human population appears to be individuals with
27 nonketotic hyperglycinemia (Section 3.1.5.1). These individuals, however, appear to be
28 less rather than more sensitive to strychnine due to their atypically high levels of glycine.

1 **3.4.5. Connected Actions**

2 The Council on Environmental Quality (CEQ), which provides the framework for
3 implementing NEPA, defines connected actions (40 CFR 1508.25) as actions which
4 occur in close association with the action of concern; in this case, the use of a pesticide.
5 Actions are considered to be connected if they: (i) Automatically trigger other actions
6 which may require environmental impact statements; (ii) Cannot or will not proceed
7 unless other actions are taken previously or simultaneously, and (iii) Are interdependent
8 parts of a larger action and depend on the larger action for their justification. Within the
9 context of this assessment of strychnine, “connected actions” include actions or the use of
10 other chemicals which are necessary and occur in close association with use of
11 strychnine. Other than milo or oat grain, no connected actions associated with the below-
12 ground use of strychnine for gopher control are apparent.

13 **3.4.6. Cumulative Effects**

14 Cumulative effects may occur with repeated exposures to a pesticide, co-exposures to
15 other chemicals with similar mechanisms of action, or exposures to other agents which
16 may impact the toxicity of the pesticide.

17
18 Repeated exposures to strychnine do not have a substantial impact on the risk
19 characterization. As detailed in Section 3.1.5 (Subchronic or Chronic Systemic Toxic
20 Effects) and discussed further in Section 3.3 (Dose-Response Assessment), repeated
21 exposures to acutely nontoxic doses of strychnine are not likely to result in toxicity. This
22 conclusion is consistent with analyses by U.S. EPA/OPP (1996a,c) and ACGIH (2001).
23 Strychnine is not the only agent that inhibits glycine (e.g., Farroni and McColl 2004);
24 nevertheless, this mechanism of action is uncommon and has not been identified in other
25 pesticides or commonly used agents to which the general public might be exposed.

26
27 Cumulative effects involving compounds that impact the toxicity of strychnine are
28 possible; however, the likelihood and nature of such interactions are unclear. As
29 discussed in Section 3.1.16, strychnine is metabolized by mixed-function oxidase, and
30 there are numerous chemicals that could potentially diminish the toxicity of strychnine
31 (by inducing mixed-function oxidase) or enhance the toxicity of strychnine (by
32 competing with strychnine as a substrate for mixed-function oxidase). The potential
33 significance of such interactions would depend on the doses of strychnine and any other
34 agent to which an individual might be exposed as well as the timing of the exposures.

35
36
37
38

4.0 ECOLOGICAL EFFECTS

4.1. HAZARD IDENTIFICATION

4.1.1. Overview

The effects of strychnine are remarkably consistent across animal species and indicate that strychnine is neurotoxic to mammals, birds, reptiles, insects, amphibians, and fish. The most extensive data are available on mammals and birds.

In mammals, the acute lethal doses and LD₅₀ values in non-dietary oral studies vary by a factor of about 50, ranging from 0.5 mg/kg bw (the approximate lethal dose in bears) to 27 mg/kg bw (the LD₅₀ in nutria). Based on an NOEC of 91.4 mg/kg bw, however, porcupines appear to be the most tolerant species. LD₅₀ values in birds are similar to although somewhat more variable than in mammals, spanning a factor of over 120 and ranging from 0.94 mg/kg bw (snowy owls) to 112 mg/kg bw (California quail). Considerable scatter is apparent in the relationship of body weight to toxicity in both mammals and birds; however, in general, larger animals appear to be more sensitive than smaller animals. Based on species sensitivity distributions (Figures 10 and 13), carnivorous mammals and birds appear to be among the most sensitive species. For birds, water fowl and perching birds (i.e., Passeriformes) are generally more sensitive to strychnine while upland game birds (Galliformes) are much more tolerant.

With respect to strychnine sensitivity, the acute dietary studies in mammals are remarkably consistent and indicate that larger mammals are more sensitive than smaller mammals. Moreover, this conclusion is consistent with the much more varied pattern in non-dietary oral toxicity studies. The dietary oral studies in mammals were conducted on only three species—i.e., pocket gophers, ferrets, and fox—and the correlation may reflect sensitivity of carnivores as much as any allometric relationship. In birds, the acute dietary studies are very scattered, and a clear allometric relationship is not apparent. The data on birds, unlike the data for mammals, include subchronic and longer-term reproduction studies in two species, quail and mallards; what is more, the pattern of sensitivity from these studies is consistent with the pattern observed in acute gavage studies: mallards (waterfowl) are much more sensitive than quail (upland game birds). For quail, the acute, subchronic, and reproduction dietary studies indicate no concentration-duration relationship, and for mallards, the acute and subchronic dietary studies suggest no concentration-duration relationship. Nonetheless, the NOEC and LOEC values from the longer-term reproduction study suggest that longer-term exposures in mallards may lead to cumulative toxicity. Notably, this is the only example of cumulative effects in the strychnine toxicity data.

Information on groups of organisms other than birds and mammals is relatively sparse. A single toxicity study in ants suggests that these organisms may be as sensitive to strychnine (administered in honey) as are mammals and birds in gavage studies. Conversely, studies on the role of insects in the decay of poisoned mammals as well as limited field observations indicate that strychnine is not remarkably toxic to several groups of insects. The discrepancies between the toxicity study and field observations

1 may simply reflect different modes of exposure —i.e., the consumption of honey versus
2 exposures to strychnine in carcasses.

3
4 Data on aquatic organisms are much more limited than data in mammals, birds, and
5 insects. Essentially, there are no data on the toxicity of strychnine to terrestrial or aquatic
6 plants. Given the expected low levels of strychnine in water, the limited toxicity data on
7 aquatic animals is of minimal concern. While the lack of toxicity data cannot be used as
8 an indication of safety, there is no apparent basis for asserting that strychnine is likely to
9 impact plants.

10 ***4.1.2. Toxicity to Terrestrial Organisms***

11 ***4.1.2.1. Mammals***

12 There is a substantial amount of information on the toxicity of strychnine to terrestrial
13 mammals, from both toxicity studies (Appendix 2) and field studies (Appendix 3). The
14 nature of the available data on mammalian toxicity is both broad (i.e., covers many
15 mammalian species) and diverse. The studies and reports include relatively standard and
16 well-documented gavage studies (e.g., Anthony et al. 1984), short-term dietary exposures
17 (Evans et al. 1990; Record 1987a,b), many brief reports of LD₅₀ values or approximate
18 lethal doses with little experimental detail (e.g., Atkins and Johnson 1975; Baker et al.
19 1982; Hatch and Funnel 1968; Nolte and Wagner 2001; Record 1987c; Rudd 1956), and
20 studies in carnivores designed to simulate feeding on poisoned animals (Marsh et al.
21 1987). Some of these studies are quite atypical. For example, Inukai (1969) reports an
22 oral bioassay in bears but provides little information on the dosing method. Another
23 unusual report involves a poisoning incident in which horses consumed grain treated with
24 strychnine (Meek and Keatts 1971). The study by Anthony et al. (1986) involves a
25 bioassay in porcupines in which the animals were exposed to strychnine in salt blocks.
26 Given this diversity of experimental design as well as the limited information on many
27 experimental details, patterns in species sensitivity are difficult to determine.
28 Consequently, this risk assessment takes into consideration parenteral routes of exposure
29 (i.e., injections).

30 ***4.1.2.1.1. Parenteral Administration***

31 Studies involving parenteral administration are useful because the dose to the animal can
32 be characterized clearly, and differences in toxicity, based on the types of injections used,
33 provide insight into the range of species sensitivity. As summarized in Table 13 and
34 illustrated in Figure 5, parenteral toxicity studies in mammals involve intravenous,
35 subcutaneous, and intraperitoneal injection. With the exception of the study by Hatcher
36 and Eggleston (1918), all of the data illustrated in Figure 5 are LD₅₀ values. The toxicity
37 values reported by Hatcher and Eggleston (1918) in dogs and cats involve gradually
38 increasing doses of strychnine administered over a brief period of time in order to
39 determine the approximate lethal dose. While not directly comparable to LD₅₀ values,
40 the approximate lethal doses in cats and dogs are the only intravenous toxicity values
41 available for these species. The intravenous toxicity values in mice, rats, cats and dogs
42 are functionally the same: 0.4-0.57 mg/kg bw. The subcutaneous and intraperitoneal

1 studies, however, suggest that smaller mammals are more sensitive than larger animals to
2 strychnine.

3
4 As discussed further in Section 4.1.2.1.3, gavage studies in mammals do not reflect a
5 clear correlation between body size and toxicity. The gavage studies display a high
6 degree of scatter; nonetheless, the general trend reflects an increasing sensitivity among
7 species with increasing body size. The rationale for this difference between
8 intraperitoneal and gavage dosing is not apparent but may reflect the much narrower
9 range of body weights in the intraperitoneal studies compared to the gavage studies.

10
11 As discussed by Kato et al (1963), the sensitivity differences within species, based on
12 subcutaneous and intraperitoneal routes of exposure, reflect the more rapid metabolism of
13 strychnine in the liver of larger mammals, relative to smaller mammals. These
14 differences in toxicity are not apparent after intravenous administration, because
15 strychnine is a very fast acting poison and the animals die very quickly after intravenous
16 dosing. Thus, for intravenous injections, the relative rate of metabolism among species is
17 not important, because the animal dies before any significant metabolism can occur.

18
19 The similar lethal toxicity values for mice, rats, cats, and dogs exposed intravenously to
20 strychnine may well suggest that potency of strychnine in mammals is essentially the
21 same in terms of plasma concentrations and perhaps the same at the receptor level—i.e.,
22 the blockage of glycine receptors. In other words, plasma volume is linearly related to
23 body weight (e.g., Davies and Morris 1993). From the data reported by Davies and
24 Morris (1993), the average plasma volume in mammals is estimated to be about 44
25 mL/kg bw. Accordingly, the intravenous doses of 0.4- 0.57 mg/kg bw correspond to
26 plasma concentrations of about 7.4-13 mg/L, which is reasonably consistent with the
27 poisoning data in human case studies. As discussed in Section 3.1.4.1, human case
28 reports of strychnine poisoning indicate that peak plasma concentrations greater than 2.2
29 mg/L were fatal in all incidents of oral poisoning, despite prompt medical attention. The
30 estimated higher plasma concentrations from the intravenous animal studies are expected
31 in that mortality in the experimental mammals occurred very quickly.

32 ***4.1.2.1.2. Dietary Toxicity***

33 As noted above, there are three relatively standard acute dietary toxicity studies on
34 strychnine, including one in the pocket gopher (Evans et al. 1990), another in the
35 European ferret (Record (1987a), and a third in the red fox (Record 1987b). The latter
36 two bioassays are 5-day dietary studies following EPA's general protocol for acute
37 dietary toxicity studies in mammalian wildlife (U.S. EPA/OPPTS 1996). These studies
38 are required for pesticide registration only when the EPA determines that a pesticide
39 poses particular risk for some groups of mammalian wildlife. The studies by Record
40 (1987a,b) were conducted at the request of the EPA and were submitted in support of the
41 registration for strychnine. These studies are summarized in the EPA ecological risk
42 assessment on strychnine (U.S. EPA/OPP 1996d); however, the full details of these
43 studies are not available. As indicated in Appendix 2, the reported LC₅₀ values are 198
44 ppm for the ferret (Record 1987a) and 70 ppm for the red fox (Record 1987b).

1 The dietary study by Evans et al. (1990) in pocket gophers was designed to assess
2 strychnine efficacy; yet, it is quite similar in design to the standard acute dietary studies
3 required by the EPA for pesticide registration. Evans et al. (1990) exposed pocket
4 gophers to oat bait containing strychnine at concentrations of 0, 0.2, 0.35, 0.5, 0.6, 0.75,
5 1.0, or 1.25% for a 3-day period. As summarized in Appendix 2, there is a clear
6 concentration-response relationship for mortality; however, the study does not provide a
7 statistical analysis of that relationship. As part of the current Forest Service risk
8 assessment, U.S. EPA's Benchmark Dose Software (U.S. EPA/OEI 2009) was used to
9 estimate the LC₅₀, LC₁₀, and the lower 95% confidence limit on the LC₁₀ based on the
10 log-dose probit model (Finney 1971). As illustrated in Figure 6, the LC₅₀ is estimated at
11 0.298%, equivalent to about 2980 ppm, a factor of about 15 higher than the LC₅₀ in
12 ferrets and a factor of more than 40 greater than the LC₅₀ in fox [2980 ppm ÷ 70 ppm ≈
13 42.6].
14

15 In addition to information on the concentration-response relationship, Evans et al. (1990)
16 provide data on food consumption and the dietary intake of strychnine. While the
17 concentration-response relationship is relatively smooth and monotonic—i.e., increasing
18 mortality with increasing concentration—a very different pattern is apparent in terms of
19 the intake of strychnine. As illustrated in Figure 7, there is an inverse relationship
20 between food consumption and dietary concentration. This is not an uncommon pattern
21 in dietary toxicity studies. For strychnine, however, the inverse relationship is marked,
22 and there is a general decrease in mortality with increasing strychnine intake (Figure 7a).
23 This pattern appears to reflect the rapid absorption and rapid toxic action of strychnine
24 (Sections 3.1.2 and 3.1.3). While the rate of strychnine absorption may be constant in
25 terms of the proportion absorbed per unit time, the absolute amount of strychnine
26 absorbed increases as the concentration of strychnine in the diet increases. At these
27 higher concentrations of strychnine in the diet, the detoxification capacity of the liver
28 may become saturated. Consequently, the animals exposed to higher dietary
29 concentrations of strychnine sicken and die rapidly. In animals exposed to lower dietary
30 concentrations, the absolute amount of strychnine absorbed per unit time is less. In these
31 animals, the liver appears to be able to detoxify the lesser absolute amounts of strychnine
32 and no adverse effects are apparent. Thus, pocket gophers given lower dietary
33 concentrations of strychnine are able to tolerate greater cumulative doses (in terms of the
34 absolute amount of strychnine ingested), compared with pocket gophers given higher
35 dietary concentrations of strychnine.
36

37 Similar experimental details are not available for the studies in ferrets (Record 1987a)
38 and foxes (Record 1987c). Based on the LC₅₀ values, however, these two carnivores
39 appear to be much more sensitive than the pocket gopher to strychnine, and these results
40 suggest that larger mammals may be more sensitive than smaller mammals to strychnine.
41 Evans et al. (1990) do not give the body weights of the pocket gophers, and U.S.
42 EPA/OPP (1996d) does not provide information on the body weights of the foxes and
43 ferrets in the Record (1987a,b) studies. To explore the relationship of body size to
44 sensitivity, the compendium of mammalian body masses by Smith et al. (2003) was used
45 to obtain estimates of body weights for pocket gophers (75 g), the European ferret (1100
46 g), and the red fox (4131.7 g). As illustrated in Figure 8, there is a statistically significant

1 ($p=0.37$) inverse relationship between body size and dietary LC₅₀ values. The statistical
2 significance, however, may be specious. While the body masses given in Smith et al.
3 (2003) appear to be reasonable and well documented, it is not likely that these body
4 weights correspond precisely with those used in the toxicity studies. Exploratory
5 analyses suggest that even minor deviations in the body weight estimates will result in the
6 loss of statistical significance. Given the minimal number of data points for assessing fit
7 to the allometric model (i.e., one degree of freedom), statistical significance would not be
8 expected.

9 ***4.1.2.1.3. Other Oral Toxicity Studies***

10 A subset of the non-dietary oral toxicity data in mammals (Appendix 2) are provided in
11 Table 14 and illustrated in Figure 9. These data represent as large a number of species as
12 possible and include LD₅₀ values associated with each species. Because of the
13 relationships between body size and toxicity in the studies involving parenteral
14 administration (Section 4.1.2.1.1) and dietary exposures (Section 4.1.2.1.2), body weights
15 are included in Table 14, and the toxicity values are plotted against body weights in
16 Figure 9. Concerning species for which multiple LD₅₀ values are available, (e.g, rats), a
17 representative toxicity value was selected. As discussed in Section 3.1.4.2.1, the
18 available data indicate that female rats are more sensitive than male rats. Although Table
19 14 includes LD₅₀ values for both male and female rats, only the average value for both
20 sexes is plotted in Figure 9. For many species, publications reporting the toxicity values
21 do not specify the body weights of the animals. In such cases, a representative body
22 weight for an adult animal is taken from the compendia on mammalian body weights by
23 Smith et al. (2003). For comparison, the approximate lethal dose for humans is included
24 as the 2.25 mg/kg bw fatal dose in an adult female (Salm 1952).

25
26 As noted in the previous two subsections, allometric relationships—i.e., correlations of
27 body weight with toxicity values—are frequently noted for many different types of
28 chemicals (e.g., Calabrese 1991). In a review of wildlife toxicity data on numerous
29 chemicals, Sample and Arenal (1999) indicate that there is an inverse relationship
30 between the body weight and sensitivity of mammals to strychnine. As discussed in the
31 previous section, this inverse relationship is apparent for dietary studies.

32
33 For the non-dietary studies, there is substantial scatter, and no statistically significant
34 pattern is apparent in Figure 9. Nonetheless, the general trend in the non-dietary studies
35 suggests that larger mammals are more sensitive than smaller mammals. If only the LD₅₀
36 data are considered in Figure 9—i.e., the data on approximate lethal doses are
37 disregarded—the inverse relationship between body size and sensitivity is apparent,
38 except in the LD₅₀ values for nutria and mule deer.

39
40 Given the diverse nature of the available information, the lack of any clear correlation
41 may be expected. In addition, some of the scatter may be due to uncertainties in some of
42 the dose estimates. For example, there is substantial uncertainty in the estimated dose to
43 horses from the report by Meek and Keatts (1971). As summarized in Appendix 3, this
44 incident involved only three horses which consumed oats bait containing 0.025%
45 strychnine. The total amount of bait consumed was estimated at 1.5 lb; however, the

1 amount consumed by each horse is not known. Since all three horses became ill, it is
2 clear that each horse consumed some amount of bait. In Table 14 and Figure 9, the dose
3 plotted is 2.2 mg/kg bw; however, the actual doses may have varied substantially. The
4 maximum dose per horse could not have exceeded about 3.75 mg/kg bw, but there is no
5 way to estimate the minimum dose.

6
7 One reasonably consistent pattern, however, involves carnivores, which appear to be
8 more sensitive than other mammals. This pattern is more clearly illustrated in Figure 10
9 as a *species sensitivity distribution*. As discussed by Posthuma et al. (2002), species
10 sensitivity distributions can be used quantitatively in risk assessments (e.g., Posthuma et
11 al. 2002) and as tools in probabilistic risk assessment. This technique is not currently
12 used quantitatively in Forest Service risk assessments. Nonetheless, species sensitivity
13 plots, such as those presented in Figure 10, are useful for illustrating differences in
14 sensitivity among different groups of organisms.

15
16 In Figure 10, the x-axis is the LD₅₀ value and the y-axis is the cumulative frequency of
17 the LD₅₀ values for each of the species. The individual values for the cumulative
18 frequency are based on the following equation:

$$Freq_i = \frac{i - 0.5}{N}$$

19
20
21 where $Freq_i$ is the cumulative frequency for the i^{th} value and N is the number of values in
22 the data set. For example, there are a total of 14 LD₅₀ values for mammals. The lowest
23 value is an estimated lethal dose of 0.5 mg/kg bw for bears (Inukai 1969). Thus, the
24 frequency for the first point ($i=1$) is calculated as $\frac{1-0.5}{14}$ or 0.037. Similarly, the second
25 lowest LD₅₀ value ($i=2$) is 0.6 mg/kg, which is assigned a frequency of $\frac{2-0.5}{14}$ or 0.107.

26
27 Note that the x-axis in Figure 10 is represents the LD₅₀ values, and these are given on a
28 logarithmic scale under the standard assumption that LD₅₀ values in different groups of
29 organisms will be log-normally distributed.

30
31 Based on estimated lethal doses, sensitivity differences among mammalian species spans
32 a factor of about 50, ranging from an approximate lethal dose of 0.5 mg/kg bw for the
33 bear (Inukai 1969) to an LD₅₀ of 27 mg/kg bw for nutria (Nolte and Wagner 2002). The
34 actual range of sensitivities may be much higher. Figure 10 does not include the NOEC
35 of 91.4 mg/kg bw for the porcupine from the study by Anthony et al. (1986). This study,
36 however, is atypical in that the method of exposure involved strychnine in salt blocks.
37 The NOEC of 91.4 mg/kg bw does suggest that porcupines may be more tolerant than
38 many other mammalian species to strychnine. Conversely, strychnine administration via
39 salt blocks may have resulted in a slow rate of exposure in which normal metabolic
40 processes could have detoxified the strychnine more rapidly than it was consumed by the
41 porcupines.

42
43 Note that the six most sensitive species of mammals are carnivores with sensitivity
44 rankings as follows: bear > mink > dog > fox > cat ≈ coyote. The latter two species, cats

1 and coyotes, are right-shifted indicating a degree of sensitivity closer to that of humans
2 and horses. For all four of these intermediate species—i.e., cat, coyote, human, and
3 horse—LD₅₀ values are not available, and the estimated lethal doses for these species are
4 not directly comparable to LD₅₀ values. As discussed above, the Inukai (1969) study was
5 conducted with only three bears, which appear to be the most sensitive species, and does
6 not report an LD₅₀ value. Despite the variability and differences in the types of available
7 data, the mean toxicity value for carnivores (1.11 mg/kg bw) is less than the mean
8 toxicity values for other mammals (11.2 mg/kg bw) by about a factor of 10. Based on a
9 standard two-sample t-test for differences in StatGraphics (Manugistics 1995), these
10 differences are statistically significant ($p < 0.05$).

11
12 Finally, the allometric relationship noted in dietary toxicity studies (Section 4.1.2.1.2) is
13 also consistent with the assertion that carnivores are more sensitive than other groups of
14 mammals. The differences in sensitivity between carnivores and other mammals are
15 considered further in the dose-response assessment (Section 4.3.2.1).

16 **4.1.2.1.4. Field Studies**

17 As summarized in Appendix 3, some of the available field studies concern the effects of
18 strychnine treated baits on both mammals and birds. Consequently, the field studies are
19 discussed in Section 4.1.2.2.4.

20 **4.1.2.2. Birds**

21 Bird toxicity data are summarized in Appendix 4. The general signs of strychnine
22 toxicity in birds appear to be similar to those in mammals—i.e., hyperactivity,
23 incoordination, aggressive behavior, seizures, paralysis, and respiratory failure (Basson
24 1987; Cheney et al. 1987; Feldman and Kruckenberg 1975; Oppenheim and Reitzel
25 1975).

26
27 Unlike the case with mammals, data are available on both the acute and chronic toxicity
28 of strychnine in birds. As noted in Section 3.1.5.2 and discussed further in Section
29 4.1.2.2.3, the longer-term toxicity studies in birds generally support the assumption that
30 strychnine does not induce cumulative toxicity. The acute toxicity studies in birds are
31 generally comparable to the acute studies in mammals. The relatively few dietary
32 exposure studies were conducted in response to registration requirements by U.S.
33 EPA/OPP for acute dietary studies in birds (Section 4.1.2.2.1). Other oral exposure
34 studies, primarily involving gavage administration were conducted on a much larger
35 number of avian species. As with the non-dietary mammalian toxicity studies, there is
36 substantial scatter in the data in terms of allometric relationships, but predatory birds
37 appear to be generally more sensitive than other groups of birds (Section 4.1.2.2.2).

38 **4.1.2.2.1. Acute Dietary Studies**

39 U.S. EPA/OPP routinely requires acute dietary studies in birds, typically quail and
40 mallards. These studies follow a standard protocol, similar to mammalian studies, in
41 which birds are fed dietary concentrations of the pesticide for 5 days followed by a 3-day
42 recovery period. As summarized in Appendix 4 (Table 2), four acute dietary studies were
43 submitted to the EPA in support of the registration of strychnine. These studies include

1 the standard test species, mallards and quail, as well as short-term dietary studies in
2 black-billed magpie and the American kestrel.

3
4 In addition to the avian dietary studies submitted to the EPA, there is a dietary study in
5 pigeons (Schafer and Eschen 1986) in the open literature. Unlike the acute dietary
6 studies required by the EPA, the Schafer and Eschen (1986) study involves only a single
7 feeding to each of two experimental groups, one group fed in the morning and another
8 group fed in the afternoon. Each exposure group consisted of 24 birds fed 0.2, 0.4 and
9 0.6% strychnine-treated whole corn bait. Apparently, no concurrent control group was
10 used. Schafer and Eschen (1986) do not report a dietary LC₅₀. As detailed in Appendix 3
11 (Table 2), the concentration-response relationship in the afternoon feeding study was not
12 monotonic. Given the scatter in the afternoon bioassay and the lack of a concurrent
13 control group, no LC₅₀ is estimated statistically in the current Forest Service risk
14 assessment. Nonetheless, in both the morning and afternoon bioassays, mortality was
15 less than 50% at 0.2% and greater than 50% at 0.4%, and the approximate LC₅₀ appears
16 to be about 0.3%.

17
18 The results of the studies summarized by U.S. EPA/OPP as well as the study by Schafer
19 and Eschen (1986) are illustrated in Figure 11. In Figure 11, estimated body weights for
20 the EPA studies are taken from Dunning (1993). An approximate body weight of 285
21 grams for pigeons is estimated from information provided by Schafer and Eschen (1986).
22 Unlike the case with mammals (Figure 8), no clear relationship between body weights
23 and LC₅₀ values is apparent, with bobwhites (BW≈ 170g) and pigeons (BW≈ 185g) being
24 much less sensitive than mallards (BW≈1,000g), kestrel (BW≈115 g) or magpie
25 (BW≈180 g). Regrettably, details of the studies cited by the EPA are not provided in the
26 summaries by U.S. EPA/OPP (1996a,d), and the studies in kestrel and magpie are not
27 referenced.

28
29 The studies in quail and mallards, however, are referenced by U.S. EPA/OPP (1996d) to
30 Pedersen. As discussed further in Section 4.1.2.2.3, Pedersen and coworkers have
31 published subchronic and reproduction studies in mallards and quail (Sterner et al. 1998;
32 Pedersen et al. 2000), and these studies are consistent with the acute dietary studies
33 indicating that mallards are more sensitive than quail to strychnine. As discussed further
34 in Section 4.1.2.2.2, the same pattern is evident in gavage studies in which mallards are
35 more sensitive than either California quail or bobwhite quail.

36
37 The reasons for the greater sensitivity of mallards, relative to quail are not clear. Sterner
38 et al. (1998) suggest that the species differences between mallards and quail could be
39 related to anatomy. Ducks and most other water fowl have a very simple crop which
40 allows food to pass rapidly into the stomach. Other groups of birds, including quail and
41 other galliformes, have a more sac-like crop, which may retard the passage of food into
42 the digestive tract (e.g., Gill 1990, Fig. 7-11). Based on gavage toxicity studies, as
43 discussed further in Section 4.1.2.2.2, mallards are also more sensitive than quail to
44 strychnine. In gavage dosing, it is not clear that anatomical differences in the crop would
45 have a substantial impact on toxicity, as happens in dietary studies. Nonetheless, and as
46 discussed further in Section 4.1.2.2.2, Passeriformes (perching birds) appear to be

1 somewhat less sensitive than waterfowl, but are also among the more sensitive bird
2 orders. While Passeriformes have crops that are more complex than those of waterfowl,
3 the crop of Passeriformes is less complex than the crops of more tolerant orders of birds.
4 Conversely, and as discussed in Section 3.1, sex-, age-, or species-related differences in
5 the sensitivity of mammals to strychnine are associated with different rates of strychnine
6 detoxification by the liver.

7 ***4.1.2.2.2. Other Acute Toxicity Studies***

8 Toxicity data from gavage studies in birds are summarized in Table 15 and illustrated in
9 Figure 12. Details of these studies are included in Appendix 4 (Table 1). In Figure 12,
10 the LD₅₀ values are plotted on the y-axis and the corresponding body weights are plotted
11 on the x-axis. Most of the LD₅₀ values are taken from Tucker and Hegel (1971) and the
12 compendia by Hudson et al. (1984). These two sources are related in that they
13 summarize studies conducted by the U.S. Fish and Wildlife Service or the predecessor
14 organization, the U.S. Bureau of Sport Fisheries and Wildlife. The Fish and Wildlife
15 Service was also involved in the publications by Anthony et al. (1984), Redig et al.
16 (1982), and Ward et al. (1942). The earlier compendium by Tucker and Crabtree (1970)
17 is from the same source but is not cited because it does not contain information other than
18 that found in Hudson et al. (1984).

19
20 The compendia from the Fish and Wildlife Service (Hudson et al. 1984; Tucker and
21 Crabtree 1970) also include information on the toxicity of strychnine sulfate. As
22 discussed in Section 2, strychnine sulfate was registered as a pesticide. Because the
23 current risk assessment only addresses the strychnine alkaloid, data on strychnine sulfate
24 are not further discussed. Notably, however, the differences between the toxicity values
25 for strychnine alkaloid and strychnine sulfate are modest and not systematic.

26
27 As with the corresponding data on mammals (Table 14 and Figure 9), substantial scatter
28 is apparent in the relationship of toxicity to body weight. Excluding the data from the
29 house sparrow, however, the LD₅₀ values appear to be inversely related to body weight—
30 i.e., larger birds tend to be somewhat more sensitive than smaller birds, consistent with
31 the general pattern noted in mammals (Section 4.1.2.1.3).

32
33 The atypically low LD₅₀ of 4.18 mg/kg bw in sparrows (Tucker and Hegele 1971) does
34 not appear to be an outlier. A similar toxicity value for sparrows—i.e., a gavage LD₅₀ of
35 1.68 mg/kg bw—is reported by Hussain et al. (1993) for strychnine chloride administered
36 in water. In the Tucker and Hegele (1971) study, the strychnine alkaloid was
37 administered in a gelatin capsule.

38
39 In gavage studies conducted with house sparrows, Hussain et al. (1993) note a
40 remarkable difference in the toxicity of strychnine chloride administered in water (LD₅₀
41 of 1.68 mg/kg bw), compared with strychnine in grains (millet, sorghum, and wheat)
42 administered by intubation (LD₅₀ values of about 10-13 mg/kg bw). In some respects,
43 this pattern does not appear to be unusual in that strychnine is probably absorbed more
44 rapidly from water than from grain. Several of the toxicity studies by Hudson et al.
45 (1984) involve administration of strychnine in water, but only one other study (Ward et

1 al. 1942) involves the administration of strychnine in grain. The studies involving a grain
2 vehicle, however, were not conducted on the same species. Thus, while the lethal dose of
3 about 20 mg/kg reported for sage grouse by Ward et al. (1942) is higher than several of
4 the LD₅₀s in other species using a water vehicle, the roles of species differences and
5 vehicle differences cannot be distinguished.

6
7 Based on the data in Table 14, the species sensitivity distribution for birds is illustrated in
8 Figure 13. The LD₅₀ values in this figure are represented by solid diamonds, with the
9 common name for the species to the left and the order for the species on the right of the
10 diamond. The only manipulation of the data in Table 14 involved the LD₅₀ values for
11 mallards and pigeons. Three LD₅₀ values for mallards are available, two from Hudson et
12 al. (1984)—i.e., 2.27 mg/kg bw and 2.83 mg/kg bw—and one from Tucker and Hegele
13 (1971)—i.e., 2.9 mg/kg bw. For pigeons, two LD₅₀ values are available, one from
14 Tucker and Hegele (1971)—i.e., 22.6 mg/kg bw—and one from Schafer and Eschen
15 (1986)—i.e., 7.73 mg/kg bw. In species sensitivity distributions, only a single point
16 should be plotted for each species, and the LD₅₀ values for mallards and pigeons are
17 averaged for plotting in Figure 13.

18
19 By comparison to the species sensitivity distribution for mammals (Figure 10), the
20 corresponding plot for bird is remarkably smooth and sigmoidal, indicating that the
21 underlying distribution of species tolerances is log-normally distributed. The plot for
22 mammals, on the hand, evidences a much more jagged pattern. This difference between
23 mammals and birds probably reflects the fact that the plot for birds is based primarily on
24 LD₅₀ values, which would be expected to have a log-normal distribution; whereas, the
25 corresponding plot for mammals is based on a combination of LD₅₀ values and estimated
26 lethal doses. For birds, the exceptions are the estimated lethal doses for the snowy owl
27 (Redig et al. 1982), the great horned owl and hawk (Anthony et al. 1984), and the eagle
28 (Hudson et al. 1984). It is reasonable to expect that the extensive use of the estimated
29 lethal doses for mammals introduces substantial random error into the estimate of the
30 underlying distribution of tolerances.

31
32 As discussed in Section 4.1.2.1.3, the variability in estimated lethal doses for mammals
33 spans a factor of about 50, ranging from 0.5 to about 25 mg/kg bw. Based on the
34 available LD₅₀ values, the variability in birds seems somewhat greater—i.e., a factor of
35 over 120—with LD₅₀ values ranging from 0.94 mg/kg bw (snowy owls) to 112 mg/kg bw
36 (California quail). Within different orders of birds, the ground feeding birds—i.e.,
37 Galliformes—are clearly more tolerant than other bird orders, and this pattern is noted in
38 several reviews of strychnine toxicity (e.g., Department of the Interior 1992; Fagerstone
39 et al. 1980; Gabrielson 1938). As noted in the early review by Gabrielson (1938), doves
40 and pigeons—i.e., Columbiformes—appear to be relatively insensitive to strychnine.
41 Based on the data plotted in Figure 13, pigeons are somewhat more sensitive than
42 Galliformes but less sensitive than other species. As with mammals (Figure 10),
43 predators—i.e., owls, hawks, and eagles—are among the more sensitive species. While
44 only represented by one species each, the LD₅₀ values in mallards and sparrows suggest
45 that water fowl (Anseriformes) and perching birds (Passeriformes) are about as sensitive
46 as predatory birds to strychnine.

1
2 Limited information is available on birds concerning gender- or age-related differences in
3 sensitivity to strychnine. As summarized in Appendix 4, the data on mallards from
4 Hudson et al. (1984) suggest that very young mallards (i.e., 36-hours- to 1-week-old)
5 with LD₅₀ values ranging from about 2 to 2.6 mg/kg bw, are somewhat more sensitive
6 than 1-month-old mallards (LD₅₀ ≈ 5.8 mg/kg bw). The LD₅₀ values of ≈ 2.3 to 2.8
7 mg/kg bw in 6-month-old mallards, however, are comparable to those in younger birds.

8 ***4.1.2.2.3. Longer-term Toxicity Studies***

9 The longer-term toxicity studies include subchronic (Appendix 4, Table 3) and
10 reproduction/chronic toxicity studies (Appendix 4, Table 4) in mallards and bobwhite
11 quail. The chronic/reproduction studies are standard studies required by U.S. EPA/OPP
12 for pesticide registration. These studies are addressed in the EPA ecological risk
13 assessment (U.S. EPA/OPP 1996d) in support of the strychnine RED (U.S. EPA/OPP
14 1996a). In addition, these studies are published in the open literature (Pedersen et al.
15 2000). The reproduction studies are not chronic in the sense that exposures involve the
16 lifespan of the birds; however, they do involve a 20-week period of exposure covering
17 mating, egg laying, and hatching.

18
19 The subchronic toxicity studies in mallards and quail involve a 28-day dietary exposure
20 (Sternier et al. 1998). These studies are not required by U.S. EPA/OPP for pesticide
21 registration; furthermore, the publication by Sternier et al. (1998) is not covered in the
22 EPA registration documents on strychnine (U.S. EPA/OPP 1996a,d).

23
24 Both the subchronic studies (Sternier et al. 1998) and the reproduction studies (Pedersen
25 et al. 2000) were conducted by the same group of investigators. In addition to the
26 summaries of these studies provided in Appendix 4, the results of the studies are
27 illustrated in Figure 14. For comparison, Figure 14 also includes the acute dietary LC₅₀
28 values discussed in Section 4.1.2.2.1. As with the subchronic and reproduction studies,
29 the acute dietary studies were also conducted at the same facility by the same group of
30 investigators.

31
32 Based on the three sets of dietary studies, quail are consistently more tolerant than
33 mallards. Based on the acute dietary LC₅₀ values—i.e., 212 ppm in mallards and 3536
34 ppm in quail—quail are more tolerant by a factor of about 17 [3536 ppm ÷ 212 ppm ≈
35 16.7]. Based on the subchronic dietary LC₅₀ values—i.e., 679.8 ppm in mallards and
36 4973 ppm in quail—quail are more tolerant by a factor of about 7 [4973 ppm ÷
37 679.8 ppm ≈ 7.3]. In both species, the LC₅₀ values for the 28-day exposures are
38 somewhat higher than the LC₅₀ values for the 5-day exposures —i.e., by factors of about
39 1.4 in quail and 3.2 in mallards. This pattern is consistent with the general observation in
40 mammals that longer-term exposures are no more hazardous than short-term exposures
41 (Section 3.1.5).

42
43 The reproduction studies (Pedersen et al. 2000) are not designed to produce mortality.
44 Consequently, LC₅₀ estimates are not available. In quail, the chronic NOEC is 1113.6

1 ppm, virtually identical to the acute NOEC (1250 ppm) and the subchronic NOEC (972.6
2 ppm). Again, this is consistent with the lack of cumulative toxicity of strychnine.

3
4 In mallards, however, the reproduction study does suggest a cumulative toxicity. In this
5 study, the dietary concentrations were 33.2, 68.9, and 140.9 ppm. The 140.9 ppm
6 concentration may be classified as a LOEC, based on signs of neurotoxicity in some adult
7 birds, decreased body weights in adult females, and decreased hatching success in the F₁
8 generation. The intermediate concentration of 68.9 ppm is also classified as a LOEC,
9 based on signs of neurotoxicity in some adult birds. In Figure 14, the lowest
10 concentration of 33.2 ppm is plotted as a NOEC because no signs of toxicity were
11 observed in adult birds. As discussed further in the dose-response assessment
12 (Section 4.3.2.2), the 33.2 ppm concentration is classified as a LOEC by U.S. EPA/OPP
13 (1996a,d) because of abnormally small testes in one bird.

14 ***4.1.2.2.4. Field Studies***

15 The number of field studies concerning the use of strychnine as a rodenticide is relatively
16 large. Field studies are summarized in Appendix 3, and Table 16 provides an overview
17 of the studies. Also, most of the field studies are reviewed in the open literature (e.g.,
18 Colvin et al. 1987; Evans et al. 1990; Hegdal et al. 1981; Nolte and Wagner 2001; Record
19 and Marsh 1988). The field study by Evans et al. (1990) appears to have been submitted
20 to the U.S. EPA and this study is discussed in the U.S. EPA/OPP (1994d) ecological risk
21 assessment as MRID 41478501.

22
23 The field studies on strychnine are particularly important to the current risk assessment.
24 As noted by Record and Marsh (1988) and discussed further in Section 4.2 (exposure
25 assessment for ecological effects), the standard HQ method used in Forest Service and
26 many other risk assessments is highly dependent on the exposure assessment. For
27 strychnine, the available data for developing exposure assessments, particularly for
28 primary exposures—i.e., the consumption of bait—is extremely limited. To develop an
29 exposure assessment using standard conservative approaches would amount to a trivial
30 exercise, leading to the conclusion that the use of strychnine treated bait in below-ground
31 applications will result in wide-spread mortality in countless numbers of species. Field
32 studies provide a resource for evaluating the usefulness of these assumptions.

33
34 As indicated in Table 16, the field studies can be generally classified according to
35 application method—i.e., below-ground hand baiting, burrow builder applications, and
36 above ground applications. While above ground applications are not currently allowed,
37 above ground applications are considered because these types of applications serve as a
38 useful comparison to below-ground applications.

1 **4.1.2.2.4.1. Hand Baiting**

2 Except for the study by James et al. (1990) on the use of strychnine to control ground
3 squirrels, all of the below-ground applications of strychnine involve the control of pocket
4 gophers. The field studies on hand baiting clearly indicate that nontarget effects are
5 likely on fossorial mammals, such as ground squirrels, chipmunks, and mice, which
6 seems intuitive. Fossorial mammals are the most likely group of organisms to enter a
7 pocket gopher burrow, and, thus, have the greatest access to strychnine treated bait.
8 Adverse effects on ground squirrels and mice are documented in the studies by Anthony
9 et al. (1984), Barnes et al. (1985), El Hani et al. (2002), Evans et al. (1990), and
10 Fagerstone et al. (1980). Fossorial mammals are also likely to be adversely affected in
11 burrow builder applications (Hegdal and Gatz 1976) as well as above ground applications
12 (Anthony et al. 1986; Howard and Bodenchuk 1984; Wood 1965).

13
14 While there is no doubt that below-ground applications of strychnine can and will kill
15 some fossorial mammals, it is far less clear that the mortality rate will be high. The low
16 mortality rate of chipmunks is demonstrated in the study by Fagerstone et al. (1980) in
17 which 30 chipmunks were tracked by radio transmitters and monitored for 5-11 days after
18 baiting. Two chipmunks were found dead with detectable levels of strychnine —i.e.,
19 0.29 and 0.35 mg/kg bw. One other chipmunk was presumed to be eaten by a raptor, and
20 three chipmunks could not be tracked. The remaining 24 chipmunks survived for the 11-
21 day monitoring period. Thus, while it is reasonable to assert that some fossorial
22 mammals will be at risk, it does not seem reasonable to assert that a substantial fraction
23 of fossorial mammals will be killed. In some studies involving above-ground baiting, no
24 substantial impacts on mice are reported (Deisch 1986; Uresk et al. 1988). Both of these
25 studies, however, involved applications for the control of prairie dogs. Deisch (1986)
26 specifically notes that the increase in mice populations was probably due to decreased
27 predation.

28
29 In the study on ground squirrel control, there was a significant ($p < 0.05$) decrease in the
30 adult body mass of burrowing owls, relative to burrowing owls at a control site (James et
31 al. 1990, p. 122, Table 1). The magnitude of the decrease was about 4.8%—i.e., 160
32 grams at the treated site versus 168 grams at the control site. Other adverse, but not
33 statistically significant effects included a 16% decrease in breeding success, a 20%
34 decrease in the number of chick per nest attempts, and a 4% decrease in the number of
35 chicks per successful pair. No effects were noted on chick body mass.

36
37 In the abstract of their publication, James et al. (1990) note that this effect—i.e.,
38 reproductive impairment—can be interpreted as ... *indicating a possible sublethal effect.*
39 The only elaboration on this point in the paper itself is a reference to the studies by
40 Cheney et al. (1987) indicating that strychnine causes impaired coordination effects in
41 owls. As noted in Section 4.1.2.2, strychnine is neurotoxic to raptors; moreover,
42 strychnine is neurotoxic to all vertebrates. In the body of their publication, however,
43 James et al. (1990) do not report any signs of neurotoxicity in the adult owls or chicks.
44

1 Decreases in adult body mass and egg production were observed in mallards in the
2 reproduction study by Pedersen et al. (2000). As discussed in Section 4.1.2.2.2 and
3 illustrated in Figure 13, mallards and owls are among the more sensitive species of birds.

4
5 James et al. (1990) present conflicting interpretations in the publication. At one point,
6 James et al. (1990) suggest that no adverse effects were observed:

7
8 *The results indicate that the use of strychnine for ground squirrel*
9 *control is not detrimental to breeding Burrowing Owls. No owls*
10 *were killed as a result of the poisoning and their reproductive*
11 *success was not significantly affected (Table 1). The owls almost*
12 *entirely ignored the dead and dying ground squirrels. The one owl*
13 *that did feed on a dead ground squirrel rejected the*
14 *gastrointestinal tract, thereby avoiding the greatest amount of*
15 *strychnine residue.*

16
17 Later in the discussion, however, James et al. (1990) suggest that the reproductive effects
18 may have been caused by strychnine:

19
20 *we cannot dismiss the possibility that some owls were affected in*
21 *this way [sublethal toxicity]. This may explain why breeding*
22 *success and adult masses were higher on the control pastures, the*
23 *latter significantly so.*

24
25 In the absence of additional data, the conflict in the interpretation of the observations
26 from James et al. (1990) cannot be fully resolved. It is worth noting that James et al.
27 (1990) report five sublethal endpoints, four of which are suggestive of an effect. The
28 assumption could be made that the likelihood of each endpoint in the control owls being
29 greater than that of the owls at the treated site is 50%—i.e., the differences are random.
30 Under this assumption, the probability of four of the five endpoints at the treated site
31 being less than the endpoints at the control site is 0.0625. While this might suggest that
32 the effects are marginally significant, the effects on chicks—i.e., number per attempts,
33 number per successes, and chick mass—are likely to be correlated.

34
35 As noted in Table 16, Anthony et al. (1984) note that risks to raptors are likely to be low
36 but that risks to mustelids (mammalian predators such as badgers) are plausible. A
37 similar assessment is given in the review by Nolte and Wagner (2001). Other than the
38 study by James et al. (1990), there are no field studies which note adverse effects or
39 observations suggestive of adverse effects in raptors. Conversely, there are no field
40 reports involving below-ground hand baiting with strychnine which document adverse
41 effects on mustelids.

42 **4.1.2.2.4.2. Burrow builder Applications**

43 As summarized in Table 16, only two reports are available on burrow builder applications
44 (Hegdal and Gatz 1976; Smallwood 1999). The study by Hegdal and Gatz (1976) is
45 relatively consistent with the field studies on below-ground hand baiting, indicating that

1 burrow builder applications of strychnine are likely to cause adverse effects in rodents
2 but not in other nontarget species, including raptors and mammalian predators. On the
3 other hand, the study by Smallwood (1999) involves an atypical application of strychnine
4 with relatively severe consequences.

5
6 As indicated in Appendix 3, the Hegdal and Gatz (1976) study involves an application of
7 strychnine which is typical of Forest Service uses—i.e., 0.5% bait at an application rate
8 of 1.25 lb formulation/acre for pocket gopher control. Effects on potential predators of
9 the pocket gopher were monitored with radio transmitters attached to groups 36 raptors
10 and 36 mammalian predators. In the 3-week post-application monitoring period, only
11 four raptors and eight of the mammalian predators could be tracked. While no adverse
12 effects were noted in these predators, the number of animals that could be tracked is
13 small.

14
15 In other groups of animals without radio transmitters, Hegdal and Gatz (1976) noted no
16 adverse effects in raptors or mammalian predators and no effects on a large population of
17 blackbirds. The only nontarget effects included a decrease in the population of small
18 rodents in the treated area relative to pre-treatment populations ($p < 0.1$). In the control
19 plots—i.e., those not treated with strychnine—the rodent populations increased ($p < 0.001$)
20 over the same period of time. The only avian death attributed to strychnine was in one
21 mourning dove. Strychnine was detected in the crop of the dove carcass; however, the
22 strychnine concentration is not reported.

23
24 In contrast to the study by Hegdal and Gatz (1976), Smallwood (1999) reports on an
25 atypical burrow builder application by the Forest Service. The Smallwood (1999)
26 publication involves an efficacy study of below-ground grain baiting versus the use of
27 paraffin pellets bait. This study was funded by the Forest Service. The efficacy study
28 itself did not monitor for or report on effects in nontarget species. In reporting on the
29 results of the efficacy study, however, Smallwood (1999) notes that the Forest Service
30 (not otherwise specified) applied a 0.89% strychnine formulation at a rate of 3400 g/ha
31 (about 3 lbs formulation/acre) to two plots on the Shasta National Forest. This
32 application rate corresponds to about 0.027 lb a.i./acre which is about twice the maximum
33 labeled rate currently allowed for burrow builder applications (Table 3). Smallwood
34 (1999, p. 62) specifically notes that the use of a burrow builder ... *was not part of my*
35 *study design.*

36
37 Smallwood (1999) does not provide data on nontarget effects of the burrow builder
38 applications but does provide the following comment:

39
40 *...the tractor-drawn burrow builder treatments applied by the US*
41 *Forest Service on my plots were far more hazardous to nontarget*
42 *animal species, because they failed to conceal the poison baits*
43 *within the artificial tunnels. Soil collapsed into the tunnels along*
44 *the tracks of the burrow builder, and the baits were readily visible*
45 *from above-ground. Many non-target animals perished when they*
46 *consumed the exposed bait.*

1 Smallwood (1999, p. 64)

2
3 According to Hegdal and Gatz (1976), burrow builders may deposit bait on the soil
4 surface during normal movement. Citing Hegdal and Gatz (1976), the U.S. EPA/OPP
5 (1996d) also notes concern for spillage in burrow builder applications. Specifically,
6 Hegdal and Gatz (1976) note:

7
8 *... small amounts of bait may become available to granivorous*
9 *birds through inadvertent spillage. Bait may also be exposed when*
10 *the burrow builder is lifted out of the ground while moving, and*
11 *when the roofs of the artificial burrow collapse.*

12 Hegdal and Gatz (1976, p. 262)

13
14 Similarly, USDA/APHIS (1994) indicates that below-ground applications of strychnine
15 result in the containment of bait within the burrow but adds the following cautionary
16 language:

17
18 *The only exception involves the use of automated burrow builders,*
19 *where incidental above ground spillage could occur. When care is*
20 *taken to avoid or clean up such spillage, it does not result in*
21 *hazardous levels of above ground exposure.*

22 USDA/APHIS (1994, Appendix P, p. 221)

23
24 While the above phrasing is much more restrained than that used by Smallwood (1999),
25 the statement can be interpreted in a similar manner. By slightly rephrasing the above
26 statement from USDA/APHIS (1994), it appears that burrow-builder applications, unlike
27 hand baiting, can lead to above ground spillage that can be hazardous unless care is taken
28 to avoid or clean up the spillage.

29
30 In attempting to reconcile the relatively detailed study by Hegdal and Gatz (1976) with
31 the almost anecdotal report by Smallwood (1999), the most obvious difference involves
32 the application rates. Again, Smallwood (1999) used about twice the maximum labeled
33 rate currently allowed for burrow builder applications of strychnine. Discounting the
34 difference in application rates, the burrow builder application discussed by Smallwood
35 (1999) might have been or might be interpreted as a misapplication—i.e., an application
36 that did not employ the care called for in USDA/APHIS (1994). In this respect, it is
37 worth noting that the product labels for burrow builder applications, both of which are
38 from the USDA/APHIS, do not specifically call for the cleanup of spilled product. As
39 discussed further in Section 4.4.2, the risk characterization for strychnine given by U.S.
40 EPA/OPP (1996d, p. 7) is influenced substantially by instructions that operators *...should*
41 *pick up spilled bait.*

42
43 In the absence of any follow-up publication or more detailed information on the
44 observations from Smallwood (1999), the study by Hegdal and Gatz (1976) offers a
45 reasonably compelling basis for asserting that widespread and obvious signs of adverse
46 effects in nontarget species other than rodents are not expected after reasonably prudent

1 burrow builder applications of strychnine, as discussed further in the risk characterization
2 (Section 4.4.2).

3 **4.1.2.2.4.3. Above Ground Applications**

4 As discussed above, the interpretation of field studies is seldom unequivocal, and it may
5 be useful to compare field studies of above-ground applications with field studies of
6 below-ground applications. In other words, if field studies on above-ground applications
7 of strychnine present a different spectrum of effects in nontarget species, compared with
8 effects observed in reasonably comparable field studies on below-ground applications,
9 then confidence in the use of the field studies on below-ground applications may be
10 enhanced. In addition, the consideration of above-ground applications of strychnine may
11 be useful in assessing the worst-case impact of below-ground applications of strychnine.
12

13 As summarized in the bottom section of Table 16, field studies on above-ground
14 applications of strychnine do present a somewhat different set of observations on
15 nontarget species. The most obvious difference involves larks. Adverse effects in
16 meadowlarks (Graham 1977) and horned larks after exposure to above-ground
17 applications of strychnine are relatively well documented (Apa et al. 1991; Holbrook and
18 Timm 1985; Howard and Bodenchuk 1984; Uresk et al. 1988). Both meadowlarks
19 (Icteridae) and horned larks (Alaudidae) are Passeriformes. The laboratory toxicity data
20 on Passeriformes are limited to the house sparrow. As illustrated in Figure 13 and
21 discussed in Section 4.1.2.2.2, the house sparrow appears to be among the more sensitive
22 species of birds—i.e., on the same order of sensitivity as mallards and raptors, which
23 suggests that adverse effects in larks might be expected. Apa et al. (1991) specifically
24 note that effects on horned larks were due to the consumption of strychnine treated bait
25 on the ground surface. Effects on other seed eating birds—i.e., other Passeriformes—
26 were not observed. The reason for the greater sensitivity of larks, relative to other
27 Passeriformes, is not apparent.
28

29 As expected, above-ground baiting with a rodenticide adversely affects rodents (Anthony
30 et al. 1986; Howard and Bodenchuk 1984; Wood 1965). Uresk et al. (1998) do not report
31 statistically significant effects on mice, which may reflect the study design and statistical
32 analysis. Rabbits appear to be only other group of mammals at substantial risk in above-
33 ground, versus below-ground, applications of strychnine (Anthony et al. 1986; Holbrook
34 and Timm 1985). The study by Wood (1965) is primarily an efficacy study, but provides
35 the following statement on potential effects in predators:
36

37 *Within the study area two gray foxes and two coyotes were found*
38 *dead. The cause of death was not known, but it may have been*
39 *from eating poisoned rodents.*

40 Wood (1965, p. 435)

41
42 This is the only report in the published literature that suggests the significance of
43 secondary exposure to strychnine in mammalian predators. The speculation by Wood
44 (1965) may have merit; however, the statement is neither well documented nor well
45 supported in the publication or in the other field studies on strychnine (Table 14 and

1 Appendix 3). Specifically, the field study by Graham (1977), although not published in
2 the open literature, provides a much more detailed set of observations suggesting the lack
3 of overt adverse effects on mammalian or avian predators, particularly raptors.

4 **4.1.2.2.4.4. U.S. EPA Incident Reports**

5 U.S. EPA/OPP (2009) summarizes numerous incidents associated with the use of
6 strychnine. These incident reports cannot be classified as field studies because they
7 contain relatively little detail. The EPA assigns each incident a unique identification
8 number which is associated with a record that provides the location of the incident, the
9 general type of site, and the likelihood that the incident was associated with the use of
10 strychnine. The *likelihood* aspect ranges from unrelated to highly probable. These
11 records are linked to another data file that specifies additional details, such as the species
12 affected and the number of individual animals affected.

13
14 The incidents involving raptors are summarized in Appendix 3 (Field Studies Involving
15 Applications of Strychnine). As indicated in Appendix 3, there were 19 reported
16 incidents of mortality in predatory or scavenger birds between 1974 and 1994 in which
17 the probability of the association between strychnine use and mortality was classified as
18 either probable or highly probable. In two of these incidents, the records explicitly note
19 that the exposures were associated with secondary poisoning.

20
21 These incident reports clearly indicate adverse effects in raptors, such as hawks or eagles,
22 which is not consistent with the results of available field studies. Moreover, as noted in
23 U.S. EPA/OPP (2009), all of the incidents occurred prior to the restriction of strychnine
24 use to below-ground applications.

25 ***4.1.2.3. Reptiles and Amphibians***

26 ***4.1.2.3.1. Reptiles***

27 Toxicity studies in reptiles are uncommon; furthermore, they are not required for
28 pesticide registration. Two compendia on reptilian toxicity data (Pauli et al. 2000;
29 Sparling et al. 2000) cite one toxicity study on strychnine, Brock (1965). Brock (1965)
30 fed various rodenticides, including strychnine, to a group of gopher snakes (*Pituophis*
31 *catenifer*) over a 2-year period, using the same snakes repeatedly in different bioassays
32 after allowing for a recovery period. The bioassay on strychnine alkaloid involved a total
33 of 12 snakes. The average body weight of snakes was 0.455 kg with a range of 0.243-
34 0.738 kg (Brock 1965, Table 1).

35
36 In the same study, Brock (1965) administered dietary concentrations of strychnine to
37 mice (BW=0.04 kg), and reports that the average amount of strychnine consumed by the
38 mice was 1.64 mg with a range of 0.03-11.7 mg. These amounts correspond to an
39 average dose of 41 mg/kg bw with a range of 0.75-1025 mg/kg bw. Brock (1956) does
40 not comment on the wide range of strychnine doses used in the study, which vary by a
41 factor of 390. The lower bound of 0.75 mg/kg bw is close to the lethal dose in bears
42 (Inukai 1969). The consumption of 11.7 mg of strychnine by a 40 gram mouse suggests a
43 high level of tolerance, similar to that noted in pocket gophers (Lee et al. 1990).

1 The poisoned rodents were then fed to individual snakes. Brock (1965) does not provide
2 details of the dosing schedule, indicating that only one mouse was fed to each snake at a
3 given time:

4
5 *After a snake accepted a poisoned rodent, it was not given another*
6 *rodent for at least 14 days. Between trials snakes were fed*
7 *nonpoisoned mice.*

8 Brock (1965, p. 245)

9
10 The study does not provide data on the amount of strychnine consumed by each mouse
11 before it was fed to a snake. From the average amount of strychnine fed to the mice and
12 the average body weight of the snakes, the average dose to the snakes can be estimated as
13 about 3.6 mg/kg bw [$1.64 \text{ mg} \div 0.455 \text{ kg} \approx 3.6044 \text{ mg/kg bw}$]. Of the 12 snakes used in
14 this study, five died, six displayed signs of toxicity, and only one showed no signs of
15 adverse effects. The signs of toxicity included signs of irritability and tremors.
16 Strychnine was the only rodenticide to cause mortality in the snakes. This study is
17 considered further in the dose-response assessment (Section 4.3.2.3).

18
19 The only other bit of information on the toxicity of strychnine to reptiles is from a case
20 report (Campbell 1982) in which a prairie rattlesnake (*Crotalus viridus*) was collected
21 from an area of New Mexico in which strychnine grain bait was used the previous day in
22 burrow baiting for rodent control. The snake displayed aggressive behavior, but it is not
23 clear that this behavior was atypical. Shortly after collection, however, the snake began
24 to convulse and died, and the body of the snake became atypically rigid. The snake was
25 not further examined or assayed for strychnine residues.

26
27 The speculation by Campbell (1982) that the snake was poisoned by strychnine through
28 the consumption of a contaminated rodent seems plausible in terms of the signs of
29 toxicity and temporal association with the use of strychnine. The amount of strychnine
30 which might have been consumed is unknown.

31
32 Based on the study by Evans et al. (1990), average residues in pocket gophers after
33 strychnine treated baiting range from about 3 to 8 mg per gopher. Campbell (1982) notes
34 that the snake was ...*an average size adult*. An average size prairie rattlesnake weighs
35 about 1 pound (0.4536 kg) (<http://sdsnake.com/Rat.htm#Snake>). From these estimates of
36 the snake's body weight and the average strychnine residues in baited gophers, the dose
37 to a rattlesnake consuming a single pocket gopher can be estimated to range from about 7
38 to 18 mg/kg bw [$3 \text{ mg to } 8 \text{ mg} \div 0.4536 \text{ kg} \approx 6.614 \text{ to } 17.64 \text{ mg/kg bw}$]. Based on
39 information the study by Brock (1965), it is reasonable to assume that this range of doses
40 would be fatal to a prairie rattlesnake, further supporting the supposition by Campbell
41 (1982) that the rattlesnake was poisoned by strychnine.

42 **4.1.2.3.2. Amphibians (Terrestrial-Phase)**

43 The toxicity of strychnine to terrestrial-phase amphibians is not well characterized. In the
44 early study by Weis and Hatcher (1922), frogs (*Rana pipiens*) were used in a classical
45 bioassay for strychnine—i.e., the responses in frogs were used quantitatively to estimate

1 concentrations of strychnine during the conduct of studies on the mammalian
2 pharmacology of strychnine. Using injections into the ventral lymph sac of frogs, Weis
3 and Hatcher (1922) noted an NOEC for hyperexcitability of approximately 0.1 mg/kg bw.
4 While detailed studies on strychnine metabolism in frogs were not conducted, Weis and
5 Hatcher (1922) noted that fasting increases the toxicity of strychnine to frogs and
6 suggested that the liver is the major organ involved in detoxification. By analogy to the
7 much more detailed studies in mammals (Section 3.1.3.1), this speculation is probably
8 correct.

9
10 The acute oral LD₅₀ of strychnine to bullfrogs (*Rana catesbeiana*) is 2.21 (1.56-3.12)
11 mg/kg bw (Tucker and Crabtree 1970; Hudson et al. 1984). As illustrated in Figures 10
12 and 13, this LD₅₀ is in the range of LD₅₀ values for relatively sensitive species of
13 mammals and birds.

14
15 As noted by the U.S. EPA/OPP (2009), amphibians have permeable non-scaly skin and
16 may be a risk to dermal contact with contaminated bait, particularly if the amphibian
17 enters gopher burrows treated with strychnine treated bait. While information is
18 available on the dermal penetration rate of strychnine in amphibians, Quaranta et al.
19 (2009) have reported that the dermal permeability of five model compounds (i.e.,
20 atrazine, antipyrine, mannitol, paraquat, and glyphosate) is 26 to 302 fold higher in adult
21 *Rana esculenta* than in preparations of pig skin.

22 **4.1.2.4. Terrestrial Invertebrates**

23 Very little information is available on the toxicity of strychnine to insects, and no
24 information is available on the toxicity of strychnine in other groups of terrestrial
25 invertebrates. Kostowski et al. (1965) report that oral doses of 0.1-.02 mg/kg strychnine
26 caused signs of neurotoxicity—i.e., ataxia and altered locomotion—as well as abnormal
27 electroencephalographic patterns in wood ants (*Formica rufa*). The dosing design is not
28 detailed in this publication other than to note that strychnine was administered in honey.
29 By analogy to oral studies in bees, it is likely that the doses were estimated based on
30 changes in the weight of honey after groups of ants were exposed to a known quantity of
31 honey containing strychnine at a known concentration. The estimated doses of 0.1-0.2
32 mg/kg bw are somewhat less than the lowest lethal dose reported in mammals—i.e., 0.5
33 mg/kg bw with an NOEC of 0.25 mg/kg bw in bears (Inukai 1969).

34
35 The only other direct information on the toxicity strychnine to insects involves an
36 extremely brief summary statement by Nolte and Wagner (2001):

37
38 *Many insects have been demonstrated to be unaffected by*
39 *strychnine, with the compound passing unchanged through the*
40 *digestive tract of beetles (unpublished USDA bibliography, no*
41 *date).*

42 Nolte and Wagner (2001, p. 66)

43
44 Further details are not provided by Nolte and Wagner (2001).

1 In a field study, Deisch (1986) surveyed a large number of insects in an area treated with
2 0.5% strychnine treated bait for the control of prairie dogs (Appendix 3). While
3 fluctuations in the density of several different groups of insects were noted, these changes
4 were associated with temporal factors and habitat alterations rather than strychnine
5 toxicity.

6
7 Notwithstanding the report by Kostowski et al. (1965) on ants, the statement by Nolte and
8 Wagner (2001) is consistent with a relatively robust literature noting the importance of
9 insects in the decomposition/consumption of poisoned rodent carcasses (Arjo et al. 2005).
10 For example, Stahl et al. (2004) noted mean and maximum strychnine concentrations of
11 0.130 and 0.338 mg/kg in ants. The highest concentration—i.e., a mean of 0.366 mg/kg
12 bw and a maximum of 0.698 mg/kg bw—were noted in Diptera larvae. While this
13 finding does not demonstrate that the insects were unaffected, the insects were live-
14 caught. The residue data on insects are considered further as a source of tertiary
15 exposures to mammals and birds in Section 4.2.

16 **4.1.2.5. Terrestrial Plants (Macrophytes)**

17 No information is available on the toxicity of strychnine in terrestrial macrophytes. As
18 discussed in Section 3.2.3.6, strychnine does not appear to be translocated by terrestrial
19 plants, and there is no basis for asserting that strychnine is likely damage terrestrial
20 plants. This qualitative assessment indicating no likely hazard to terrestrial plants is
21 essentially identical to the assessment given by the U.S. EPA:

22 *Since there is no above-ground exposure to strychnine, effects to*
23 *plants are not expected. There is no evidence that roots of plants*
24 *encountering bait in burrows take up the strychnine and transport*
25 *it to the above-ground portions of the plant.*

26 –U.S. EPA/OPP 2009, p. 44
27

28 **4.1.2.6. Terrestrial Microorganisms**

29 No studies have been conducted on the toxicity of strychnine to terrestrial
30 microorganisms. Starr et al. (1995, 1996) examined the degradation of strychnine in two
31 soils treated with 10 ppm strychnine. As is typical in the microbial degradation of many
32 chemicals, lag phases were noted in the degradation of strychnine. This lag phase is
33 associated with enzyme induction—i.e., microbial adaptation—rather than toxicity.
34 Changes in populations of total bacteria, Actinomycetes (a type of gram-positive
35 bacteria), and fungi were noted between the two soils and at different times after
36 incubation; however, significant differences were not observed in microbial populations
37 between treated and control soils.

38 **4.1.3. Aquatic Organisms**

39 **4.1.3.1. Fish**

40 The acute toxicity data in fish exposed to strychnine are summarized in Appendix 5.
41 Consistent with effects seen in other groups of organisms, like mammals, birds, snakes,
42 and insects, the signs of strychnine toxicity in fish include hyperactivity, spasms, and

1 convulsions (Baradbury et al. 1991; Carlson et al. 1998). These similarities seem to
2 reflect a common mechanism of action—i.e., strychnine blocks the normal neuro-
3 inhibitory action of glycine (Shen et al. 2005).

4
5 Typically, U.S. EPA/OPP requires a standard set of acute studies in fish as well as an
6 early life stage (a.k.a. egg-to-fry) study. For strychnine, however, the EPA waived the
7 requirement for an early life stage study (U.S. EPA/OPP 1996a, p. 50). As noted in
8 Section 3.2.3.1.1 (Likelihood and Magnitude of Exposure), U.S. EPA/OPP (1996a, p. 8)
9 expresses minimal concern for the contamination of surface water given the restrictions
10 on the uses of strychnine, specifically that only below-ground applications are permitted.
11 As detailed in Section 3.2.3.4.3 and summarized in Table 11 of the current Forest Service
12 risk assessment, the minimal concern appears to be justified in that the maximum peak
13 concentrations of strychnine should not exceed about 0.003 mg/L and the maximum
14 concentrations in surface water associated with atypical events should not exceed about
15 0.03 mg/L.

16
17 Two acute toxicity studies in fish were submitted to and reviewed by the U.S. EPA/OPP
18 (1996a,d). The lowest LC₅₀ is 0.76 mg/L in bluegill sunfish. Based on this toxicity
19 value, the U.S. EPA/OPP (1996d) classifies strychnine as highly toxic. The other LC₅₀ is
20 2.3 mg/L for rainbow trout. Based on this toxicity value, strychnine is moderately toxic.
21 Other toxicity values are available in the open literature, and all of the LC₅₀ values from
22 the open literature are above the LC₅₀ of 0.76 mg/L in bluegill sunfish. Thus, U.S.
23 EPA/OPP (1996d) uses the most sensitive toxicity value available when classifying
24 strychnine as highly toxic to some species of fish. As discussed further in the risk
25 characterization for fish (Section 4.4.3.1), the LC₅₀ of 0.76 mg/L leads to estimated HQs
26 below the level of concern.

27 **4.1.3.2. Amphibians (Aquatic-Phase)**

28 The only study of aquatic-phase amphibians is the report by Cuome et al. (1978) which
29 notes that embryos of the common toad (*Bufo vulgaris*) were immobilized immediately
30 by strychnine concentrations of 50 mg/L. At a concentration of 5 mg/L, abnormalities of
31 the digestive tract and eyes were noted. An NOEC for the developmental effects was not
32 determined.

33
34 The only other strychnine studies conducted with amphibians involve its use to assess
35 mechanisms of action in photoreceptors (Shen et al. 2008) and the control of spinal and
36 hindbrain neurons (Boothby and Roberts 1992). In these studies, strychnine as well as
37 other agents whose mechanism of action is well understood are used as tools to better
38 understand the control of specific biological processes. These studies do not provide
39 information that is directly relevant to the current risk assessment on strychnine.

40 **4.1.3.3. Aquatic Invertebrates**

41 As summarized in Appendix 5, only one standard bioassay is available on strychnine
42 exposure in aquatic invertebrates. This study, summarized in U.S. EPA/OPP (1996d),
43 reports a 48-hour LC₅₀ of 8 mg/L (10-12 mg/L) in *Daphnia magna*. As with the acute
44 toxicity data in fish, this LC₅₀ is far above any plausible concentrations of strychnine in

1 surface water. This matter is discussed further in the risk characterization for aquatic
2 invertebrates (Section 4.4.3.3).

3
4 The only study encountered in the open literature regarding the effects of strychnine on
5 aquatic invertebrates is the neurophysiology study by Gola and Ducreux (1984)
6 conducted with the sea slug (*Aplysia californica*). In this study, strychnine
7 concentrations of 0.1-1 mM (i.e., about 33.4-334.4 mg/L) were used to assay very
8 specific effects on neural activity in the slug. Like some of the mechanistic studies on
9 amphibians, this study does not provide information which is directly relevant to the
10 current risk assessment on strychnine.

11 ***4.1.3.4. Aquatic Plants***

12 As with terrestrial plants (Section 4.1.2.5), no information is available on the toxicity of
13 strychnine to aquatic plants; however, there is no basis for asserting that strychnine is
14 likely to have an impact on aquatic plants.

15

1 4.2. EXPOSURE ASSESSMENT

2 4.2.1. Overview

3 The exposure scenarios for terrestrial species are summarized in Worksheet G01 of the
4 Excel workbook that accompanies this risk assessment. The exposures to aquatic species
5 are summarized in Worksheet G03 of this workbook.

6
7 Forest Service risk assessments generally employ a relatively standard set of exposure
8 scenarios which are applied uniformly to different pesticides. While not all scenarios are
9 included for all types of pesticides, the structures of the exposure assessments are similar.
10 This approach is not taken for below-ground applications of strychnine because the
11 nature and details of potential exposures differ substantially from those of other
12 pesticides.

13
14 The literature on strychnine and other rodenticides generally classifies exposures as
15 primary, secondary, or tertiary, and this convention is adopted in the current Forest
16 Service risk assessment. *Primary exposures* involve the direct consumption of bait, and
17 primary exposure scenarios are developed for small mammals as well as some types of
18 birds. *Secondary exposures* involve the consumption of strychnine-contaminated prey
19 (i.e., prey poisoned as a result of primary exposure, like pocket gophers). Secondary
20 exposure scenarios are developed for predatory mammals, birds (i.e., raptors), and
21 reptiles. *Tertiary exposures* involve the consumption of prey containing strychnine as a
22 result of feeding on a primary consumer—e.g., the consumption of an insect that had fed
23 on a poisoned carcass. Tertiary exposure scenarios are developed for an insectivorous
24 mammal, bird, and terrestrial-phase amphibian. Other standard exposure scenarios
25 include the consumption of contaminated water as well as the consumption of
26 contaminated fish.

27
28 A summary of the animals used in the exposure assessments (i.e., ecological receptors) is
29 given in Table 17. Most Forest Service risk assessments use a relatively small number of
30 receptors intended to represent worst-case exposures. In the current ecological risk
31 assessment of strychnine, the standard set of receptors is used for exposure scenarios
32 involving the consumption of contaminated water—i.e., a small mammal (20 g mouse), a
33 large mammal (70 kg deer), as small bird (20 g passerine), and a large bird (4 kg Canada
34 goose), as discussed in Section 4.2.2. For other exposure scenarios involving strychnine,
35 the receptors are elaborated. For mammals, primary exposure scenarios include the
36 standard mouse and deer as well as the pocket gopher and ground squirrel. As discussed
37 in Section 4.2.2, the pocket gopher is used only to calibrate plausible exposures to
38 strychnine treated bait. The ground squirrel is used as a larger fossorial mammal that will
39 consume strychnine treated bait. This species is selected because field studies are
40 available that document effects in ground squirrels (Section 4.1.2.2.4). Thus, the
41 exposure assessments and subsequent risk estimates can be used as a tool to assess the
42 plausibility of the risk characterization (Section 4.4). For the same reasons, the exposure
43 scenarios for birds are elaborated to include small and larger tolerant species (Galliformes
44 and Columbiformes).

1 Generally, Forest Service risk assessments attempt to use exposure scenarios compatible
2 with or at least comparable to those used by U.S. EPA/OPP. For strychnine, however,
3 the EPA did not conduct a quantitative exposure assessment for any exposure pathways
4 (U.S. EPA/OPP 1996d). Consequently, as discussed further in Section 4.4, the EPA does
5 not provide a quantitative risk characterization for nontarget species, which is comparable
6 to the EPA decision not to provide a quantitative exposure assessment for workers
7 (Section 3.2.2.1).

8
9 Like its decision regarding worker exposure, the EPA’s decision not to conduct an
10 exposure assessment for nontarget species has merit. As discussed below, the data
11 supporting many of the exposure scenarios are extremely limited, particularly for primary
12 exposures to some groups of nontargets and secondary exposures to all nontargets.
13 Nonetheless, for certain groups of organisms, the risk characterization can be based with
14 confidence on the existing field studies. Then again, as discussed in Section 4.1.2.2.4,
15 some of the available field studies offer conflicting information or are subject to
16 ambiguous interpretations, and what is more, some groups of nontarget organisms are not
17 well encompassed by the field studies. Consequently, the current Forest Service risk
18 assessment develops exposure assessments that are as complete as possible, even though
19 several of the exposure scenarios are tenuous. The limitations of these exposure
20 scenarios are emphasized in the following subsections and considered further in the risk
21 characterization (Section 4.4).

22 ***4.2.2. Primary Exposures***

23 Three classes of primary exposure scenarios are considered: an accidental spill (Section
24 4.2.2.1), a misapplication in which surface contamination occurs (Section 4.2.2.2), and an
25 expected or typical application in which minimal surface contamination occurs (Section
26 4.2.2.3). As detailed in the following subsection, field monitoring data adequately
27 demonstrate that pocket gophers in the field will not consume strychnine treated bait as
28 the sole component of their diet. Thus, adjustment factors are used to estimate the
29 proportion of strychnine treated bait that different groups of animals may consume as a
30 fraction of their total diet. These factors are summarized in Table 18, and the rationale
31 for these factors is detailed below.

32 ***4.2.2.1. Primary Exposures, Accidental Spill***

33 All Forest Service risk assessments include exposure scenarios involving some sort of
34 accidental spill. The usual concern for an accidental spill is the contamination of surface
35 water—e.g., a spill into a small pond, which is considered below for both terrestrial
36 species (Sections 4.2.4) and aquatic species (Section 4.2.5). For strychnine, however, an
37 accidental spill could also involve a large spill of bait onto the ground, which is then
38 consumed by terrestrial organisms.

39
40 Primary exposures involve the consumption of contaminated bait. Superficially, this is a
41 simple scenario in which the amount of bait consumed might be estimated from the food
42 consumption rates of the receptor. As in all Forest Service risk assessments, food
43 consumption rates are estimated from allometric relationships developed by U.S.
44 EPA/ORD (1993)—i.e., the Wildlife Exposure Factors Handbook. Allometric

1 relationships scale the amount of food consumed per day to the body weight of the
2 animal—i.e., $FC = aW^b$ —where FC is the food consumption in grams, W is the body
3 weight in grams, and a and b are coefficients. Different allometric relationships are
4 developed for different groups of organisms. For example, the allometric equations for
5 rodents is given as $FC = 0.621W^{0.584}$ (U.S. EPA/ORD 1993, Eq. 3-8, p. 3-6). Based on
6 this equation, a 75 gram pocket gopher is estimated to consume 7.7 grams of food per
7 day. This estimate is reasonably close to the mean bait consumption of 6.46 grams for
8 pocket gophers given in Evans et al. (1990).

9
10 If the simple and conservative assumption were made that the pocket gopher consumed
11 7.7 grams of a 0.5% bait, the dose to the gopher would be somewhat greater than 500
12 mg/kg bw [7.7 grams x 1000 mg/g x 0.005 ÷ 0.075 kg ≈ 513.333 mg/kg]. As discussed
13 in Section 4.1.2.1.2 and illustrated in Figure 7, the study by Evans et al. (1990) clearly
14 demonstrates that the estimated dose of 500 mg/kg bw would grossly overestimate
15 exposure. In other words, the animal would either die before the dose of 500 mg/kg
16 could be consumed or the animal would self-limit consumption.

17
18 Taste aversion to strychnine has been studied in a few species (Howard et al. 1990;
19 Brockhoff et al. 2007); however, generalizations about field consumption cannot be
20 made, based on these studies. Nonetheless, the available data, including the dietary study
21 by Evans et al. (1990), additional field monitoring data from the Evans study, and several
22 additional field studies summarized in Table 16, clearly indicate that doses of 500 mg/kg
23 bw are not plausible. If it is not reasonable to assume that a pocket gopher will consume
24 strychnine treated bait equal to an amount estimated from allometric relationships, it is
25 also not reasonable to assume that other species will other species will consume bait
26 equal to the estimated total food intake based on allometric relationships.

27
28 For the accidental ground spill scenario, it is assumed that the amount of bait consumed
29 as a fraction of the total diet is 0.02 (0.002 to 0.2). This adjustment is functionally a
30 model calibration. As detailed in Worksheet F01b, this calibration leads to dose
31 estimates of about 10 (1 to 100) mg/kg bw for the pocket gopher, which encompass the
32 body burdens in pocket gophers from the dietary study by Evans et al. (1990). As
33 summarized in Appendix 2 and illustrated in Figure 7, the dietary studies using 0.2-
34 1.25% strychnine treated bait resulted in intakes of about 3.73-7.5 mg of strychnine.
35 Using an approximate body weight of 0.075 kg for the gopher, these intakes correspond
36 to doses of about 50-100 mg/kg bw. In field monitoring study of poisoned pocket
37 gophers, Evans et al. (1990, Table 2) report that carcass concentrations ranged about 0.2
38 to 90 mg/kg bw. Thus, the calibration of bait consumption of 0.02 (0.002 to 0.2) as a
39 fraction of total dietary consumption leads to estimated doses for the pocket gopher
40 which are consistent with the available laboratory and field monitoring data on pocket
41 gophers.

42
43 Applying these ratios to other animals assumes that the animals will respond to readily
44 available bait in the same manner as the pocket gopher. This assumption is obviously
45 tenuous but is made in the absence of data to support alternative assumptions.

1 **4.2.2.2. Primary Exposures, Misapplication**

2 Typically, strychnine treated bait will be deposited directly into gopher burrows or in
3 artificial burrows made by burrow builders. In either case, it is reasonable to assume that
4 very little bait will be available to receptors who might consume bait but do not enter
5 burrows—i.e., all primary consumers, except fossorial mammals.

6
7 As discussed in Section 4.1.2.2.4.2 (Burrow builder Applications), Smallwood (1999)
8 recounts an incident in which a substantial amount of strychnine treated bait was
9 available to above-ground primary consumers and implies that this exposure scenario is
10 characteristic of burrow builder applications. The field study by Hegdal and Gatz (1976)
11 contradicts the presumption; however, both Hegdal and Gatz (1976) and USDA/APHIS
12 (1994) acknowledge that above ground spillage may occur during burrow builder
13 applications. The USDA/APHIS (1994) seems to imply that the amount of above ground
14 spillage could be hazardous. Consequently, misapplications of strychnine appear to be a
15 concern for burrow builder applications.

16
17 As discussed further in Section 4.4.2, the U.S. EPA/OPP (1996d, p.7) has also expressed
18 concern with burrow builder applications but notes that *... recent instructions for the*
19 *burrow builder say that the operators should pick up spilled bait.* Based on these
20 instructions, the Agency appears to conclude that burrow builder applications will not
21 pose any risk to nontarget species. It is not clear that or how well spilled bait will be
22 picked up subsequent to large-scale burrow builder applications. As noted in Section
23 3.2.2.1.2, the study by Hegdal and Gatz (1976) involved three burrow builders working
24 14 hours per day for 8 days in applying strychnine treated bait to over 1500 acres. In the
25 absence of clear and well-documented studies demonstrating the spillage in not an issue
26 in burrow builder applications, it seems prudent to consider misapplication as a separate
27 exposure scenario.

28
29 In below-ground hand baiting, the available field studies give no indication that
30 misapplications would lead to potentially hazardous amounts of bait on the soil surface.
31 Thus, with the exception of gross mishandling, it does not appear that misapplication
32 scenarios are applicable to hand baiting.

33
34 While misapplications are of concern in this risk assessment, data to directly support such
35 an exposure assessment are not available. As noted above, no studies are available with
36 burrow builder applications that give a quantitative estimate of the amount of spilled
37 during application and the amount remaining after typical clean-up measures. As an
38 alternative, a surrogate exposure assessment is based on the assumption that a gross
39 misapplication of strychnine treated bait could lead to conditions in which the availability
40 of the bait is equivalent to the availability of the bait to fossorial mammals, in normal
41 applications.

42
43 As summarized in Table 16, normal below-ground hand baiting with strychnine will lead
44 to exposures in fossorial mammals including ground squirrels, chipmunks, and mice.
45 These exposures, however, appear to be less than the upper bound exposures to gophers.
46 Clearly, strychnine exposure will be less for fossorial mammals than for the most heavily

1 exposed pocket gophers, given that strychnine treated bait is deposited in the burrow of
2 pocket gophers. Monitoring data from field studies indicate that strychnine residues in
3 fossorial mammals range from about 0.6 to 13 mg/kg bw (Anthony et al. 1984; Barnes et
4 al. 1985; Fagerstone et al. 1980). The upper bound of this range, rounded to one
5 significant digit, is about a factor of 10 below the upper bound of 100 mg/kg bw for
6 pocket gophers (Section 4.2.2.1).

7
8 Accordingly, strychnine exposures to fossorial mammals under normal conditions of
9 application are based on consumption factors of 0.002 (0.002 to 0.02). As detailed in
10 Worksheet F05a, this assumption leads to dose estimates for a 20 g mouse of about 1.8
11 (0.2 to 18) mg/kg bw. This range encompasses the monitored body burdens in fossorial
12 mammals of 0.6-13 mg/kg bw, as referenced above and summarized in Table 16.

13
14 For the misapplication scenario, the consumption factors of 0.002 (0.002 to 0.02) are
15 applied to all groups of nontarget primary consumers, other than fossorial mammals. The
16 misapplication scenario assumes that exposure factors for fossorial mammals are
17 equivalent to those of gophers—i.e., consumption factors of 0.02 (0.02 to 0.2).

18
19 The large mammal—i.e., a 70 kg deer—is not included in the misapplication scenario.
20 As summarized in Worksheet F01g (the accidental exposure scenario for the deer), the
21 accidental exposure scenario assumes the deer would consume 190 (19 to 1900) mg of
22 strychnine. For the misapplication scenario, this amount is adjusted to 19 (1.9 to 190) mg
23 of strychnine. An application rate of 1 lb formulation/acre corresponds to 0.005 lb
24 a.i./acre or about 2200 mg/acre [$\approx 453,600 \text{ mg/lb} \times 0.005 = 2268 \text{ mg}$]. Thus, for a deer to
25 consume 190 mg, it must be assumed that about 10% of the bait is effectively applied to
26 the ground surface and the deer systematically consumes all of the available bait over an
27 area of about 1 acre. While the former assumption may be plausible under conditions of
28 gross misapplication, the latter assumption seems implausible.

29 ***4.2.2.3. Primary Exposures, Typical Applications***

30 Elaborate details are provided for each of three primary exposure scenarios involving
31 typical applications of strychnine treated bait: the foraging of gopher dens by fossorial
32 mammals (Section 4.2.2.3.1), the consumption of incidental above-ground spillage by
33 birds (Section 4.2.2.3.2), and foraging of gopher burrows by larger omnivorous mammals
34 (Section 4.2.2.3.3).

35 ***4.2.2.3.1. Fossorial Mammals***

36 It is likely that fossorial mammals, like mice and squirrels, will enter gopher dens and
37 directly consume strychnine treated bait; accordingly, effects of exposure on fossorial
38 mammals are well documented in below-ground applications of strychnine (Section
39 4.1.2.2.4). As summarized in the previous section, consumption factors for fossorial
40 mammals in typical below-ground applications of strychnine are assumed to be 0.002
41 (0.0002 to 0.02). This assumption is based on field monitoring data and probably leads to
42 reasonably realistic estimates of exposure. Exposure estimates are made for three
43 receptors, a very small mammal (i.e., a mouse in Worksheet F05a), a somewhat larger

1 fossorial mammal (i.e., a ground squirrel in Worksheet F05b), and substantially larger
2 fossorial mammal (i.e., a skunk in Worksheet F05c).

3 **4.2.2.3.2. Ground Surface Feeders**

4 Unlike the case with pocket gophers and other fossorial mammals, monitoring data to
5 support a calibration of consumption factors for surface dwelling mammals as well as
6 birds that might feed on incidental surface deposits of bait are extremely limited. As
7 summarized in Table 16, the only monitoring information encountered in the literature
8 comes from the field study by Barnes et al. (1985). The only information from this study
9 is that strychnine was not detected in a blue grouse (*Dendragapus obscurus*) found dead
10 after an application of 0.5% strychnine treated bait. The limit of detection is given by
11 Barnes et al. (1985) as less than 0.01 ppm. The lack of strychnine residues in grouse,
12 even if strychnine were available, may be expected. In the toxicity study on sage grouse,
13 Ward et al. (1942) noted that sage grouse will not voluntarily consume strychnine treated
14 bait.

15
16 Other than small mammals and ground squirrels, the groups of vertebrates that might
17 consume incidental amounts of strychnine treated bait on the ground surface are birds.
18 Not all birds will consume bait, despite its availability above ground. In fact, some birds,
19 such as grouse, may avoid strychnine, while other species, such as ducks, will freely
20 consume strychnine treated bait if it is available (Wobeser and Blakley 1987). In the
21 field study on owls, James et al. (1990) indicate that several bird species appear to be
22 attracted to treated fields.

23
24 Because of the lack of adequate monitoring data, the risk characterization for the primary
25 consumption of bait in typical below-ground applications of strychnine is based primarily
26 on field studies, as discussed further in Section 4.4.2.2. Nonetheless and as a purely
27 exploratory effort, consumption factors of 2×10^{-5} (2×10^{-6} to 2×10^{-4}) are used for birds that
28 might consume incidental amounts of strychnine treated bait from the ground surface. As
29 detailed in Worksheet F05g, these consumption factors lead to estimated doses of about
30 0.008 (0.0008 to 0.08) mg/kg bw. The central estimate is somewhat below the 0.01 ppm
31 limit of detection in the study by Barnes et al. (1985) in which no strychnine was found in
32 a dead grouse. As with the other primary exposure scenario, the birds specifically used in
33 exposure assessments are the small passerine (Worksheet F05d), mallard (Worksheet
34 F05e), pigeon (Worksheet F05f), and quail (Worksheet F05g). These exposure estimates
35 are regarded as little more than a rationalization of the reported lack of effects in birds,
36 other than raptors, in field studies involving below-ground hand baiting.

37 **4.2.2.3.3. Bears Foraging on Gopher Caches**

38 As with the exposure scenarios for misapplications (Section 4.2.2.2), large grazing
39 mammals, such as deer, are not included in the exposure scenarios for primary
40 consumption. While deer and other mammals might consume incidental amounts of bait,
41 there is no basis for asserting that these exposures might be toxicologically significant.

42
43 Grizzly bears, on the other hand, do feed on pocket gopher food caches—i.e., below-
44 ground areas where gophers store food, including strychnine treated bait. Grizzly bear

1 foraging for pocket gopher food caches is well documented and appears to occur
2 primarily in early to mid-spring (e.g., Mattson 2004; National Park Service 2000, p. 41).
3 The potential risk to grizzly bears from the consumption of gopher caches is the primary
4 focus of the Barnes et al. (1985) study. Consequently, the exposure assessment for bears
5 feeding on gopher caches given in the current Forest Service risk assessment relies
6 heavily on the publication by Barnes et al. (1985).

7
8 As noted in Table 5, the use of strychnine in grizzly bear habitats is prohibited ... *except*
9 *under programs and procedures approved by the U.S. EPA*. Thus, grizzly bear exposure
10 to strychnine resulting from foraging on the food caches of pocket gophers may be a very
11 atypical event. Also, the notion of other bear species foraging on gopher food caches
12 seems unlikely. Black bears will only occasionally forage on pocket gopher food caches,
13 because black bears are less well adapted than grizzly bears to digging (Mattson no date).
14 Black bears would most likely forage for gopher food caches only in areas with a
15 significant snow pack and only in early spring during snow melt (Mattson 2010). The
16 application of strychnine during a time in which there is a significant snow pack is
17 improbable. No information is available on other mammals that might feed on of pocket
18 gopher food caches.

19
20 The current Forest Service risk assessment includes an exposure scenario for the
21 consumption of a pocket gopher food cache by a grizzly bear. This exposure scenario
22 involves what is likely to be a very rare event and is given primarily to illustrate the
23 potential hazards of using strychnine in grizzly bear habitat, as well as to encompass
24 incidents in which other mammals might occasionally forage on gopher food caches.

25
26 The body weight of grizzly bears is highly variable. Smith et al. (2003) give weights
27 ranging from 139 to 206 kg. Barnes et al. (1985) consider grizzly bear body weights of
28 34 kg (presumably a young bear) to 155 kg. For this exposure scenario, a body weight of
29 100 kg is used—i.e., a relatively small adult bear with a body weight typical of an adult
30 black bear (Smith et al. 2003).

31
32 Unlike other primary exposure scenarios, the amount of food, hence the amount of
33 strychnine, consumed will not depend on the food consumption rates of the receptor.
34 Again using allometric relationships from U.S. EPA/ORD (1993, Eq. 3-7, p. 3-6), the
35 amount of food that would be consumed per day by a 100 kg mammal is about 3 kg dry
36 weight—i.e., $0.0687 \times (100 \text{ kg})^{0.822} \approx 3.025 \text{ kg}$. Barnes et al. (1985) excavated 10 food
37 caches and noted dry weights of 22-196 grams, and Mattson (2004) reports a mean (\pm SE)
38 mass of 38.8 (\pm 9.4) grams, also for 10 food caches. All of these amounts are far less than
39 the daily food requirements of a 100 kg bear. Thus, the exposure of the bear to
40 strychnine from the consumption of a food cache will be limited only by the amount of
41 strychnine in the cache and the proportion of the cache that the bear consumes.

42
43 In the exposure assessment developed for a grizzly bear by Barnes et al. (1985), the
44 assumption is made that the bear consumes all of the cache. As noted by Barnes et al.
45 (1985) this is a conservative assumption because bears will often consume only succulent
46 vegetation. As also noted by Mattson (2004, p. 735), grizzly bears may only partially

1 consume the contents of the cache—i.e., only about 6 g of a 44-g food cache or 13%. In
2 the current Forest Service risk assessment, the working assumption is that a bear may
3 consume from 10 to 100% of the caches with a central estimate of 30%, the approximate
4 geometric mean of the range.

5
6 The amount of strychnine in the food cache is based on monitoring data from Barnes et
7 al. (1985). Barnes et al. (1987) monitored 10 caches and found detectable strychnine
8 residues in three caches, reporting an average amount of 17 mg with a range of 6.8-36.3
9 mg. Thus, the three monitored values were 6.8, 7.9, and 36.3 mg. The reported amounts
10 in gopher nests are an average of 11.2 mg with a range of 0.2-51.2 mg (Barnes et al.
11 1985, Table 3, p. 555). In their exposure assessment, Barnes et al. (1985, p. 556) use an
12 upper bound exposure of 51.2 mg. The current Forest Service risk assessment takes a
13 modestly more conservative approach. Assuming a log-normal distribution, the three
14 values for the food caches are used to calculate a mean and 95% confidence interval of
15 12.5 (1.25 to 125) mg.

16
17 As detailed in Worksheet G08, the estimated doses to the bear are about 0.04 (0.001 to
18 1.25) mg/kg bw. Barnes et al. (1985) do not explicitly report mg/kg bw doses; however
19 the study provides the example of a 34 kg bear consuming 51.2 mg of strychnine. This
20 amount corresponds to a dose of about 1.5 mg/kg bw [$51.2 \text{ mg} \div 34 \text{ kg} \approx 1.506 \text{ mg/kg}$
21 bw], which is a somewhat higher dose estimate than the upper bound used in the current
22 Forest Service risk assessment. As discussed further in Section 4.4.2.1, this minor
23 difference has no impact on the risk characterization.

24 **4.2.3. Secondary Exposures**

25 Secondary exposures—i.e., the consumption of prey contaminated with strychnine—are
26 handled similarly to the consumption of gopher caches by a bear, detailed in the previous
27 subsection (Section 4.2.2.3.3).

28
29 The predator species used in the exposure scenario are a 13 kg coyote (Worksheet F09a),
30 a 7 kg badger (Worksheet F09b), a 1 kg mink (Worksheet F09c), a 1.5 kg great horned
31 owl (Worksheet F09d), and a 0.5 kg rattlesnake (Worksheet F09e). The coyote and mink
32 are selected because toxicity data are available on these species (Table 14). In addition,
33 coyotes and mink (as well as several other types of mustelids) will prey on and consume
34 pocket gophers (e.g., Anthony et al. 1984; Marsh et al. 1987; Prince 1994). The badger is
35 included as a fossorial predatory mammal that preys on pocket gophers. As discussed in
36 Section 4.1.2.2.4, mustelids are presumed to be a species at risk (Anthony et al. 1984;
37 Nolte and Wagner 2001), although adverse effects on mustelids have not been
38 documented in field studies. The great horned owl is selected as a predator species to
39 represent a relatively small but sensitive raptor (Table 15) and to explore the plausibility
40 of potential adverse effects in owls noted in the field study by James et al. (1990). The
41 rattlesnake is selected as a representative predatory reptile and because the anecdotal
42 report by Campbell (1982) indicates that rattlesnakes prey on poisoned rodents.

43
44 The most likely prey species are pocket gophers or ground squirrels. As summarized in
45 Table 16, field studies provide adequate information on the concentrations of strychnine

1 in pocket gophers and ground squirrels. Concentrations in pocket gophers are higher at
2 the upper bounds of documented concentrations —i.e., about 90 ppm (Evans et al. 1990),
3 compared with an upper bound of about 13 ppm in mice, based on field monitoring data
4 (Barnes et al. 1985). For the current Forest Service risk assessment, a 75 gram pocket
5 gopher is used as the prey species. The estimated concentration in the gopher is 10 (1 to
6 100) ppm, which is equivalent to 10 (1 to 100) mg a.i./kg bw. For each of the receptors,
7 the working assumption is that a single gopher is consumed. For the mink, owl, and
8 snake, this assumption is a reasonable upper limit. A coyote might consume more than
9 one gopher, and this possibility is considered in the risk characterization (Section 4.4).

10
11 The most difficult aspect of the exposure assessment involves the proportion of the prey
12 that will be consumed by the predator as well as the body parts that will be consumed.
13 Consistent with distribution in experimental mammals (Section 3.1.3.1), numerous
14 studies in mammalian wildlife indicate that a substantial proportion of strychnine will
15 remain in the gastrointestinal tract or cheek pouches of poisoned pocket gophers and
16 other rodents (e.g., Anthony et al. 1984; Barnes et al. 1985; Colvin et al. 1987; Hegdal
17 and Gatz 1976; Marsh et al. 1987; Record and Marsh 1988; Redig et al. 1982; Schitoskey
18 1975). Anthony et al. (1984) provide the most extreme data, indicating the
19 approximately 99% of the ingested strychnine remains in the gastrointestinal tract of
20 ground squirrels. In pocket gophers, the field monitoring data from Barnes et al. (1985)
21 indicate that about 70% of the body burden in pocket gophers is found in the
22 gastrointestinal tract. Conversely, Fagerstone et al. (1980) noted concentrations of 0.29
23 and 0.35 ppm in the bodies of two poisoned chipmunks. In one chipmunk, the
24 concentration of strychnine was only 0.1 ppm, and no strychnine was found in the
25 gastrointestinal tract of the other chipmunk. It seems reasonable to suppose that animals
26 that hastily feed on bait will rapidly absorb a lethal amount of strychnine, very large
27 proportions of which will remain in the gastrointestinal tract. Conversely, animals that
28 consume contaminated bait at a slower rate might be able to absorb a greater proportion
29 of the ingested strychnine.

30
31 The amount of strychnine in the gastrointestinal tract, relative to the amount of strychnine
32 in the muscle tissue and other organs is important because field observations indicate that
33 some mammalian predators (Marsh et al. 1987) as well as some avian predators and
34 scavengers (Graham 1977) generally avoid consuming the gastrointestinal tract of
35 poisoned rodents.

36
37 The working assumption in the current Forest Service risk assessment is that mammalian
38 or avian predators might consume 30% (1 to 80%) of the strychnine in a gopher. This
39 assumption is based on various reports of the amount of strychnine detected in the
40 gastrointestinal tract of rodents. The lower bound of 1% is based on the observations
41 from Anthony et al. (1984)—i.e., 99% of the strychnine in the gastrointestinal tract. The
42 central estimate of 30% is based on the study by Barnes et al. (1985)—i.e., 70% of the
43 strychnine in the gastrointestinal tract. The upper bound of 80% is judgmentally based
44 on the data from Fagerstone et al. (1980) indicating that a substantial amount of
45 strychnine may be absorbed from the gastrointestinal tract of some poisoned rodents. In
46 addition, except for the snake, it is plausible to assume that the predator might not

1 consume all of the prey species. This supposition is similar to the variations in the
2 proportion of a food cache consumed by a bear, as discussed above. For reptiles, a
3 simpler approach is justified, and the assumption is that the reptile completely consumes
4 the gopher.

5 **4.2.4. Tertiary Exposures**

6 Tertiary exposures refer to the consumption of a lower order of contaminated prey (e.g., a
7 mink that ate a poisoned gopher—i.e., *secondary exposure*) by a higher order of prey
8 (e.g., a coyote or raptor—i.e., *tertiary exposure*). Any number of tertiary exposure
9 scenarios could be developed; however, the current Forest Service risk assessment
10 focuses on small predators that consume contaminated insects and develops exposure
11 scenarios for a small mammal (Worksheet 10a), a small bird (Worksheet 10b), and a
12 bullfrog (Worksheet 10c). The consumption of contaminated insects by a small mammal
13 (20 g) and small bird (10 g) are standard exposure scenarios in most Forest Service risk
14 assessments. In the current ecological risk assessment, the reasons for considering a
15 young (20 g) bullfrog are that data are available on this species (Section 4.1.2.3.2), this
16 species is considered in the assessment of strychnine by Arjo et al. (2006), and
17 information is available on the consumption of insects by this species.

18
19 For Forest Service risk assessments on insecticides and herbicides, the residues of
20 pesticides on insects are based on the empirical relationships between broadcast
21 application rates and residues on insects recommended by Fletcher et al. (1994). These
22 methods are not applicable to applications of strychnine for rodent control. Stahl et al.
23 (2004) assayed strychnine residues in insects feeding on the carcasses of poisoned
24 gophers, and these data are used in the assessment by Arjo et al. (2006) of risks to small
25 mammals, small birds, and the bullfrog. Arjo et al. (2006, p. 184) uses 0.2756 µg/g as
26 the concentration of strychnine in insects, which is same as the upper 95th percentile from
27 the analysis of strychnine residues in adult Diptera feeding on gopher carcasses from
28 Stahl et al. (2004).

29
30 Forest Service risk assessments prefer to assess risks based on central estimates as well as
31 upper and lower bounds. Stahl et al. (2004) do not specify percentile values for the seven
32 groups of insects covered in their analysis. As summarized in Table 19, Stahl et al.
33 (2004) assayed strychnine residues in seven groups of insects that had fed on pocket
34 gophers poisoned with strychnine following a baiting application in a national forest.
35 Maximum concentrations in the different groups of insects range from about 0.05 µg/g
36 (wasps) to about 0.7 µg/g (Diptera larvae). Assuming a log-normal distribution, the 95%
37 confidence interval for the maximum values is 0.196 (0.067 to 0.572) µg/g (Table 19).
38 As a modestly more conservative approach than that taken by Arjo et al. (2006), these
39 values are rounded to one significant place—i.e., 0.2 (0.07 to 0.6) µg/g—and used in the
40 EXCEL worksheets to estimate doses to the tertiary receptors.

41
42 Arjo et al. (2006) assume that 100% of the receptors' diet is contaminated. This is the
43 standard assumption in exposure assessments for insectivores in most Forest Service risk
44 assessments involving broadcast applications. For broadcast applications, this
45 assumption is plausible; however, it is less plausible for hand baiting of strychnine. In

1 the absence of monitoring data which could be used to set objective bounds, the
2 assumption is made that 30% (10 to 100%) of the diet of the predators consists of
3 contaminated insects.

4
5 The mass of the insects which the receptors might consume is based on allometric
6 relationships from the EPA for the small mammal (U.S. EPA/ORD 1993, Eq. 3-8, p. 3-6)
7 and small bird (U.S. EPA/ORD 1993, Eq. 3-3, p. 3-3). The EPA has not developed an
8 allometric relationship for the bullfrog, but provides sufficient information to do so.
9 Consequently, an allometric relationship is developed for the bullfrog, as summarized in
10 Figure 15. For a small (20 g) bullfrog, the estimated food consumption is 1.82 g or about
11 9% of body weight. This estimate is modestly higher than the 7% estimate used by Arjo
12 et al. (2005). Arjo et al. (2005) do not specify the body weight of the frog; nonetheless, a
13 fractional food consumption rate of 0.07 is consistent with a 27 g frog.

14 ***4.2.4. Consumption of Surface Water and Fish***

15 The exposure assessments associated with the consumption of contaminated surface
16 water and contaminated fish parallel those used in the human health risk assessment.
17 Exposure scenarios are presented for the consumption of contaminated surface water or
18 fish following an accidental spill as well as the consumption of water or contaminated
19 fish associated with peak and longer-term concentrations of strychnine in surface water
20 which might be expected from runoff, sediment loss, and percolation. The exposure
21 scenario for the accidental spill is detailed in Section 3.2.3.4.1. As discussed in this
22 section, the accidental scenario involves the spill of 30 (20-40) pounds of a 0.5%
23 formulation into a small pond in which estimated water concentrations of strychnine are
24 68 (45 to 91) ppb ($\mu\text{g/L}$). This range of concentrations also encompasses reports from
25 the Forest Service indicating that strychnine concentrations of 13-23 ppb were monitored
26 after below-ground applications of strychnine were followed by severe rainstorms—i.e.,
27 the report by Podsiadlo (1998) discussed in Section 3.2.3.4.5.

28
29 At an application rate of 1 lb/acre of a 0.5% formulation, the peak and longer-term
30 expected concentrations of strychnine in surface water are much lower. The estimated
31 peak concentrations are 0.01 (0.0035 to 0.125) ppb (e.g., Worksheet D05), and the
32 longer-term estimated concentrations are 0.005(0.0035 to 0.014) ppb (e.g., Worksheet
33 D07). Notably, the worksheets specify the concentrations in units of mg/L or ppm rather
34 than $\mu\text{g/L}$ or ppb. Units of mg/L follow the convention used for pesticide concentrations
35 in ambient water in all worksheets developed by WorksheetMaker (SERA 2009).

36
37 The receptors used in these exposure assessments include a small mammal (20 g), a canid
38 (5 kg), a large mammal (70 kg), a small bird (20 g), and a large bird (4 kg). These are
39 standard receptors used in all Forest Service risk assessments for the exposure scenarios
40 associated with the consumption of contaminated water. As discussed further in Section
41 4.3 (the dose-response assessment for the ecological risk assessment), the current Forest
42 Service risk assessment is somewhat atypical in that separate toxicity values are
43 developed for raptors (highly sensitive species), waterfowl and passerines (sensitive
44 species), pigeons (intermediate sensitivity), and game fowl (tolerant species).

1 In standard Forest Service risk assessments, the consumption of contaminated water by a
2 large bird is typically based on a 4 kg Canada goose. The consumption of contaminated
3 fish is typically represented generically using toxicity data on the most sensitive group of
4 birds. Because of the high sensitivity of raptors to strychnine, a 4 kg raptor is used rather
5 than the Canada goose as the representative large bird consuming contaminated water and
6 fish. For the small bird, the receptor is taken as a sensitive passerine.

7 ***4.2.5. Aquatic Organisms***

8 The exposure assessment for aquatic organisms parallels the exposure assessment for the
9 consumption of surface water by nontarget terrestrial species. As discussed in the
10 previous subsection, exposure scenarios are presented for the consumption of
11 contaminated surface water following an accidental spill as well as expected peak and
12 longer-term concentrations of strychnine in surface water.
13

1 **4.3. DOSE-RESPONSE ASSESSMENT**

2 **4.3.1. Overview**

3 Table 20 summarizes the toxicity values used in the ecological risk assessment. The
4 derivation of each of these values is discussed below. The available toxicity data support
5 separate dose-response assessments in two subgroups of mammals (carnivores and
6 omnivores), three subgroups of birds (raptors, sensitive species of non-raptors, and other
7 tolerant orders of birds), reptiles, terrestrial phase amphibians, and three subgroups of
8 aquatic organisms (fish, aquatic phase amphibians, and aquatic invertebrates). The units
9 of measure are different for the various groups of organisms, depending on the nature of
10 exposure and the way in which the toxicity data are expressed.

11
12 The dose-response assessments for mammals and birds are the most complex, reflecting
13 the types and amounts of available data. To the extent possible, the toxicity data used for
14 each subgroup are based on the nature of exposure. For carnivores, including terrestrial
15 phase amphibians and reptiles, the dose-response is based on studies involving the
16 consumption of contaminated prey. In the absence of these types of studies, the dose-
17 response assessment is based on gavage studies. For the other subgroups, plausible
18 exposures involve the consumption of contaminated bait (primary exposure), and the
19 dose-response assessment is based on dietary studies. Particularly for birds, this
20 approach results in less than conservative dose-response values; however, the approach is
21 justified by the mode of plausible exposures.

22
23 Although the dose-response values derived for aquatic animals are relatively standard, the
24 dose-response assessment is abbreviated because the amount of data is limited and
25 because the potential for exposure is fairly low for these organisms. A dose-response
26 assessment is not developed for plants, since strychnine does not appear to be hazardous
27 to plants. Similarly, no dose-response assessment is developed for terrestrial
28 invertebrates or soil microorganisms because of limitations in the available data. As an
29 alternative, risks to terrestrial invertebrates and soil microorganisms are addressed
30 qualitatively in the risk characterization.

31 **4.3.2. Toxicity to Terrestrial Organisms**

32 **4.3.2.1. Mammals**

33 In typical pesticide risk assessments conducted by the Forest Service, the dose-response
34 assessment for mammalian wildlife is adopted directly from the human health risk
35 assessment, and a single toxicity value is derived for the most sensitive mammalian
36 species. Occasionally, a separate toxicity value is derived for carnivorous mammals.

37
38 As discussed in Section 4.1.2.1, strychnine toxicity data for mammalian wildlife are
39 atypically robust and clearly justify the derivation of separate toxicity values for different
40 mammalian species. Also, as noted in Section 4.2.2 (Exposure Assessment for Mammals
41 and Birds), strychnine exposures vary according to particular characteristics of
42 mammalian species—e.g., habit, size, diet, etc. Small mammals, such as the target
43 species and certain other small fossorial rodents, are at greatest risk of exposure from the

1 consumption of strychnine treated bait—i.e., primary exposure. Predatory mammals,
2 such as weasels and coyotes, are at greatest risk from the consumption of poisoned
3 mammals—i.e., secondary exposures. Omnivorous mammals might be exposed to
4 strychnine from the consumption of insects which feed on the decaying carcasses of
5 poisoned mammals—i.e., tertiary exposure. To accommodate the various types of
6 exposures as well as the available data regarding differences in the toxicity of strychnine
7 to various groups of mammals, separate toxicity values are derived for mammalian
8 carnivores and omnivores.

9 ***4.3.2.1.1. Carnivores***

10 Among mammals, carnivores are more sensitive than omnivores or herbivores to
11 strychnine (Section 4.1.2.1, Figures 8 and 10). Sensitivity to strychnine varies among
12 carnivores with estimates of lethal doses ranging from 0.5 mg/kg bw—i.e., bears (Inukai
13 1969)—to about 2.1 mg/kg bw—i.e., coyotes (Marsh et al. 1987). The range of
14 sensitivities, however, is relatively modest and does not justify the derivation of separate
15 toxicity values.

16
17 While the hazard identification for mammals focuses on lethal dose estimates, the Forest
18 Service approach differs from that of the EPA. The Forest Service prefers to use NOEC
19 values rather than LD₅₀ values for dose-response assessments, even for acute effects.
20 Bears appear to be the most sensitive species, based on the study by Inukai (1969), which
21 reports an NOEC of 0.25 mg/kg bw in one of only three bears studied. This value is
22 supported by an NOEC of 0.286 mg/kg bw in coyotes (Marsh et al. 1987). Both of these
23 NOECs, however, are very close to the lethal dose of 0.5 mg/kg bw in bears; moreover,
24 both NOECs are based on very small numbers of animals. Given the substantial
25 variability in strychnine toxicity within species (Section 3.1.4), it seems reasonable to
26 assert that NOECs ranging from 0.25 to 0.286 mg/kg bw might not be protective of
27 mammalian carnivores, in general.

28
29 As discussed in Section 3.3.2, the acute RfD used in the human health risk assessment is
30 0.02 mg/kg bw. This RfD is derived from the threshold limit value proposed by the
31 American Conference of Governmental Industrial Hygienists (ACGIH 2001). This TLV
32 is based on the lower bound of the range of therapeutic doses once prescribed to humans.

33
34 The dose of 0.02 mg/kg bw is used as a reasonably protective NOEC for mammalian
35 carnivores. Using this NOEC is fundamentally equivalent to using the NOEC of 0.25
36 mg/kg bw in bears (Inukai 1969) and applying an uncertainty factor of 10 to account for
37 sensitivity differences within populations of mammalian carnivores. Uncertainty factors
38 are not typically used in ecological risk assessments; however, the approach seems
39 justified for strychnine. The approach is analogous to the one used in most human health
40 risk assessments of applying an uncertainty factor of 10 to account for sensitive
41 individuals within the general population (e.g., SERA 2007a, Table 3-5).

42
43 Adopting the acute surrogate RfD of 0.02 mg/kg bw does not appear to be overly
44 conservative. As illustrated in Figure 10, humans appear to be somewhat less sensitive
45 than mammalian carnivores to strychnine—i.e., the lowest documented lethal dose in an

1 adult human is about 2.25 mg/kg bw (Salm 1952), a factor of about 5 greater than the
2 lowest documented lethal dose of 0.5 mg/kg bw in a mammalian carnivore (Inukai 1969).

3 **4.3.2.1.2. Other Mammals**

4 While pocket gophers are the target species for strychnine, they are clearly not the most
5 sensitive species, even excluding mammalian carnivores. As summarized in Table 14
6 and illustrated in Figure 10, horses (Meek and Keatts 1971) and ground squirrels
7 (Anthony et al. 1984) appear to somewhat more sensitive than pocket gophers to
8 strychnine. More tolerant species include nutria, opossum, and mule deer.

9
10 As discussed in Section 4.2, exposures of large herbivorous mammals to strychnine are
11 likely to be negligible in below-ground applications of strychnine treated bait. The
12 species at greatest risk are likely to be burrowing mammals, such as mice and chipmunks.
13 As discussed further in Section 4.4.2.1 (risk characterization for mammals), incidental
14 mortality in mice and chipmunks are documented in field studies (Section 4.4.2.1).

15
16 The intraperitoneal LD₅₀ values for mice exposed to strychnine range from 14 to 48
17 mg/kg bw (Lamanna and Hart 1968), as summarized in Appendix 2 and discussed in
18 Section 4.1.2.1.1. The lower bound of this range is higher than the oral LD₅₀ of 3.6
19 mg/kg bw in ground squirrels (Anthony et al. 1984). In general, it is reasonable to expect
20 that oral LD₅₀ values will be greater than intraperitoneal LD₅₀ values. Thus, the data on
21 mice and ground squirrels suggest that the oral LD₅₀ in ground squirrels could serve as a
22 conservative toxicity value for small mammals, like mice and chipmunks. In the absence
23 of an oral NOEC, the LD₅₀ of 3.6 mg/kg bw is divided by a factor of 10 to approximate
24 an NOEC of 0.36 mg/kg bw. This estimated NOEC is rounded to 0.4 mg/kg bw and is
25 used as the toxicity value for herbivorous mammals. This approach is analogous to the
26 use of a 0.1 level of concern in EPA risk characterizations for acute toxicity in threatened
27 and endangered terrestrial animals, based on an LD₅₀ (SERA 2007a, Table 4-2).

28 **4.3.2.2. Birds**

29 As with the toxicity data on mammals, the available toxicity data on birds suggest that
30 some orders of birds, including predatory birds (i.e., raptors), are more sensitive than
31 others (Section 4.1.2.2) to strychnine. Furthermore, sensitive orders of birds include not
32 only carnivorous orders but also avian waterfowl (Anseriformes) and perching birds
33 (Passeriformes). The more tolerant groups of birds include game birds or fowl
34 (Galliformes) and pigeons (Columbiformes).

35 **4.3.2.2.1. Raptors**

36 Based on data summarized in Table 15 and illustrated in Figure 13, raptors (Strigiformes,
37 Accipitriformes, and to a lesser extent the Accipitriformes, appear to be among the birds
38 most sensitive to strychnine. Within these groups, sensitivity varies substantially with
39 estimated lethal doses ranging from 0.94 mg/kg bw for the snowy owl (Redig et al. 1982)
40 to 10.75 mg/kg bw for the red-tailed hawk (Anthony et al. 1984).

41
42 As noted in the dose-response assessment for mammals, Forest Service risk assessments
43 do not use LD₅₀ values or estimated lethal doses in dose-response assessments. No

1 details are available on the estimated lethal dose of 0.94 mg/kg bw for the snowy owl
2 from Redig et al. (1982). Both Anthony et al. (1984) and Cheney et al. (1987) do provide
3 considerable detail on dose-response relationships in owls and hawks. In the great
4 horned owls, which are less sensitive than snowy owls, Cheney et al. (1987) reports an
5 NOEC of 1.0 mg/kg bw and frank effect levels (severe incoordination) at 2.5 mg/kg bw.
6 Anthony et al. (1984) do not identify an NOEC for great horned owls but note a similar
7 frank effect level (convulsions) at 2.1 mg/kg bw. In hawks, Cheney et al. (1987) reports
8 a NOEC of 2.0 mg/kg bw with an LOEC (mild incoordination) at 2.3 mg/kg bw.
9 Anthony et al. (1984) reports an NOEC in hawks of 2.9 mg/kg bw with a corresponding
10 frank effect level of 4.6 mg/kg bw. These studies involve small numbers of animals and
11 are similar to dose titrations in human clinical studies in which the dose is gradually
12 increased in order to identify a toxic threshold (Section 3.1.5.1). The very narrow ranges
13 between apparently nontoxic and toxic doses do not justify a reduced scaling factor for
14 estimating an NOEC from an LD₅₀.

15
16 The lowest reported lethal dose for raptors is 0.675 mg/kg bw, the lower bound on the
17 estimated lethal dose reported in Redig et al. (1982). Applying the standard factor of 10
18 and rounding to one significant digit, the toxicity value for raptors is taken as 0.07 mg/kg
19 bw. This value is very close to the NOEC of 0.02 mg/kg bw used for mammalian
20 carnivores (Section 4.3.2.1.1), and this similarity is appropriate given the overall
21 similarities in the toxicity of strychnine to mammals and birds.

22 ***4.3.2.2.2. Sensitive Non-Raptors (Waterfowl and Passerines)***

23 As discussed above and illustrated in Figure 13, the sensitivity of waterfowl and perching
24 birds (Passerines) to strychnine is in the range of sensitivities of raptors. The exposures
25 of raptors and sensitive non-raptors, however, are different. Raptors will typically be
26 exposed to strychnine through the consumption of poisoned prey (secondary exposure).
27 Waterfowl and Passeriformes are most likely to be exposed to strychnine through the
28 consumption of treated grain (primary exposure).

29
30 The dietary toxicity studies in mallards, discussed in Section 4.1.2.2.1, are the studies
31 most relevant to the dose-response assessment for sensitive avian species other than
32 raptors. The principal concern, however, with the dose-response assessment for
33 waterfowl is the duration of exposure. As discussed in Section 4.1.2.2.3 and illustrated in
34 Figure 14, mallards are the only species in which a dose-duration relationship is apparent;
35 however, this relationship is evident only between the 28-day (Sternier et al. 1998) and
36 20-week studies (Pedersen et al. 2000). Although the Pedersen et al. (2000) study is
37 relatively detailed, the focus of the study is on reproductive success rather than toxicity.
38 While signs of neurotoxicity were noted in the reproduction study at a dietary
39 concentration (68.9 ppm), which is below the NOECs in the subchronic studies (91.1
40 ppm), Pedersen et al. (2000) do not indicate when the onset of toxicity was observed.

41
42 As a very conservative approach, it can be assumed that the chronic NOEC for
43 neurotoxicity (33.2 ppm) should be applicable to acute exposures. In other words, the
44 group of mallards used in the reproduction study may have been more sensitive than the
45 groups used in the acute dietary or subchronic studies. This type of variability has been

1 noted in studies on pocket gophers (Section 4.1.2.1.2). Pedersen et al. (2000) do not
2 report specific values for food consumption in mallards. Using the standard food
3 consumption factor of 0.07 kg food/kg bw, the dietary concentration of 33.2 ppm would
4 correspond to a dose of about 2.3 mg/kg bw. This NOEC is virtually identical to the
5 lowest reported gavage LD₅₀ values in adult mallards—i.e., about 2.7 mg/kg bw from the
6 study by Hudson et al. (1984). Thus, even though the NOEC of 2.3 mg/kg bw is based
7 on a conservative assumption in terms of dietary toxicity—i.e., the chronic NOEC should
8 be applied to acute exposures—that toxicity value itself is very close to the LD₅₀ for
9 gavage exposure.

10
11 It is reasonable to assume that dietary exposures are less hazardous than gavage
12 exposures. As discussed extensively in the human health risk assessment, dietary
13 exposures entail a more gradual rate of exposure and probably a more gradual rate of
14 absorption. Thus, detoxification by the liver will permit the animal to consume a greater
15 amount of strychnine. This pattern is demonstrated clearly in the study by Evans et al.
16 (1990), as illustrated in Figure 7. Consequently, the current Forest Service risk
17 assessment uses the estimated NOEC of 2.3 mg/kg bw from the dietary study by
18 Pedersen et al. (2000) to characterize risks in sensitive avian species other than raptors.
19 Although this approach is not necessarily the most conservative in nature, it should
20 provide the most reasonable and realistic assessment of risks.

21 **4.3.2.2.3. Tolerant Orders of Birds**

22 The dose-response assessment for tolerant orders of birds parallels the approach used for
23 sensitive avian species other than non-raptors. As discussed in Section 4.1.2.2.2 and
24 illustrated in Figure 13, tolerant groups of birds include fowl (Galliformes) as well as
25 pigeons and related species (Columbiformes). Like waterfowl and perching birds, these
26 types of birds are most likely to be exposed to strychnine through the consumption of
27 contaminated bait (primary exposure). Thus, dietary toxicity studies are the most
28 relevant data.

29 **4.3.2.2.3.1. Fowl (Galliformes)**

30 As discussed in Section 4.1.2.2.3 and illustrated in Figure 14, the dietary studies in quail
31 require little interpretation. The dietary NOECs are virtually identical in acute, subacute,
32 and chronic studies, and the selection of the specific NOEC is inconsequential. Food
33 consumption estimates are available for both the subchronic study (Sterner et al. 1998) as
34 well as the chronic study (Pedersen et al. 2000). Body weight data, however, are most
35 clearly specified in the chronic study—i.e., about 200 g for quail—with a dietary
36 consumption of about 19 g/day. Thus, the NOEC of 1113.6 ppm is associated with a
37 dose of about $[1110 \text{ mg/kg diet} \times 19 \text{ g diet/bird} \div 200 \text{ g bw} \approx 105 \text{ mg/kg bw}]$. This is
38 higher than the estimated NOEC of 2.3 mg/kg bw for mallards by a factor of about 45.
39 The calculated NOEC of 105 mg/kg is rounded to 100 mg/kg bw and is used for the risk
40 characterization for tolerant orders of fowl (Galliformes).

41
42 As summarized in Table 15, the average gavage LD₅₀ for mallards is about 2.67 mg/kg
43 bw, and the average gavage LD₅₀ for quail is about 67.3 mg/kg bw. Thus, based on the
44 oral LD₅₀ studies, mallards are more sensitive than quail by a factor of about 26, which is

1 reasonably consistent with the differences in dietary NOECs—i.e., ≈ 1100 ppm for quail
2 and ≈ 33 ppm for mallard, differing by a factor of about 33. As with the dose-response
3 assessment for sensitive non-raptors (Section 4.3.2.2.3), using the NOEC based on
4 dietary toxicity studies is not necessarily the most conservative approach; nonetheless,
5 this toxicity value is most applicable to the types of exposures to which fowl would be
6 subject—i.e., the direct consumption of strychnine treated bait.

7 **4.3.2.2.3.2. Pigeons and Related Species (Columbiformes)**

8 As illustrated in Figure 13, pigeons may be classified as more tolerant to strychnine than
9 the more sensitive groups of birds—i.e., passerines, waterfowl, and raptors—but pigeons
10 appear to be somewhat more sensitive to strychnine than Galliformes. This difference is
11 also reflected in the acute dietary studies (Appendix 4, Table 2). The acute dietary LC_{50}
12 for quail is about 3500 ppm with an NOEC of 1250 ppm (U.S. EPA/OPP 1996d). As
13 discussed in Section 4.1.2.2.1, the study in pigeons by Schafer and Eschen (1986) does
14 not provide a statistical estimate of the acute dietary LC_{50} ; however, the LC_{50} can be
15 crudely approximated at about 3000 ppm.

16
17 More significantly, the dietary concentration of 0.2% or 2000 ppm is a frank effect
18 level—i.e., mortality rates were 17 and 33% at the 2000 ppm dietary level in the two
19 studies conducted by Schafer and Eschen (1986). Based on the dietary consumption data
20 provided by Schafer and Eschen (1986, Table 4, p. 278), fatally exposed pigeons in the
21 0.2% groups consumed strychnine at doses equivalent to about 27-70 mg/kg bw. Thus,
22 while the NOEC of 100 mg/kg bw is supported for Galliformes, as detailed in the
23 previous subsection, it cannot be applied to Columbiformes.

24
25 As discussed by Schafer and Eschen (1986), pigeons surviving the 0.2% dietary
26 concentration consumed less strychnine than the fatally exposed pigeon, and the authors
27 estimate a nonlethal dose of about 13 mg/kg bw. The signs of toxicity in the surviving
28 birds are characterized only as *...transient nonlethal effects*. As also noted by Schafer
29 and Eschen (1986), this nonlethal dose is above the gavage LD_{50} of about 7.7 mg/kg bw
30 as well as the LD_{90} of about 11 mg/kg bw. Thus, as with quail, dietary exposures of
31 pigeons to strychnine are less toxic than gavage exposures. For pigeons, however, the
32 differences between the gavage LD_{50} and lethal dietary exposures are not remarkable.

33
34 For the current Forest Service risk assessment, the non-lethal dose of 13 mg/kg bw noted
35 by Schafer and Eschen (1986) may be classified as an LOEC. This value is divided by a
36 factor of 3 to estimate an NOEC of 4 mg/kg bw [$13 \text{ mg/kg bw} \div 3 \approx 4.33 \text{ mg/kg bw}$]. As
37 detailed in SERA (2007a, Table 3-5), the EPA sometimes uses a factor of 3 rather than 10
38 to estimate an NOEC from an LOEC. The uncertainty factor of 3 for pigeons is justified
39 for two reasons. First, while Schafer and Eschen (1986) do not describe the toxic effects
40 in detail, they do indicate that the effects were transient. Second, and more importantly,
41 dividing the LOEC of 13 mg/kg bw by 10 yields an NOEC of about 1 mg/kg bw, is lower
42 than the estimated NOEC of 2.3 mg/kg bw for sensitive waterfowl and passerines
43 (Section 4.3.2.2.2). Given the sensitivities of waterfowl and passerines, relative to
44 pigeons (Figure 13), having a toxicity value for pigeons which is lower than the toxicity
45 value for waterfowl and passerines is not be sensible.

1 **4.3.2.3. Reptiles and Terrestrial Phase Amphibians**

2 **4.3.2.3.1. Reptiles**

3 As discussed in Section 4.2.3, reptiles may be exposed to strychnine through the
4 consumption of poisoned mammals, particularly poisoned pocket gophers, and one such
5 probable incident of exposure is documented by Campbell (1982). In the absence of
6 toxicity data in reptiles, U.S. EPA/OPP suggests that risk characterizations for reptiles
7 may be based on risk characterizations in birds. For strychnine, the relevant surrogate
8 species would be raptors. Using the risk characterization for raptors as a surrogate for the
9 risk characterization for reptiles is not an ideal approach for strychnine, because raptors
10 often avoid consuming the digestive tract of prey, which tends to reduce exposure. This,
11 however, is not the case with reptiles such as snakes.

12
13 As summarized in Section 4.1.2.3, one toxicity study is available in reptiles (Brock
14 1965). This is not an ideal study because the snakes used in the bioassay were used as
15 well in bioassays of other rodenticides. In addition, the doses to the individual snakes
16 cannot be determined. The estimated average dose is about 3.6 mg/kg bw. As illustrated
17 in Figure 13, the estimated oral LD₅₀ of 3.6 mg/kg bw is in the range of toxicity values
18 for predatory birds. Applying the standard approach to estimating an NOEC by dividing
19 the LD₅₀ by a factor of 10 and rounding to one significant place, the LD₅₀ of 3.6 mg/kg
20 bw could be used to estimate an NOEC of about 0.4 mg/kg bw. Given the limitations in
21 the toxicity study by Brock (1965), however, a more conservative approach is justified,
22 and the estimated NOEC of 0.07 mg/kg bw for raptors is used. In other words, rather
23 than using the risk characterization for raptors as a surrogate for the risk characterization
24 in reptiles, the toxicity data on raptors are used as a surrogate for toxicity to reptiles.

25
26 The estimated NOEC for raptors of 0.07 mg/kg bw (Section 4.3.2.2.1) is about a factor of
27 about 50 below the estimated oral LD₅₀ of 3.6 mg/kg bw in snakes from the Brock (1965)
28 study. Thus, the estimated NOEC for snakes is about a factor of 5 below the toxicity
29 value that could be derived from the Brock (1965) study—i.e., the approach used in the
30 dose response assessment for reptiles is equivalent to dividing the LD₅₀ by a factor of 50
31 rather than the more conventional factor of 10. Given the uncertainties in the dose
32 estimates from the Brock (1965) study—i.e., the lethal doses in some of the snakes may
33 have been substantially below 3.6 mg/kg bw—using the more conservative toxicity value
34 for raptors seems warranted.

35 **4.3.2.3.2. Terrestrial Phase Amphibians**

36 Toxicity data are available on terrestrial phase amphibians (Section 4.1.3.2), and
37 plausible exposures involve the consumption of contaminated insects (Section 4.2.3.2).
38 As discussed in Section 4.1.3.2, the only available oral LD₅₀ value is the LD₅₀ of 2.21
39 mg/kg bw in the bullfrog, *Rana catesbeiana* (Tucker and Crabtree 1970; Hudson et al.
40 1984).

41
42 In the absence of an NOEC, Forest Service risk assessments generally divide an LD₅₀ for
43 a terrestrial organism by 10 to estimate the NOEC and use a level of concern of 1
44 (HQ=1=LOC). This is mathematically equivalent to the approach used by U.S.

1 EPA/OPP to base acute risk characterizations for threatened and endangered terrestrial
2 species on an LC₅₀ and use a level of concern of 0.1. Taking this approach and rounding
3 to one significant place, the estimated NOEC for the frog is 0.2 mg/kg bw. Furthermore,
4 this estimate is supported by the parenteral NOEC of 0.1 mg/kg bw reported for another
5 species of frog (*Rana pipiens*) in the early study by Weis and Hatcher (1922).

6
7 Because an oral NOEC can be estimated for only one species, it is assumed that NOEC
8 applies to tolerant species. Potential risks to sensitive species are discussed qualitatively
9 in Section 4.4.2.3.2.

10 **4.3.3.4. Terrestrial Invertebrates**

11 No toxicity values are proposed for terrestrial invertebrates. While exposures to
12 terrestrial invertebrates will occur, the single toxicity study on terrestrial invertebrates—
13 i.e., the study on ants by Kostowski et al. (1965)—is not well documented in terms of
14 estimating doses; moreover, the exposure vehicle (honey) is not applicable to bait
15 applications. In addition, one very detailed field study (Deisch 1986) as well as less
16 detailed but credible observations from Nolte and Wagner (2001) suggests that toxicity to
17 insects will not be substantial. Consequently, risks to insects are addressed qualitatively
18 in this risk assessment (Section 4.4.2.3).

19 **4.3.2.5. Terrestrial Plants (Macrophytes)**

20 Given the lack of an identified hazard to terrestrial plants as well as the lack of toxicity
21 data on terrestrial plants, no dose-response assessment for this group of organisms is
22 proposed.

23 **4.3.2.6. Terrestrial Microorganisms**

24 As with terrestrial plants and for the same reasons, no dose-response assessment for
25 terrestrial microorganisms is proposed.

26 **4.3.3. Aquatic Organisms**

27 Forest Service risk assessments typically attempt to derive dose-response assessments for
28 acute and chronic toxicity in fish, amphibians, and aquatic invertebrates as well as
29 toxicity to aquatic macrophytes, algae, and sometimes aquatic microorganisms. When
30 possible, separate toxicity values are derived for sensitive and tolerant species. As
31 summarized in Section 4.2.5 and detailed further in Section 3.2.3.4, below-ground
32 applications of strychnine are not expected to lead to wide-spread or substantial
33 concentrations of strychnine in water. Nonetheless, some contamination of surface water
34 is plausible, and monitoring data provided by the Forest Service indicate that atypical
35 events may lead to somewhat higher concentrations of strychnine in surface water. Thus,
36 the standard approach to the derivation of acute toxicity values is taken in the following
37 subsections for fish, amphibians, and aquatic invertebrates. Because of the very limited
38 data available on these groups as well as the fact that the focus of this risk assessment is
39 on terrestrial organisms, the dose-response assessments for fish (Section 4.3.3.1),
40 amphibians (Section 4.3.3.2), and aquatic invertebrates (Section 4.3.3.3) are abbreviated.
41 No hazard to aquatic plants can be identified (Section 4.3.3.4).

1 **4.3.3.1. Fish**

2 Only acute toxicity data are available in fish. The NOEC reported is an NOEC of 0.5
3 mg/L for mortality in silversides (Dawson et al. 1977). This NOEC for mortality,
4 however, was associated with *slight effects*. No other details are available.

5
6 Following standard Forest Service practice, the lowest LC₅₀ of 0.76 mg/L—i.e., the
7 toxicity value for Bluegill sunfish summarized by U.S. EPA/OPP (1996d) is divided by a
8 factor of 20 and rounded to one significant digit to estimate an NOEC of 0.04 mg/L. This
9 approach is equivalent to the practice of U.S. EPA/OPP to base acute risk
10 characterizations for threatened and endangered species of aquatic animals on an LC₅₀
11 using a level of concern of 0.05 (e.g., SERA 2007a, Table 4-2).

12
13 The most tolerant species of fish appears to be the Japanese medaka with an LC₅₀ of
14 5.7 mg/L (Rice et al. 1997). Following the same approach used with sensitive species of
15 fish, the estimated NOEC is 0.3 mg/L [$5.7 \text{ mg/L} \div 20 = 0.285 \text{ mg/L} \approx 0.3 \text{ mg/L}$].

16 **4.3.3.2. Aquatic Phase Amphibians**

17 Very little data are available on aquatic phase amphibians. The study by Cuome et al.
18 (1978) notes developmental effects in toad embryos at 5 mg/L. While this is not a
19 standard toxicity study, it is plausible that embryos are a very sensitive life stage. In the
20 absence of an NOEC, the LOEC of 5 mg/L is divided by a factor of 10 to estimate an
21 NOEC of 0.5 mg/L.

22
23 Because data are available on only one species of aquatic phase-amphibians, the working
24 assumption is that toads are tolerant species. Accordingly, risks to potentially sensitive
25 species are addressed qualitatively (Section 4.4.3.2).

26 **4.3.3.3. Aquatic Invertebrates**

27 Only one toxicity study is available in invertebrates, an acute toxicity in *Daphnia magna*
28 with a reported LC₅₀ of 8 mg/L (U.S. EPA/OPP 1996d, MRID 41126503). Because this
29 is the only available toxicity study, the working assumption is that daphnids are tolerant,
30 not sensitive species. Following the same approach used with fish, the LC₅₀ is divided by
31 20 to estimate an NOEC of 0.4 mg/L.

32 **4.3.3.4. Aquatic Plants**

33 As with terrestrial plants, there is no identifiable hazard to aquatic plants. Consequently,
34 no dose-response assessment for this group of organisms is proposed.

35
36

1 4.4. RISK CHARACTERIZATION

2 4.4.1. Overview

3 In the normal and anticipated below-ground application of strychnine to control pocket
4 gophers, adverse effects on fossorial rodents are inevitable. Adverse effects on this group
5 of organisms are amply demonstrated in multiple field studies. While not demonstrated
6 in field studies, adverse effects on mustelids and predatory snakes appear to be likely. At
7 least for predatory snakes, a probable case of a fatal exposure has been reported.

8
9 Strychnine cannot be applied in grizzly bear habits or in the habitats of some species of
10 fox or wolves without specific approval from the U.S. EPA. In the absence of this
11 limitation, adverse effects on grizzly bears through foraging on pocket gopher food
12 caches are plausible. Adverse effects on canid predators such as coyotes may be less
13 likely but effects in canid predators also appear to be plausible.

14
15 Many other aspects of the risk characterization for strychnine are accompanied by
16 substantial uncertainties and ambiguities. Almost all the uncertainty is associated with
17 the nature of or limitations in the data available to support the exposure assessments.
18 Several field studies indicate that adverse effects on raptors are not likely. A single field
19 study reports reduced body weight in adult owls and equivocal effects on reproductive
20 success that might be related to the consumption of poisoned rodents after a below-
21 ground application of strychnine. While this concern is supported by toxicity data in
22 sensitive species of birds, the association in the field observation is weak. Incident data
23 reported by the U.S. EPA indicate that adverse effects in raptors are possible; however,
24 all of the reported incidents occurred prior to the restriction of strychnine to below-
25 ground applications. Thus, the probability of observing adverse effects in raptors
26 associated with below-ground applications of strychnine is remote.

27
28 Accidental events or misapplications could lead to effects on a broader range of species.
29 If a large amount of strychnine is spilled onto the ground surface and not effectively and
30 promptly remediated, adverse effects are plausible in many species of birds and
31 mammals. The probability of misapplication of strychnine is not clear; however, this
32 issue is likely to be a concern only with burrow builder applications.

33
34 Very little information is available on the toxicity of strychnine to aquatic organisms.
35 Nonetheless, most exposures for aquatic organisms are below the level of concern. The
36 only exception involves fish in the event of an accidental spill or other atypical event. In
37 these cases, the upper bound of the concentration in water would modestly exceed the
38 level of concern.

39 4.4.2. Terrestrial Organisms

40 The risk characterization for terrestrial organisms could be based exclusively on field
41 studies (Table 16). This is essentially the approach taken in U.S. EPA/OPP (1994d). As
42 noted in Section 4.1.2.2.4, the field study by Evans et al. (1990) was submitted to the
43 U.S. EPA (MRID 42488601) in support of the registration of strychnine.

1
2 Forest Service risk assessments attempt to maintain consistency with the EPA. When
3 differing approaches are taken or when differing conclusions are reached, these
4 differences are explicated, as is the case with strychnine. Another complication is that
5 risk assessments sometimes present apparently ambivalent conclusions, which is also the
6 case with strychnine. Consequently, the conclusions reached by the U.S. EPA are quoted
7 below for clarity.

8
9 Based on field study data—i.e., the Evans study submitted to EPA and designated as
10 MRID 42488601—the Agency makes the following statements:

- 11
- 12 • *Hazards to nontarget avian species (and possibly*
13 *mammals) occur when using the burrow builder because of*
14 *spillage of the poisoned baits...*
 - 15
 - 16 • *Residues of strychnine in the gastro-intestinal tract of*
17 *pocket gophers exceed the Agency's unacceptable risk*
18 *criteria for nontarget organisms. Residues at those levels*
19 *could kill secondary consumers.*
 - 20
 - 21 • *There are sufficient data to presume that the proposed use*
22 *poses a "may effect" situation to endangered species, and*
23 *exposure to endangered species is expected if the baiting*
24 *operation is conducted in their currently occupied habit.*

25
26 *However, recent instructions for the burrow builder say that*
27 *the operators should pick up spilled bait; therefore, the*
28 *underground use of strychnine to control pocket gophers does*
29 *not pose an unacceptable risk to nontarget wildlife (MRID*
30 *42489601).*

31 U.S. EPA/OPP (1996d, p. 6-7)

32
33 Forest Service risk assessments sometimes base the risk characterization for ecological
34 effects in some receptors solely on field studies—e.g., the effects of *B.t.k.* on terrestrial
35 invertebrates (SERA 2004a). In other cases, the risk characterization can be based on
36 both field studies and independent estimates of exposure and toxicity using the hazard
37 quotient approach—e.g., the effects of tebufenozide on terrestrial invertebrates (SERA
38 2004b).

39
40 For strychnine, the risk characterization given in the current Forest Service risk
41 assessment is not based solely on field studies. Field studies are not used exclusively
42 because of limitations and ambiguities in these studies. For example, Hegdal and Gatz
43 (1976) provide an exceptionally detailed and large field study on burrow builder
44 applications. As discussed in Section 4.1.2.2.4.2, this study involved radio tracking of
45 groups of 36 raptors and 36 mammalian predators. While no adverse effects were noted,
46 only four raptors and eight of the mammalian predators could be tracked over the 3-week

1 post-application monitoring period. Thus, the actual observations consist of 0/4
2 responses in raptors and 0/8 responses in mammalian predators. Using the Wilson
3 interval (Brown et al. 2001; Wilson 1927) to take the upper 95% confidence limits on
4 these binomial responses, these data are consistent with upper bound risks of 40% for
5 raptors and 25% for mammalian carnivores. Ambiguities are illustrated in the study by
6 James et al. (1990) in owls. As discussed in Section 4.1.2.2.4.1 and noted further below,
7 this study is open to conflicting interpretations. Finally, none of the field studies
8 specifically addresses risks to mustelids, reptiles, or amphibians.

9
10 Because of these limitations, the use of the hazard quotient (HQ) approach for risk
11 characterization —i.e., the ratio of the anticipated exposure to a toxicity value—is used
12 along with the available field studies. While the toxicity data on strychnine are in many
13 ways exceptionally detailed (Section 4.3), many of the exposure assessments involve
14 substantial uncertainty and ranges of estimated doses that are very large (Section 4.2).
15 Consequently, the risk characterization for several groups of receptors involves hazard
16 quotients that range from far below a level of concern to substantially above a level of
17 concern. In other words, the risk characterization for strychnine is unavoidably
18 ambiguous.

19
20 A final limitation in the risk characterization for strychnine involves the use of field
21 studies. High confidence can be placed in risk characterizations that are based on
22 consistency between field studies and the independent application of the HQ method.
23 This is not the case with strychnine. As detailed in Section 4.2, field monitoring data are
24 used for several groups of receptors to calibrate the exposure assessment. Because of
25 this, several of the HQs are not independent of the field observations. Thus, while the
26 HQ method is consistent with field studies for several groups of receptors, this
27 consistency may be viewed as an artifact of the manner in which the exposure
28 assessments are developed.

29
30 Worksheet G02 includes the HQs for accidental and non-accidental acute exposures as
31 well as chronic exposures. None of the chronic exposures approach a level of concern,
32 and the risk characterization for these exposure scenarios is not otherwise considered.

33 ***4.4.2.1. Mammals***

34 ***4.4.2.1.1. Primary Consumers, Mammals***

35 While many uncertainties and ambiguities are inherent in the risk characterization for
36 strychnine, adverse effects including death in some fossorial rodents are virtually
37 inevitable even in properly conducted below-ground hand baiting. These effects are
38 documented in numerous field studies (Table 16). The hazard quotients for fossorial
39 mammals given in Worksheet G02 provide no substantial elaboration to this risk
40 characterization. As noted at the start of Section 4.4.2, these hazard quotients are
41 calibrated to the field observations.

42
43 The only nuance to the risk characterization for fossorial mammals involves the
44 prevalence of the adverse effects. The field study by Anthony et al. (1984, Table 1)
45 suggests that effects on ground squirrel populations could be substantial shortly after

1 baiting but that the populations would recover within a month or two. The lack of long-
2 term adverse effects is likely to be a pattern with many receptor groups. Citing several of
3 the field studies summarized in Table 16, Nolte and Wagner (2001) state that ...
4 *underground baiting of forest pocket gophers with 0.5 % strychnine-treated grain is*
5 *unlikely to induce long-term adverse effects on non-target wildlife species.* As noted in
6 Section 3.1.5 of the human health risk assessment, most uses of strychnine are unlikely to
7 produce any long-term adverse effects.

8
9 A 70 kg deer is considered as a primary consumer only in the event of an accidental spill.
10 This is an extreme exposure scenario in which it is assumed that a large amount of bait is
11 spilled and that effective remedial action is not taken. As with all accidental exposure
12 scenarios in Forest Service risk assessments, this scenario is provided only to indicate the
13 need for effective remediation. For a large accidental spill of strychnine, the need is
14 obvious, as reflected in the HQs of 7 (0.7 to 69) for the deer.

15
16 The only other primary consumer considered in this risk assessment is the grizzly bear.
17 As noted in Section 4.2.2.3.3, grizzly bears will forage for and consume gopher food
18 caches. The assessment of risks to grizzly bears from foraging on pocket nests or gopher
19 food caches is the focus of the field study by Barnes et al. (1985). Barnes et al. (1985) is
20 essentially a field study, designed to obtain information on potential grizzly bear
21 exposures to strychnine, and a mini-risk assessment.

22
23 The risk characterization from Barnes et al. (1985) mirrors the ambivalence and
24 ambiguity in the current Forest Service risk assessment on strychnine. Discussing the
25 two sites assayed in this paper, designated as *SAF* and *WBC*, these investigators note:

26
27 *...bait in pocket gopher nests and bait sets presents a low risk to*
28 *bears. The mean strychnine content nest of from SAF and WBC*
29 *(11.2 mg) represents a potentially lethal dose for bears weighing*
30 *≤34 kg; the maximum amount found (51.2 mg) could affect a 155-*
31 *kg bear.*

32 Barnes et al. (1985, p. 556)

33
34 As indicated in Worksheet G02, the HQs for a grizzly bear feeding on a gopher food
35 cache are 1.9 (0.06 to 63). These HQs are based on the exposure data from Barnes et al.
36 (1985) but use a lower toxicity value—i.e., the acute surrogate RfD of 0.02 mg/kg bw
37 from the human health risk assessment (Section 4.3.2.1.1). The central and lower bound
38 of the HQs are consistent with the above assessment from Barnes et al. (1985). In these
39 ranges of exposures, risks to bears would be low to negligible. The upper bound HQ of
40 63 is associated with a dose of 1.25 mg/kg bw. Based on the study by Inukai (1969), a
41 dose of 1.25 mg/kg would be lethal to a bear.

42
43 U.S. EPA/OPP (1996a,d) does not explicitly discuss risks to bears; however, the EPA
44 reflects concern for exposures to grizzly bears in that the product labels for all
45 formulations considered in the current Forest Service risk assessment place restrictions
46 on the use of strychnine in grizzly bear habitats.

4.4.2.1.2. Secondary Consumers, Mammals

Three secondary consumers are considered, a coyote, a badger, and a mink. The exposure scenarios for the coyote and badger are essentially a unit risk scenario for the consumption of one gopher. The exposure scenario for the mink also involves a single gopher, although it does not seem likely that a mink would consume more than one gopher in a single feeding event (Section 4.2.3). As with the grizzly bear, the HQs are based on a toxicity value of 0.02 mg/kg bw, the surrogate acute RfD derived in the human health risk assessment.

As with the HQs for the grizzly bears, the HQs for the secondary consumers vary from far below the level of concern to far above the level of concern—i.e., 0.9 (0.003 to 33) for the coyote, 2 (0.005 to 43) for the badger, and 11 (0.04 to 300) for the mink. The differences between these species reflect the differences in body size— i.e., coyote > badger > mink.

The lower bounds of the HQs are based on the assumption that most of the strychnine in the gopher will be in the gastrointestinal tract and that the predator will not consume the gastrointestinal tract. The rationale for these assumptions is discussed in Section 4.2.3. For the coyote, Marsh et al. (1987) provide support for the notion that coyotes will avoid consuming the intestinal tract of ground squirrels. It is less clear that this would be the case with small prey such as the pocket gopher. The study by Anthony et al. (1984) indicates that the toxicity of strychnine to mink may be modestly less when strychnine is administered in ground squirrel carcasses relative to gavage dosing—i.e., a gavage LD₅₀ of 0.6 mg/kg bw versus death in 2/5 mink fed strychnine in ground squirrel carcasses at a dose of about 0.96 mg/kg bw (Appendix 2). The extent to which mink or other mustelids would avoid feeding on the gastrointestinal tract of a poisoned gopher is not clear. Finally, as discussed in Section 4.2.3, the proportion of strychnine that would remain in the gastrointestinal tract of a poisoned pocket gopher or other rodent may be highly variable. As indicated in Worksheets G09a (coyote), G09b (badger), and G09c (mink), this uncertainty is encompassed by assuming that the predator consumes 0.3 (0.01 to 0.8) of the gopher without making an explicit assumption about the distribution of strychnine in the gopher or the parts of the gopher that are consumed.

While substantial uncertainty is reflected in the range of hazard quotients, these hazard quotients do clearly suggest a potential for risk. If a coyote were to completely consume a poisoned pocket gopher or consume parts of more than one pocket gopher, the dose to the animal could reach about 0.5 mg/kg bw, approaching an observed lethal dose for the coyote (Table 14). While many pocket gophers will die below ground and not be available to surface predators such as the coyote, some field studies indicate that a substantial proportion of poisoned rodents may be found on the ground surface (e.g., ground squirrels in Anthony et al. 1984).

Mink and other mustelids appear to be at substantially greater risk than coyotes. As illustrated in Figure 9, mink are among the mammalian species most sensitive to strychnine. In addition, mink and other mustelids will prey on gophers below ground. The central estimate of the HQ is associated with a dose of about 0.225 mg/kg bw, about

1 one-third of the LD₅₀ of 0.6 mg/kg bw (Anthony et al. 1984). The upper bound HQ is
2 associated with a dose of 6 mg/kg bw, above the LD₅₀ by a factor of 10. This severe risk
3 characterization for mustelids is consistent with more qualitative expressions of concern
4 for mustelids (Anthony et al. 1984; Nolte and Wagner 2001).

5
6 As with grizzly bears, U.S. EPA/OPP (1996a,d) does not provide risk quotients, which
7 are quantitative estimates of risk analogous to a hazard quotient, for secondary
8 consumers. Nonetheless, as with grizzly bears, the EPA's concern for secondary
9 consumers is reflected in use restrictions on habitats of the San Joaquin kit fox and the
10 gray wolf (Table 5). The determination that secondary consumers may be at risk is also
11 consistent with the U.S. EPA/OPP assessment that the below-ground application of
12 strychnine treated bait is *likely to adversely affect* the San Joaquin kit fox (U.S. EPA/OPP
13 2009, p.9, Table 1.1).

14
15 The clear potential for adverse effects in secondary consumers does not suggest that these
16 effects will be prevalent. Unlike the case with fossorial mammals (Section 4.4.2.1.1),
17 there are no field studies that note prevalent adverse effects in secondary consumers. The
18 field observations from Marsh et al. (1987) suggest that effects on coyotes are not likely
19 to be common and may be extremely rare. There are no field observations about
20 mustelids. While somewhat speculative, mortality or other adverse effects on mustelids
21 would seem to be more difficult to document in field studies, relative to effects on larger
22 surface-dwelling mammals.

23 ***4.4.2.1.3. Tertiary Consumers, Mammals***

24 In a conservative exposure scenario in which the upper bound of exposure is derived
25 from the assumption that a small mammal consumes only contaminated insects with an
26 upper bound residue based on maximum detected residues in insects (Section 4.2.4), the
27 HQs for tertiary consumption by a small mammals are below the level of concern by
28 factors of about 3 to 1250—i.e., HQs of 0.009 (0.0008 to 0.3). Relative to primary and
29 secondary consumers, risks to mammalian tertiary consumers are negligible. The risk
30 characterization is consistent with the risk characterization presented by Arjo et al.
31 (2005).

32 ***4.4.2.1.4. Water Consumption, Mammals***

33 As detailed in Section 3.2.3.4, the expected peak concentrations of strychnine in surface
34 water are based on extraordinarily conservative assumptions—i.e., that strychnine is
35 applied above ground. Based on these very conservative assumptions, the upper bounds
36 of the hazard quotients for mammals range from 0.00002 to 0.0005, which is below the
37 level of concern by factors of 2000-50,000.

38
39 As detailed in Section 3.2.3.4.5, the Forest Service has monitored strychnine in surface
40 water at concentrations exceeding those expected from estimates based on modeling
41 (Podsiadlo 1998). These higher than expected concentrations cannot be explained, but
42 they are encompassed by the accidental exposure scenario for the spill of a large amount
43 of strychnine into a small pond (Section 3.2.3.4.1). As summarized in Worksheet G02,
44 the upper bound hazard quotients for this accidental spill scenario range from 0.02 to 0.4,

1 below the level of concern by factors of 2.5-50. Given the risks to primary and secondary
2 consumers, these HQs are insubstantial.

3 **4.4.2.2. Birds**

4 **4.4.2.2.1. Primary Consumers, Birds**

5 The risk characterization for birds is tenuous at best. As discussed at the start of Section
6 4.4.2 and summarized in Table 18, the exposure assessment for primary consumers is
7 based on a calibration of exposure assumptions from field studies. These exposure
8 factors are based primarily on observations in mammals.

9
10 The non-accidental exposure scenarios in which no substantial amount of strychnine is
11 anticipated on the soil surface—i.e., the expected outcome in Forest Service
12 applications—risks to birds consuming bait are negligible. This statement is not based
13 primarily on the HQs given in Worksheet G02. Instead, this conclusion is based on field
14 studies involving hand baiting and one burrow builder application in which no adverse
15 effects on birds were observed (Table 16). In addition, Table 16 also summarizes field
16 studies on above-ground applications of strychnine in which adverse effects were not
17 observed on birds other than larks and pigeons.

18
19 Accidental exposures involve a large spill of bait that is not mitigated properly or
20 quickly. While there are uncertainties in this exposure scenario, the hazard quotients
21 reflecting concern for passerines, mallards, and pigeons appear to be plausible. Cases of
22 poisonings in mallards are reported in cases involving the misapplications of strychnine
23 (Wobeser and Blakley 1987) as well as in surface applications (Redig et al. 1982). Given
24 the well-characterized toxicity of strychnine to birds, it seems reasonable to assume that
25 mortality in birds can be expected in the event of a severe ground spill.

26
27 Risks associated with misapplications of strychnine cannot be clearly characterized
28 because of uncertainties in the exposure assessments. Based on differences in the toxicity
29 to different species of birds (Section 4.3.2.2), it seems reasonable to suggest that
30 passerines would be at greatest risk. Other than to suggest concern for the potential
31 effects of misapplications, the report by Smallwood (1999) does not contain sufficient
32 detail for elaboration of the risk characterization.

33 **4.4.2.2.2. Secondary Consumers, Birds**

34 Several field studies note no adverse effects in raptors in areas where strychnine was
35 applied for rodent control (Table 16). This is the case for hand baiting (Anthony et al.
36 1984; Barnes et al. 1985), burrow builder applications (Hegdal and Gatz 1976), and
37 above-ground applications (Graham 1977). While these field studies have limitations
38 (Section 4.4.2.), they provide a reasonable basis for a benign risk characterization.

39
40 The only field study suggesting a potentially adverse effect is the field study in burrowing
41 owls by James et al. (1990). As discussed in Section 4.1.2.2.4.1, James et al. (1990)
42 present a conflicting interpretation of their study indicating that the study suggests that
43 below ground applications of strychnine are ... *not detrimental to breeding Burrowing*

1 *Owls* but also indicating that sublethal effects ... *may explain why breeding success and*
2 *adult masses were higher on the control pastures.* As also noted in Section 4.1.2.2.4.1,
3 decreases in adult body mass and egg production were observed in mallards in the
4 reproduction study by Pedersen et al. (2000), and the sensitivity of mallards and owls is
5 similar (Figure 13).

6
7 Based on the exposure assessment for owls discussed in Section 4.2.3 and detailed in
8 Worksheet F09d, the HQs for the owl are 2 (0.007 to 57). These HQs are associated with
9 estimated doses of 0.15 (0.0005 to 4) mg/kg bw. The upper bound of this dose is above
10 the approximate lethal dose for snowy owls (≈ 1 mg/kg bw from Redig et al. 1982) and
11 below the approximate lethal dose of 7.6 mg/kg in the great horned owl (Anthony et al.
12 1994). The central estimate of the dose is below the level in which frank adverse effects
13 would be expected in either species of owl. Thus, the HQs and the corresponding doses
14 are generally consistent with the lack of overt toxic effects in burrowing owls (James et
15 al. 1990). The lower bound of the dose, 0.0005 mg/kg bw, is also be consistent with the
16 general observation that raptors will eviscerate their prey and will not consume the
17 gastrointestinal tract (e.g., James et al. 1990). While the HQ approach suggests that
18 adverse effects in raptors are not impossible, the HQs do not help in resolving the
19 uncertainties expressed by James et al. (1990).

20
21 As discussed in Section 4.1.2.2.4.4 and detailed in the supplemental table at the end of
22 Appendix 3, the incident reports from U.S. EPA/OPP (2009) suggest that raptors may be
23 adversely affected by strychnine. All of these incidents, however, occurred before
24 strychnine was limited to below-ground applications. Combined with the field studies
25 discussed above and the HQs given in Worksheet G03, the weight-of-evidences suggests
26 that adverse effects in raptors are possible; however, the probability of adverse effects in
27 raptors as a result of below-ground applications of strychnine is remote.

28 ***4.4.2.2.3. Tertiary Consumers, Birds***

29 As with mammals (Section 4.4.2.1.3), the HQs for insectivorous birds are based on a
30 conservative exposure assessment, and these HQs are very low—i.e., 0.003 (0.0004 to
31 0.07) and below the level of concern by factors of about 14-2500. While primary
32 consumers and perhaps secondary consumers may be at some risk under extreme
33 exposures, risks to insectivorous birds are negligible.

34 ***4.4.2.2.4. Water Consumption, Birds***

35 Also as with mammals (Section 4.4.2.1.4), risks to birds consuming surface water are
36 negligible. The upper bounds of the HQs associated with expected peak concentrations
37 of strychnine in water range from 0.00001 to 0.000002, below the level of concern by
38 factors of 100,000-500,000. In the case of an accidental spill, the upper bound HQs
39 range from 0.001 to 0.008, below the level of concern by factors of 125-1000.

40
41 The other exposure scenario associated with contaminated water is the consumption of
42 contaminated fish by a raptor. This is a common exposure scenario used in most Forest
43 Service risk assessments and is not modified for the risk assessment on strychnine
44 (Section 4.2.4). As detailed in Worksheet G02, the consumption of contaminated fish by

1 a bird at expected peak concentrations of strychnine in water leads to HQs of 0.0001
2 (0.00005 to 0.003), below the level of concern by factors greater than 300-20,000.

3
4 For an accidental spill, the upper bound of the HQ for the fish consumption scenario does
5 modestly exceed the level of concern—HQs of 0.8 (0.3 to 1.7). As discussed in Section
6 3.2.3.4.5, the exposure scenario is somewhat atypical for strychnine in that it is used to
7 encompass monitoring data provided by the Forest Service, which indicates
8 concentrations that cannot be rationalized, based on extensive modeling efforts using a
9 number of different surface water models. Consequently, concern with this exposure
10 scenario is greater than that in other Forest Service risk assessments in which this
11 scenario is used only to illustrate the consequences of an accidental spill.
12 Notwithstanding these concerns and as discussed more fully in Section 4.4.2.2.2, the
13 weight of evidence does not support a substantial concern for adverse effects in predatory
14 birds.

15 ***4.4.2.3. Reptiles and Terrestrial Phase Amphibians***

16 ***4.4.2.3.1. Reptiles***

17 The risk characterization for reptiles is based on the consumption of a poisoned gopher
18 by a rattlesnake. The HQs are 21 (2 to 214) and are associated with doses of 1.5 (0.15 to
19 15) mg/kg bw. As detailed in Worksheet F09d, this variability is associated only with the
20 variability in well-documented strychnine residues in pocket gophers. The central
21 estimate of the dose could be lethal to a snake—i.e., it is about one-half of the LD₅₀—and
22 the upper bound of the dose would most certainly be lethal—i.e., the dose is about four
23 times the LD₅₀. The lower bound of the dose would probably not be associated with
24 overt toxic effects (Section 4.3.2.3.1). While there are limitations in the toxicity study in
25 snakes (Section 4.1.2.3.1) and no field studies have reported adverse effects in snakes, the
26 anecdotal report by Campbell (1982) supports the risk characterization that adverse
27 effects and probably lethal effects are likely in predatory snakes in areas in which below-
28 ground baiting of strychnine is conducted. Compared to many other aspects of the risk
29 characterization for strychnine, this assessment is accompanied by little uncertainty.

30 ***4.4.2.3.2. Terrestrial Phase Amphibians***

31 Risks to terrestrial phase amphibians are characterized quantitatively based on the
32 consumption of contaminated insects by a bullfrog. As with the risk characterizations for
33 the small mammal (Section 4.4.2.1.3) and small bird (4.4.2.2.3), the HQs are below the
34 level of concern—i.e., 0.02 (0.002 to 0.5). Given the conservative nature of the exposure
35 assessment (Section 4.2.4), there is no basis for asserting that adverse effects in terrestrial
36 phase amphibians are likely.

37
38 In a risk assessment for the California Red-legged Frog (CRLF) and the California Tiger
39 Salamander (CTS), U.S. EPA/OPP (2009) has determined that the below-ground use of
40 strychnine treated bait may adversely affect these endangered species:

41
42 *Although exposures via dermal absorption and via consumption of*
43 *invertebrates cannot be estimated, the potential exists for dermal*

1 *exposure and consumption of invertebrates that have been in*
2 *contact with the bait. Therefore, due to the high toxicity of*
3 *strychnine, risk cannot be discounted.*

4 U.S. EPA/OPP 2009, p. 9

5
6 Based on the quantitative estimates of oral exposure presented in the current Forest
7 Service risk assessment, the consumption of contaminated insects does not appear to pose
8 a risk to terrestrial phase amphibians. As discussed in Section 4.1.2.3.2, the skin of
9 terrestrial phase amphibians appears to be much more permeable to several organic
10 compounds, compared with mammalian skin (Quaranta et al. 2009). In the absence of
11 any quantitative exposure assessments for dermal contact with strychnine treated bait,
12 however, any determination that below-ground applications of strychnine are likely to
13 adversely affect terrestrial phase amphibians are merely speculative.

14 **4.4.2.3. Terrestrial Invertebrates**

15 As discussed in Section 4.1.2.4, one study suggests that strychnine administered in honey
16 may be toxic to some insects (Kostowski et al. 1965). Nonetheless, field studies indicate
17 that insects play a major role in the decomposition of poisoned rodents, and adverse
18 effects on insects feeding on rodent carcasses have not been reported (Arjo et al. 2005).
19 In addition, one field study notes that insect populations in areas where strychnine was
20 applied were not adversely affected by exposure (Deisch 1986). A quantitative risk
21 characterization is not developed for insects because no potential hazard can be
22 identified.

23 **4.4.3. Aquatic Organisms**

24 Risks to aquatic organisms are summarized in Worksheet G03. As detailed in
25 Section 4.3.3, the information on the toxicity of strychnine to aquatic organisms is limited
26 to acute bioassays of strychnine in fish, amphibian embryos, and aquatic invertebrates.
27 The estimated NOEC values are based on an LOEC for amphibian embryos and LC₅₀
28 values for fish and aquatic invertebrates. Given the limitations in the toxicity data,
29 confidence in the risk characterization is limited.

30
31 To some extent, the limitations in the toxicity data are offset by the very conservative
32 nature of the exposure assessment (Section 3.2.3.4). Based on expected peak
33 concentrations in surface water, the upper bounds of HQs for aquatic organisms range
34 from 0.0003 to 0.003, which is below the level of concern by factors of over 300 to over
35 3000. The HQs are within the range of the 0.00122 EPA Risk Quotient (RQ) derived for
36 fish (U.S. EPA/OPP 2009). The EPA RQ and the HQs derived for fish in the current
37 Forest Service risk assessment are far below the level of concern.

38
39 For the accidental spill scenario, the level of concern for fish is exceeded across the range
40 of HQs—i.e., 1.7 (1.1 to 2). While this situation is not unusual in Forest Service risk
41 assessments, the accidental spill scenario itself is somewhat unusual in that this scenario
42 is also used to encompass unexpectedly high and unexplained concentrations in streams.
43 These concentrations are discussed in detail in Section 3.2.3.4.5. Given the limitations in
44 the available toxicity studies in fish, these hazard quotients cannot be well understood.

1 Based on the U.S. EPA/OPP levels of concern for RQs (e.g., SERA 2007a, Table 4-2),
2 the HQs are below the level of concern for acute toxicity—i.e., mortality is an unlikely
3 effect of exposure. The HQs, however, are above the level of concern for threatened and
4 endangered species of fish.

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 [] indicates the source for identifying the reference.

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FOAI02	Request for additional DERs.
E-Docket01	Docket ID: EPA-HQ-OPP-2006-0955: Rodenticides, Proposed Mitigation Decision.
E-Docket02	Docket ID: EPA-HQ-OPP-2009-0815: Petition for Reclassification of Strychnine as Restricted Use
Internet	References obtained from various sites on the Internet.
SET00	Papers from preliminary scoping.
SET01-TOXL	Preliminary TOXLINE literature search.
SET01-ECOT	Preliminary ECOTOX literature search.
SET01-Suppl	References from supplemental searched.
SET01-RED	Open literature references from EPA-RED.
SET02	Supplemental searches for program description.
SET03	Tree search of bibliographies and references provided by Forest Service R5.
SET04	Tree search of bibliographies for Sets 01 to 03.
SET05	Additional supplemental searches of various topics and tree search of SET04.
SET06	Studies on treatment of nonketotic hyperglycinemia
Sec	Summary of citation from a secondary source.
Std	Standard references used in most Forest Service risk assessments.

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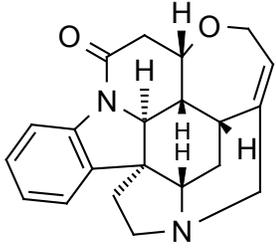
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Table 1: Physical and chemical properties of strychnine		
Property	Value	Reference
Nomenclature		
Common Name	strychnine	Tomlin 2004
IUPAC Name	strychnidin-10-one	Tomlin 2004
CAS Name	strychnidin-10-one	Tomlin 2004
Structure		Tomlin 2004
Appearance/state, ambient	Colorless crystals	Tomlin 2004
Bioconcentration	8.718 L/kg (wet-wt)	EPI Suite 2008
	2	HSDB 2010
CAS number	Alkaloid: 57-24-9 Sulfate: 60-41-3 Nitrate: 66-32-0	Tomlin 2004; Cornell University 1991; http://www.chemnet.com/dict
log K _{ow}	4.0 (pH 7) [K _{ow} = 10,000]	Tomlin 2004
	Reported as K _{ow} and not Log K _{ow} but this is clearly a typographic error. 0.9 (pH 5) 4.0 (pH 7) 114.0 (pH 9)	U.S. EPA/OPP 1996a
	1.93 [K _{ow} = 85.1] (experimental)	EPI Suite 2008; U.S. EPA/OAQ 1985
Koc (mL/g)	2082 to 8506	Kookana et al. 1997, 1998
	Loam and loamy sand: ≈15,850 Sandy loam: 13,800 Sandy clay loam: 9,330	Starr et al. 1996 (Table 2 of paper)
	267	USDA/APHIS 1994 citing HSDB
Kd (mL/g)	20.82 to 173.19	Kookana et al. 1997, 1998
	40 to 169	HSDB 2010
Melting point	270-280 °C	Tomlin 2004
	273 °C	U.S. EPA/OPP 1996a, 2009
Molecular formula	C ₂₁ H ₂₂ N ₂ O ₂	Tomlin 2004
Molecular weight (g/mole) [conversion factor to alkaloid equivalents]	Alkaloid: 334.4 Nitrate: 397.43 [334.4 ÷ 397.43 ≈ 0.8414] Sulfate: 432.49 [334.4 ÷ 432.49 ≈ 0.7732]	Tomlin 2004 http://www.chemnet.com/dict
pK _a	8.26 (K _a =5.4x10 ⁻⁹)	Tomlin 2004; U.S. EPA/OPP 1996a

SMILES Notation	<chem>O=C1C[C@@H]2OCC=C3CN4CC[C@]56[C@@H]4C[C@@H]3[C@@H]2[C@@H]6N1c7cccc75</chem>	Tomlin 2004
Soil photolysis half life	180 days [1 st order kinetics may not apply]	U.S. EPA/OPP 1996a
Soil halftime	32-127 days	Rogers et al. 1997; Kookana et al. 1998
	24-27 days	Starr et al. 1995,1996
Specific gravity	0.25 at 25 C	U.S. EPA/OPP 1996a
U.S. EPA Docket Number(s)	EPA-HQ-OPP-2006-0955, Rodenticides; Notice of Availability of Proposed Mitigation Decision	http://www.regulations.gov
Vapor pressure	Negligible	U.S. EPA/OPP 1996a
Water hydrolysis halftime	Stable	U.S. EPA/OPP 1996a
Water solubility (mg/L)	143 mg/L	Tomlin 2004; ACGIH 2001
	115 mg/L (0.0115 g/100 mL)	U.S. EPA/OPP 1996a
	160 mg/L (experimental)	EPI Suite 2008

Table 2: Currently Active Registrations for Strychnine

Formulation Name	U.S. EPA Reg. No.	Restricted Use	Registrant
Petersens Pocket Gopher Killer I For Pocket Gopher Control Only	10031-1	Yes	Petersen Seeds Inc.
Petersens Pocket Gopher Killer II For Pocket Gopher Control Only	10031-2	Yes	Petersen Seeds Inc.
Petersens Pocket Gopher Killer III For Pocket Gopher Control Only	10031-3	Yes	Petersen Seeds Inc.
Petersen's Pocket Gopher Bait	10031-6	Yes	Petersen Seeds Inc.
Strychnine Alkaloid N.F. Powder	27995-1	No	H Interdonati Inc.
Fort Dodge Gopher Bait	322-1	Yes	Fort Dodge Chemical Company
Elston Gopher Getter Bait	35380-1	Yes	Elston Manufacturing, Inc.
G.G. Jr. Hand Probe Gopher Getter Bait	35380-3	No	Elston Manufacturing, Inc.
Wilco Gopher Getter Type 1 Bait	36029-1	No	Wilco Distributors, Inc.
Strychnine Alkaloid N.F.	36029-14	No	Wilco Distributors, Inc.
Wilco Pocket Gopher Milo Bait For Hand Baiting	36029-16	No	Wilco Distributors, Inc.
Wilco Gopher Getter Ag Bait	36029-7	Yes	Wilco Distributors, Inc.
Strychnine Alkaloid NFX	37259-1	No	Noris Chemical Corp.
Pocket Gopher Bait Containing Strychnine 1-10 Formulation On Oats	4271-10	Yes	R & M Exterminators Inc.
Pocket Gopher Bait Containing Strychnine 1-10 Formulation On Milo	4271-17	Yes	R & M Exterminators Inc.
Omega Gopher Grain Bait	5042-32	No	RCO International Inc.
RCO Avalon Mixed Grain Gopher Bait	5042-34	Yes	RCO International Inc.
Martin's Gopher Bait 50	53883-23	No	Control Solutions, Inc.
Martin's Gopher Bait 50r	53883-24	Yes	Control Solutions, Inc.
0.5% Strychnine Milo	56228-11	Yes	USDA
0.5% Strychnine Pocket Gopher Oat Bait For Use In Burrow Builders	56228-12	Yes	USDA
0.5% Strychnine Milo For Hand-Baiting Pocket Gophers	56228-19	No	USDA
0.5% Strychnine On Oats For Hand Baiting Gopher-Go	56228-20	No	USDA
Gopher-Go	641-1	No	Southwest Chemical Company
Gopher-Go A G Bait	641-2	Yes	Southwest Chemical Company
Force's Ro-Dex	814-4	No	Carajon Chemical Company Inc.
Eckroat Gopher Getter Bait	84224-1	Yes	Wild West Pest, LLC
Cooke Quick Action Gopher Mix	909-2	No	Central Garden & Pet D/B/A Lilly Miller Brands/Excel Garden

Source: <http://www.pesticideinfo.org>.

Table 3: Strychnine Formulations Designated for Use by the Forest Service

Trade Name	Supplier	EPA Reg. No. (Date of most recent EPA label)	Type of Formulation (% a.i.)	Application Rate lb formulation per acre (lb a.i./acre)	Forest Service Region Where Used
Fort Dodge Gopher Bait	Fort Dodge Chemical Company	322-1 (11/07/08)	bait NOS (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R6
Wilco Gopher Getter Type 1 Bait	Wilco Distributors Inc	36029-1 (11/20/08)	bait NOS (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R5
Wilco Gopher Getter Restricted Use Bait	Wilco Distributors Inc	Special need label for CA and NV	milo grain (1.8%)	0.125 to 1.0 (0.00225 to 0.018 lb a.i./acre)	R5
Wilco Gopher Getter AG bait	Wilco Distributors Inc	36029-7 36029-1 (11/17/08)	milo grain (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R5 and R6
Omega Gopher Grain Bait	RCO International	5042-32 (7/29/08)	oats (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R5 and R6
0.5% strychnine milo pocket gopher bait for use in burrow builders	USDA/APHIS	56228-11 (7/11/05)	milo grain (0.5%)	1.0 to 2.5 (0.005 to 0.0125 lb a.i./acre)	R6
0.5% strychnine pocket gopher oat bait for use in burrow builders	USDA/APHIS	56228-12 (7/11/05)	oats (0.5%)	1.0 to 2.0 (0.005 to 0.01 lb a.i./acre)	R6
0.5% strychnine milo for hand-baiting pocket gophers	USDA/APHIS	56228-19 (7/11/05)	milo grain (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R6
0.5% strychnine oats for hand-baiting pocket gophers ^b	USDA/APHIS	56228-20 (7/11/05)	oats (0.5%)	0.125 to 1.0 (0.000625 to 0.005 lb a.i./acre)	R6

^a R5 designated this formulation as EPA No. 36029-1. This registration number is for Wilco Gopher Getter Type 1 Bait. The 1.8% bait has a Special Needs Label for California and Nevada.

^b The name designated in the R6 spreadsheet is: “*pocket gopher oat bait for use in burrow builders*”. The name used in the above table is from the U.S. EPA label.

Table 4: Use of Strychnine by the Forest Service (2000 to 2004)

Region Name (Designation)	Pounds Strychnine	Treated Acres	Lbs/acre	Proportion of Pounds of Total Forest Service Use
Northern (R1)	840.77	12244.00	0.06867	0.501
Rocky Mountain (R2)	0.75	2.00	0.37500 ^a	<0.001
Southwestern (R3)	0	0	N/A	0
Intermountain (R4)	601.28	9328.00	0.06446	0.359
Pacific Southwest (R5)	28.62	16809.50	0.00170	0.017
Pacific Northwest (R6)	205.67	47514.00	0.00433	0.123
Southern (R8)	0	0	N/A	0
Northern (R9)	0	0	N/A	0
Total	1677.09	85897.50	0.01952	

^a This application may be reported in units of formulation rather than a.i.

Region 1 Use of Strychnine in Bait Stations for Animal Damage Control (2000 to 2004)

Year	Pounds Strychnine	Number of Bait Stations	Pounds per Station^a
2002	0.1	1395	0.000072
2003	0.14	1952	0.000072
2004	0.6	856	0.00070

^a See the discussion of bait stations in Section 2.5.

Source: USDA/Forest Service Pesticide Use Reports
<http://www.fs.fed.us/foresthealth/pesticide/reports.shtml>

Table 5: Restrictions on Strychnine Applications

Species	U.S. EPA Registration Number ^a								
	322-1	36029-1	SNL/CA	36029-7	5042-32	56228-11	56228-12	56228-19	56228-20
Bear, Grizzly	X	X	X	X	X	X	X	X	X
Condor, California					X	X	X	X	X
Fox, San Joaquin kit	X	X	X	X	X	X	X	X	X
Goose, Aleutian Canada	X								
Kangaroo Rat, Morro Bay	X	X	X	X	X	X	X	X	X
Mouse, Salt Marsh Harvest	X	X	X	X		X	X	X	X
Wolf, Gray	X	X	X	X	X	X	X	X	X

^a See Table 3 for common names of formulations. SNL/CA refers to Wilco Gopher Getter Restricted Use Bait. In order to apply strychnine in areas inhabited by the listed species, special permission must be obtained from the U.S. EPA.

Table 6: Estimates of fatal and non-fatal exposures in humans

Dose (mg/kg bw)	Peak Serum Conc. (mg/L)	Fatal	Not fatal	Sex, Comment	Reference
1.0	N/A		X	M, Snorted	Boyd et al. 1983
N/A	2		X	M	Edmunds et al. 1986
1.4	N/A	X		F, Infant	Stannard 1969
1.7	N/A		X	F, Snorted	Boyd et al. 1983
2.25	N/A	X		F	Salm 1952
N/A	2.45		X	F	Hernandez et al. 1988
3.4	N/A		X	M	Teitelbaum and Ott 1970
4.3	N/A		X	M	Teitelbaum and Ott 1970
4.3	N/A		X	F	Lambret et al. 1981
6.5	N/A		X	M	Swissman and Jacoby 1964
9.4 ^b	≈0.8 ^b		X	F	Greene and Meatherall 2001
9.8	N.D. ^a		X	M	Sgaragli and Mannaioni 1973
25	2.12		X	M	Palatnick et al. 1996
	2.6	X		M	Perper 1985
69	5	X		M	Heiser et al. 1989
80	0.8	X		M	Lloyd and Pedley 1953

M= Male; F=Female; N/A=Not available;

^a Blood assay but no strychnine detected. The limit of detection is not specified.

^b Dermal exposure. See Sections 3.1.3.2 and 3.1.12 for discussion.

See Appendix 1 for details.

Table 7: Standard worker exposure rates used in Forest Service risk assessments

Worker Group	Rate (mg/kg bw/day per lb applied)		
	Central	Lower	Upper
Directed foliar	0.003	0.0003	0.01
Broadcast foliar	0.0002	0.00001	0.0009
Aerial	0.00003	0.000001	0.0001

Source: SERA 2007a, Table 3-4.

Table 8: Worker exposure rates for standard PHED Scenarios

Scenario	mg/lb a.i. handled			
	No clothing	Single Layer, No gloves	Single layer, Gloves	Inhalation
1. Dry flowable, open mixing and loading	1.1	0.066	0.066	0.00077
2. Granular, open mixing and loading	0.032	0.0084	0.0069	0.0017
3. All liquids, open mixing and loading	3.1	2.9	0.023	0.0012
4. Wettable powder, open mixing and loading	6.7	3.7	0.17	0.04342
5. Wettable powder, water soluble bags	0.039	0.021	0.0098	0.00024
6. All liquids, closed mixing and loading			0.0086	0.000083
7. Aerial-fixed wing, enclosed cockpit/liquid	0.0050	0.0050	0.0022	0.000068
8. Aerial-fixed wing, enclosed cockpit/granular	0.0044	0.0017	0.0017	0.0013
9. Helicopter application, enclosed cockpit		0.0019	0.0019	0.0000018
10. Aerosol application	480	190	81	1.3
11. Airblast application, open cockpit	2.2	0.36	0.24	0.0045
12. Airblast application, enclosed cockpit			0.019	0.00045
13. Groundboom applications, open cab	0.046	0.014	0.014	0.00074
14. Groundboom applications, enclosed cab	0.010	0.0050	0.0051	0.000043
15. Solid broadcast spreader, open cab, AG	0.039	0.0099		0.0012
16. Solid broadcast spreader, enclosed cab, AG	0.0021	0.0021	0.0020	0.00022
17. Granular bait dispersed by hand			71	0.47
18. Low pressure handwand	25	12	7.1	0.94
19. High pressure handwand	13	1.8	0.64	0.079
20. Backpack applications	680			0.33
21. Hand gun (lawn) sprayer			0.34	0.0014
22. Paintbrush applications	260	180		0.280
23. Airless sprayer (exterior house stain)	110	38		0.830
24. Right-of-way sprayer	1.9	1.3	0.39	0.0039
25. Flagger/Liquid	0.053	0.011	0.012	0.00035
26. Flagger/Granular	0.0050			0.00015
27. WP or liquid/open pour/airblast/open cab	26			0.021
28. WP or liquid/open pour/airblast/closed cab	0.88	0.37	0.057	0.0013
29. Liquid or DF /open pour/ground boom/closed cab	0.22	0.089	0.029	0.00035
30. Granule/open pour/belly grinder	210	10	9.3	0.062
31. Push type granular spreader		2.9		0.0063
32. Liquid/open pour/low pressure handwand	110	100	0.43	0.030
33. WP/open pour/low pressure handwand			8.6	1.1
34. Liquid/open pour/backpack			2.5	0.03
35. Liquid/open pour/high pressure handwand			2.5	0.12
36. Liquid/open pour/garden hose end sprayer	34			0.0095
37. Liquid/open pour/termicide injection			0.36	0.0022

Source: Keigwin 1998.

Note: The above values are in mg a.i./lb handled and not in mg a.i./kg bw per lb handled. Scenarios 17, 30, and 34 are bolded because these scenarios are discussed in Section 3.2.2.1 of the current Forest Service risk assessment.

Table 9: Modeled and monitored concentrations in surface water

Scenario	Concentrations (ppb or µg/L) ^a	
	Peak	Long-Term Average
MODELING FOR THIS RISK ASSESSMENT		
Accidental Spills (Section 3.2.3.4.2)		
30 (20 to 40) lbs of a 0.5% formulation or 0.15 (0.1 to 0.2 lbs a.i.	68 (45 to 91)	N/A
Gleams-Driver (Section 3.2.3.4.3)		
Broadcast surface application at 1 lb a.i./acre		
Pond (Section 3.2.3.4.4)	0.96 (0 - 14.1)	0.026 (0 - 0.4)
Stream (Section 3.2.3.4.4)	1.82 (0 - 25.2)	0.032 (0 - 0.6)
Broadcast surface application at 0.005 lb a.i./acre		
Pond (Section 3.2.3.4.4)	0.0048 (0 – 0.071)	0.00013 (0 – 0.002)
Stream (Section 3.2.3.4.4)	0.0091 (0 – 0.13)	0.00016 (0 – 0.00001)
U.S. EPA Models (Section 3.2.3.4.4)		
PRZM-EXAMS, OR Christmas Tree Scenario, Index Reservoir, Upper 10 th Percentile and range, 1 lb a.i./acre	3.68 (2.66 – 5.66)	0.975 (0.712 – 1.566)
PRZM-EXAMS, OR Christmas Tree Scenario, Farm Pond, Upper 10 th Percentile and range, 1 lb a.i./acre	1.16 (0.684 – 2.14)	0.368 (0.188 – 0.498)
GENEEC, 1 lb a.i./acre	6.47	3.54 [90-day average]
FIRST, a lb a.i./acre	18.975	2.8
USDA/Forest Service Monitoring (Section 3.2.3.4.5)		
48 acres treated with 15.4 lbs/bait [0.32 lb/acre]	13 [≈41 ppb per lb a.i./acre]	N/A
14 acres treated with 4.8 lbs/bait [0.34 lb/acre]	23 [≈ 67 ppb per lb a.i./acre]	N/A

^a Values in **bold type** are the **expected or monitored concentrations**. Values in plain type are concentrations for a unit application rate of 1 lb a.i./acre.

Table 10: Chemical and site parameters used in GLEAMS modeling

Parameter^a	Clay	Loam	Sand	Note/ Reference
Half-lives (days)				
Aquatic Sediment		165 (72-381)		Note 1
Foliar		35		Note 2
Soil		55 (24-127)		Note 3
Water		1095		Note 4
Soil K_{oc} , mL/g		5,700 (2,000 to 16,000)		Note 5
Sediment K_d , mL/g		60 (20 to 170)		Note 6
Water Solubility, mg/L		143		Tomlin 2004
Foliar wash-off fraction		0.5		Note 2
Fraction applied to foliage		0		Note 2
Depth of Soil Injection		1 cm		Section 2.3.1.
Irrigation after application		none		Section 2.3.1.

Note 1 No data are available. Use EPA default approach and assume 3x soil half-life (see Note 4).

Note 2 Use default values for foliar half-life and wash-off. These do not impact the modeling because no compound is applied to foliage.

Note 3 Range of reported soil in Table 1 with a central estimate taken as the geometric mean of the range.

Note 4 Strychnine is stable in water (U.S. EPA/OPP 1996a). Use a half-life of 3 years to reflect negligible degradation.

Note 5 Reported K_{oc} values are highly variable and the K_{oc} model may not be valid. Use triangular distribution based on the values summarized in Table 1.

Note 6 Based on range of 20.82 to 173.19 from Kookana et al. 1997, 1998 rounded to 20-170. Use geometric mean (≈ 60) for central estimate.

Table 11: Water Contamination Rates Used in Risk Assessment

(see Section 3.2.3.4.6 for discussion)

Water contamination rate in mg/L per lb/acre applied ^a

Expected Concentrations	Peak	Longer-term
Central	0.002	0.001
Lower	0.0007	0.0007
Upper	0.025	0.0028

^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 12: Estimates of Dose-Severity Relationships in Humans

NOTE: The dose-severity relationships detailed in this table and discussed in Section 3.3.4 should not be interpreted as suggesting that exposures above the surrogate RfD of 0.02 mg/kg bw are acceptable.

Dose (mg/kg bw) ^a	Corresponding Hazard Quotient ^b	Organism (number of individuals): Effect	Reference
Oral, Inhalation, or Ocular			
0.02	1	Surrogate acute and chronic RfD. No effects anticipated.	Section 3.3.3.1/2
0.06	2	Short-term exposure limit from 1976-1985. No acute effects anticipated.	ACGIH 2001
0.1	5	Typical therapeutic doses. No acute effects anticipated.	Hayes 1982
1	50	Signs of strychnine toxicity and potentially lethal without prompt and effective medical intervention.	Table 6 and Section 3.1.4.
>1	>50	Signs of toxicity and potentially lethal despite prompt medical care.	Table 6., Stannard 1969
≈25	≈1250	Likely to be lethal despite prompt medical care.	Table 6., Perper 1985; Heiser et al. 1989; Lloyd and Pedley 1953
Dermal Exposures Only			
10 Dermal Only	500	Signs of strychnine toxicity after dermal exposure. Potential for lethality not clear.	Greene and Meatherall (2001), Appendix 1 and Sections 3.1.3.2 and 3.1.12.

Table 13: Toxicity of Strychnine to mammals on perenteral administration

Species	Route	Sex	BW (kg)	LD ₅₀ or Lethal Dose (mg/kg bw)	Reference
Intravenous					
Mouse	i.v.	NS	0.02	0.41	HSDB 2010
Rats	i.v.	M	0.2	0.57	Kato et al. 1962
Rats	i.v.	F	0.2	0.57	Kato et al. 1962
Cat	i.v.	F	2.56	0.325 ^b	Hatcher and Eggleston 1918
Dog	i.v.	M	12.4	0.4 ^b	Hatcher and Eggleston 1918
Intraperitoneal					
Mouse	i.p.	B	0.01	1.45	Lamanna and Hart 1968
Mouse	i.p.	B	0.018	1.69	Lamanna and Hart 1968
Mouse	i.p.	B	0.025	1.8	Lamanna and Hart 1968
Rats	i.p.	M	0.2	2.82	Kato et al. 1962
Rats	i.p.	F	0.2	1.62	Kato et al. 1962
Guinea pigs	i.p.	F	0.5	10.9	Kato et al. 1963
Subcutaneous					
Mice	s.c.	NS	0.017	0.474	Sandberg and Kristainson 1970
Rats	s.c.	M	0.2	4.01	Kato et al. 1962
Rats	s.c.	F	0.2	1.81	Kato et al. 1962

^a Data from Poe et al. (1936) and Davis and Yeh (1969) are not given because the body weights of the rats are not specified.

^b Approximate lethal dose.

These data are plotted in Figure 4 and discussed in Section 4.1.2.1.

Table 14: Selected studies on the oral toxicity of strychnine in mammals

Species	Average or Approximate Body Weight (kg) ^a	LD ₅₀ (mg/kg bw)	Approximate/ Minimum Lethal Dose	Reference [note]
Western pocket gophers (<i>Thomomys mazama</i>)	0.075	8		Nolte and Wagner 2002
Golden-mantled ground squirrel (<i>Spermophilus lateralis</i>)	0.191	3.6		Anthony et al. 1984
Rat (<i>Rattus norvegicus</i>)	0.32	4.3 [2.2 F; 6.4 M]		U.S. EPA/OPP 1996d
Mink (<i>Mustela vison</i>)	0.945	0.6		Anthony et al. 1984
Kit fox (<i>Vulpes macrotis mutica</i>)	1.7	0.75		Schitoskey 1975
Cat (NOS) ^e	2.5		2	Atkins and Johnson 1975
Opossum (<i>Trichosurus vulpecula</i>)	2.65	22.36	10	Bell 1972
Nutria (<i>Myocastor coypus</i>) ^c	5.4	27		Nolte and Wagner 2002
Porcupine (<i>Erethizon dorsatum</i>)	≈8.4		> 91.4 [NOEC]	Anthony et al. 1986 [salt blocks]
Dog	10	0.7		Baker et al. 1982
Coyote	13 [10-16.1]		2.1 [1.3-2.9]	Marsh et al. 1987 [squirrel carcasses]
Mule deer (<i>Odocoileus hemionus</i>)	54.2	20.5 [17-24]		Tucker and Crabtree 1970
Humans	60			
Bear (<i>Ursus arctos yesoensis</i>), n=3	206	≈0.5	0.25 [NOEC] 0.5 [13 hours] 1.0 [30 min.]	Inukai 1969
Horses	≈1000	≈2.2	<3.75	Meek and Keatts 1971 [poisoning with oat bait]

^a Body weight from Smith et al. 2003 except for body weights bold which are taken from publication or other source as indicated.

^b This is not a true LD₅₀ but is the dose in terms of mg/kg bw in which 5/10 animals died. See Appendix 2 for details of nonlinear dose/response relationship and Section 4.1.2 for discussion.

^c <http://icwdm.org/handbook/rodents/nutria.asp>

^d Arithmetic mean of LD₅₀s for males and females.

^e Body weight of 2.5 kg taken from Hatcher and Eggleston 1918

See Figure 6 for illustration and discussion in Section 4.1.2.1.2.

Table 15: Gavage toxicity of strychnine alkaloid in adult birds

Order	Species (Sex)	Weight (g) ⁽¹⁾	LD ₅₀ (mg/kg bw)	Reference
Anseriformes	Mallard (M&F)	1082	2.9	Tucker and Hegele 1971
Galliformes	Pheasant (M) ⁽²⁾	1317	24.7	Tucker and Hegele 1971
Galliformes	Chukar (M&F) ⁽²⁾	615	16.0	Tucker and Hegele 1971
Galliformes	Japanese quail (F) ⁽²⁾	90	22.6	Tucker and Hegele 1971
Columbiformes	Pigeon (M&F) ⁽²⁾	354.5	21.3	Tucker and Hegele 1971
Passeriformes	House Sparrow (M)	28	4.18	Tucker and Hegele 1971
Anseriformes	Mallard (M&F)	1082	2.27	Hudson et al. 1984
Anseriformes	Mallard (M&F)	1082	2.83	Hudson et al. 1984
Accipitriformes	Golden eagle (M) ⁽³⁾	3477	6.45	Hudson et al. 1984
Galliformes	California quail	176	112.	Hudson et al. 1984
Strigiformes	Snowy owl ⁽³⁾	3500	0.94	Redig et al. 1982
Columbiformes	Pigeon	285	7.73	Schafer and Eschen 1986
Strigiformes	Great horned owl ⁽³⁾	1500	7.6	Anthony et al. 1984
Accipitriformes	Red-tailed hawk ⁽³⁾	1250	10.75	Anthony et al. 1984
Galliformes	Sage grouse	1100	42.5	Ward et al. 1942

⁽¹⁾ Body weights in bold are taken from the referenced publication for the toxicity value. Other body weights are taken from Dunning (1993) as indicated below.

⁽²⁾ The same data (not shown) are given in Hudson et al. (1984).

⁽³⁾ Estimated lethal dose. See Appendix 4 for details.

Body weights used in Table 15 (above)

Common Name	Body Weight (g)			Reference
	M	F	Average	
California quail	176	170	173	Dunning (1993, p. 49)
Chukar partridge	700	530	615	Dunning (1993, p. 42)*
Golden eagle	3477	4913		Dunning (1993, p. 36)
Japanese quail			90	Dunning (1993, p. 44)
Mallard ducks			1082	Dunning (1993, p. 22)
House sparrow	28	27	27.5	Dunning (1993, p. 260)
Ring-necked pheasant	1317	953	1135	Dunning (1993, p. 47)
Pigeon	369	340	354.5	Dunning (1993, p. 72)

Table 16: Field studies concerning mammals and birds

Application % formulation, application rate as lb formulation/acre (if specified)	Affected Nontargets, Residues (if given)	Unaffected Nontargets ⁽⁴⁾	Reference
Hand baiting, below ground (for pocket gopher control unless otherwise specified)			
0.5%, up to 3 lb/acre	Ground squirrels, 2.3 (0.6 – 7) ppm. Mustelids *	Raptors *	Anthony et al. 1984
0.5%, ≈1 to 2 lb/acre	Gopher, 3 (0.6-5.2) ppm Mice, 10 (7-13) ppm	Grouse, <0.01 ppm	Barnes et al. 1985
0.5%, ≈0.4 lb/acre	Squirrels and chipmunks		El Hani et al. 2002
0.5 to 1.25%	Gophers, 1.05 – 90 ppm Mice		Evans et al. 1990
0.5%, ≈0.9 lb/acre	Chipmunks, 0.3 - 0.35 ppm ⁽²⁾ Mice, 2.6 - 5.4 ppm		Fagerstone et al. 1980
0.25% (Ground squirrel control)	Gophers, 0.9 to 9.5 ppm Burrowing owls ⁽³⁾		James et al. 1990
0.35% to 1.3%, 0.3 to 0.4 lb/acre	Gophers, 0.9 to 9.5 ppm		Ramey et al. 2002
Burrow-builder, below ground			
0.5%, 1.25 lb/acre	Mice Ground squirrels Mourning dove	Red-winged blackbirds. Raptors Mammalian predators	Hegdal and Gatz 1976
0.5%, 3 lb/acre	<i>Many non-target animals perished</i>		Smallwood 1999
Above ground (for prairie dog control unless otherwise specified)			
5.79%, salt bait blocks for porcupine control	Chipmunks, squirrels, cottontails, deer mice		Anthony et al. 1986
0.5%	Horned larks	Other passerines	Apa et al. 1991
0.5%		Mice ⁽¹⁾	Deisch 1986
0.44%, 1-5.7 lb/acre	Meadowlark, pigeon.	Carnivorous mammals and birds.	Graham 1977
0.5% Prairie dog control	Rabbits Horned larks		Holbrook and Timm 1985
0.15 to 0.5%, kangaroo rat control	Mice Horned lark		Howard and Bodenchuk 1984
0.5%	Horned larks	Deer mice Rabbits	Uresk et al. 1988
Kangaroo rat control	Rodents including deer mice. Mammalian predators??		Wood 1965

*Authors assert a potential risk or lack of risk but risks to the species/groups are not reported, observed, or otherwise documented in publication. Risks to mustelids supported by Nolte and Wagner (2001).

⁽¹⁾ Beneficial effects on deer mice associated with decreased predation.

⁽²⁾ Strychnine induced mortality documented in 2/30 but 24/30 chipmunks survived.

⁽³⁾ Decrease (4.8%) in adult body weights (p<0.05) noted in treated relative to control areas. See Section 4.1.2.2.4. for discussion. Other effects not statistically significant.

⁽⁴⁾ General statements on the lack of observed effects not included.

Table 17: Terrestrial Ecological Receptors Considered in Assessment

Receptor	Body Weight (kg)	Comment
Primary Exposure Scenarios (Consumption of Bait)		
Deer	70	Used only in accidental primary exposure scenario.
Grizzly bear	100	Used only for foraging on pocket gopher food caches.
Mallard	1	Representative of relatively small sensitive waterfowl.
Mouse	0.02	Representative of small fossorial mammal.
Pigeon	0.35	Representative of tolerant Columbiformes.
Pocket gopher	0.075	Used only in accidental exposure scenario to calibrate field intake rates for primary exposures. See Section 4.2.2. for discussion.
Skunk	2.0	Large fossorial which may forage for gopher bait.
Quail	0.2	Representative of tolerant Galliformes.
Raptor	4	Representative of larger predatory bird. Used only in water consumption scenarios as a standard Forest Service receptor.
House sparrow	0.02	Representative of small sensitive passerine.
Squirrel	0.15	Representative of a larger fossorial mammal.
Secondary Exposure Scenarios (Consumption of Prey)		
Coyote	13	Consumption of part of a 75 g pocket gopher
Badger	7	Consumption of part of a 75 g pocket gopher
Mink	1	Consumption of part of a 75 g pocket gopher
Owl (Great horned)	1.5	Consumption of part of a 75 g pocket gopher
Rattle snake	0.5	Consumption of all of a 75 g pocket gopher
Eagle	N/A	Consumption of fish by a raptor. See Section 4.2.4.
Tertiary Exposure Scenarios (Consumption of Insects)		
Small mammal	0.02	Generic and standard Forest Service receptor.
Small bird	0.01	Generic and standard Forest Service receptor.
Bullfrog, young	0.02	Consumption of contaminated insects
Surface Water Exposure Scenarios		
Canid	5	Generic and standard Forest Service receptor.
Large Mammal	70	Generic and standard Forest Service receptor.
Large Bird	4	Standard Forest Service receptor is a Canada goose. For strychnine, a raptor is used as the most sensitive class of birds.
Small Mammal	0.02	Generic and standard Forest Service receptor.
Small Bird	0.01	Generic and standard Forest Service receptor. Toxicity value for the more sensitive passerines is used in risk characterization.

See Section 4.2.1 for discussion.

Table 18: General Assumptions for Primary Exposures

Scenario	Group	Proportion of Bait Consumed Relative to Total Food Consumption		
		Central	Lower	Upper
Accidental Spill	All organisms	0.02	0.002	0.2
Misapplication	Fossorial mammals	0.02	0.002	0.2
	All other groups	0.002	0.0002	0.02
Proper Application	Fossorial mammals	0.002	0.0002	0.02
	All other groups	0.00002	0.000002	0.0002

See Section 4.2.2. for discussion.

Table 19: Strychnine residues in insects

Insect	Mean	S.D.	N	t ($\alpha=0.05$)	95% upper limit of mean	Log ₁₀ Maximum	Maximum
Ants	0.130	0.149	12	1.812	0.208	-0.471	0.338
Wasps	0.006	0.016	10	1.833	0.015	-1.292	0.051
Other Hymenoptera	0.031	0.064	6	2.015	0.084	-0.793	0.161
Coleoptera	0.004	0.011	13	1.782	0.009	-1.469	0.034
Diptera adults	0.040	0.112	25	1.711	0.078	-0.467	0.341
Diptera larvae	0.366	0.232	4	2.353	0.639	-0.156	0.698
Other Insects	0.167	0.289	5	2.132	0.443	-0.300	0.501
Average of Means	0.106				Average of Maximum	-0.707	0.196
					Lower Limit:	-1.171	0.067
					Upper Limit:	-0.243	0.572
					S.D.	0.502	
					N	7	
					t ($\alpha=0.025$)	2.447	

Data from Stahl et al. (2004, Table 2, p. 261

See Section 4.2.4 for discussion.

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

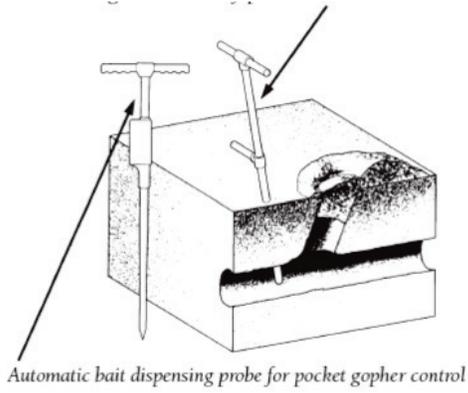
Group/Duration	Organism	Endpoint/Basis of Toxicity Value	Toxicity Value ¹	Reference
Terrestrial Animals				
Mammals				
	Carnivores	NOEC for neurotoxicity, human acute RfD	0.02 mg/kg bw	Section 4.3.2.1.1.
	Omnivores	LD ₅₀ for squirrels ÷ 10	0.4 mg/kg bw	Section 4.3.2.1.2.
Birds				
	Raptors (Highly Sensitive)	Approximate lethal dose (snowy owl) ÷ 10	0.07 mg/kg bw	Section 4.3.2.2.1.
	Waterfowl and Passerines (Sensitive)	Dietary NOEC	2.3 mg/kg bw	Section 4.3.2.2.2.
	Game Fowl (Tolerant)	Dietary NOEC	100 mg/kg bw	Section 4.3.2.2.3.1.
	Pigeons (Intermediate)	Dietary LOEC ÷ 3	4 mg/kg bw	Section 4.3.2.2.3.2.
Reptiles				
		Toxicity value for raptors	0.07 mg/kg bw	Section 4.3.2.3.1.
Amphibians²				
		LD ₅₀ for bullfrog ÷ 10	0.2 mg/kg bw	Section 4.3.2.3.2.
Aquatic Animals				
Fish				
	Sensitive	LC ₅₀ for bluegills ÷ 20	0.04 mg/L	Section 4.3.3.1.
	Tolerant	LC ₅₀ for medaka ÷ 20	0.3 mg/L	Section 4.3.3.1.
Amphibians³				
	Sensitive		N/A	Section 4.3.3.2.
	Tolerant	LOEC in toad embryos ÷ 10	0.5 mg/L	Section 4.3.3.2.
Invertebrates				
	Sensitive		N/A	Section 4.3.3.3.
	Tolerant	LC ₅₀ for daphnids ÷ 20	0.4 mg/L	Section 4.3.3.3.

¹ Toxicity values derived with adjustment or uncertainty factors are rounded to one significant digit. Toxicity values based on experimental NOECs are rounded to 2 significant digits.

² Terrestrial phase amphibians.

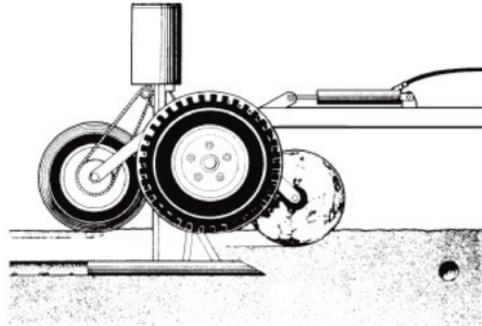
³ Aquatic phase amphibians.

MamCrn	Ac		0.02 mg/kg bw	Section 4.3.2.1.1.
Mam	Ac		0.4 mg/kg bw	Section 4.3.2.1.2.
BrdRapt	Ac		0.07 mg/kg bw	Section 4.3.2.2.1.
BrdSn	Ac		2.3 mg/kg bw	Section 4.3.2.2.2.1.
BrdTl	Ac		100 mg/kg bw	Section 4.3.2.2.3.
Rept	Ac		0.07 mg/kg bw	Section 4.3.2.3.1.
AmphTr	Ac		0.2 mg/kg bw	Section 4.3.2.3.2.
Fsh	Ac	Sn	0.04 mg/L	Section 4.3.3.1.
Fsh	Ac	Tl	0.3 mg/L	Section 4.3.3.1.
Amph	Ac	Tl	0.5 mg/L	Section 4.3.3.2.
AqInv	Ac	Tl	0.4 mg/L	Section 4.3.3.3.
BrdAve	Ac		4 mg/kg bw	Section 4.3.2.2.3.2.



Hand Baiting

Figure 1: Application Methods for Strychnine



Mechanical Baiting

Source: Iowa State University 1992

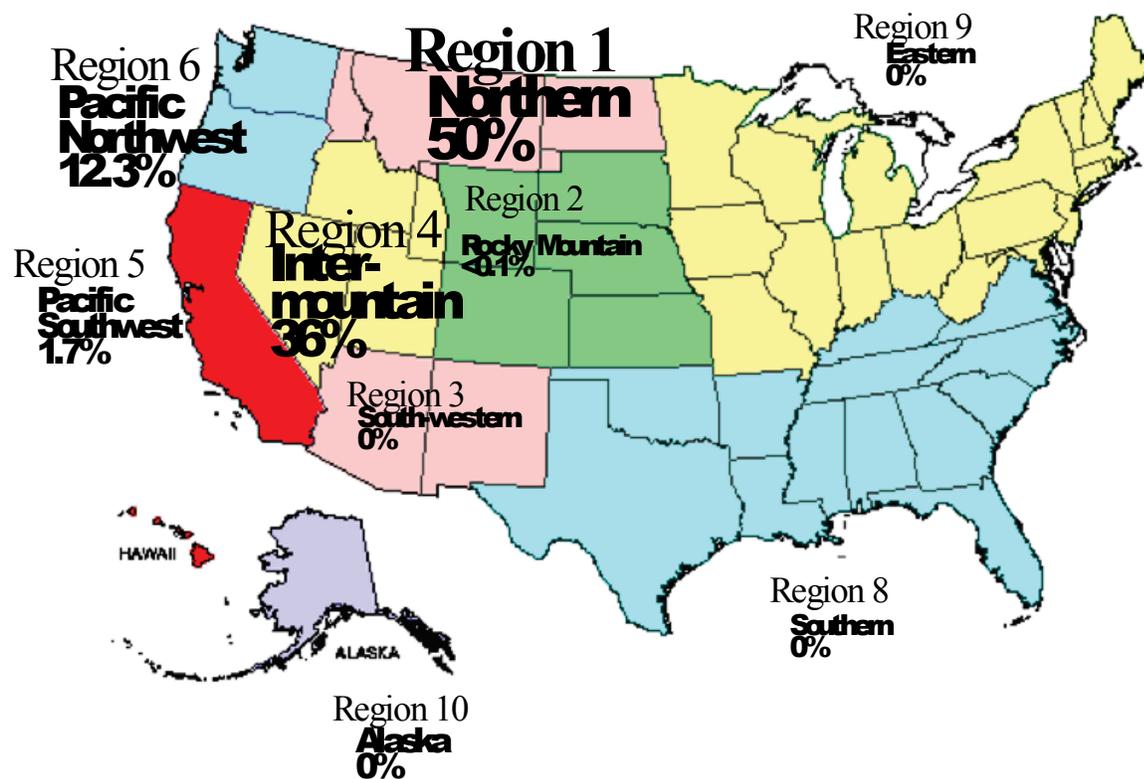


Figure 2: Relative Uses of Strychnine in Forest Service Regions

Source: *USDA/Forest Service Pesticide Use Reports*
<http://www.fs.fed.us/foresthealth/pesticide/reports.shtml>

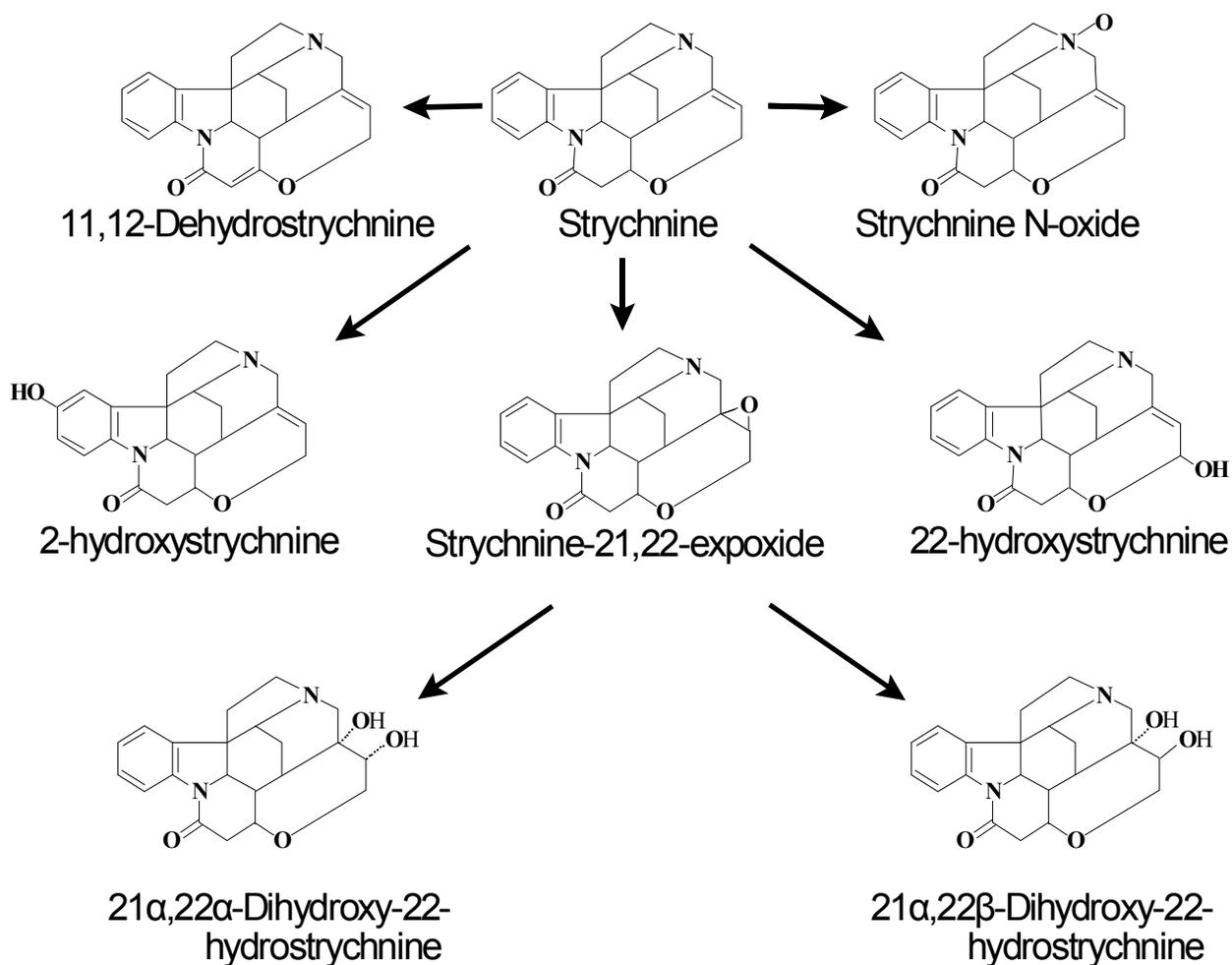


Figure 3: Metabolic pathways of strychnine

Based on Mishima et al. (1985, Figure 6), Oguri et al. (1989, Figure 4), and Tanimoto et al. (1991, Figure 6)

Note: 21 α , 22 α –dihydroxy-22- strychnine and 21 α , 22 β –dihydroxy-22-hydrostrychnine differ only in the orientation of one hydroxyl-group with respect to the ring system.

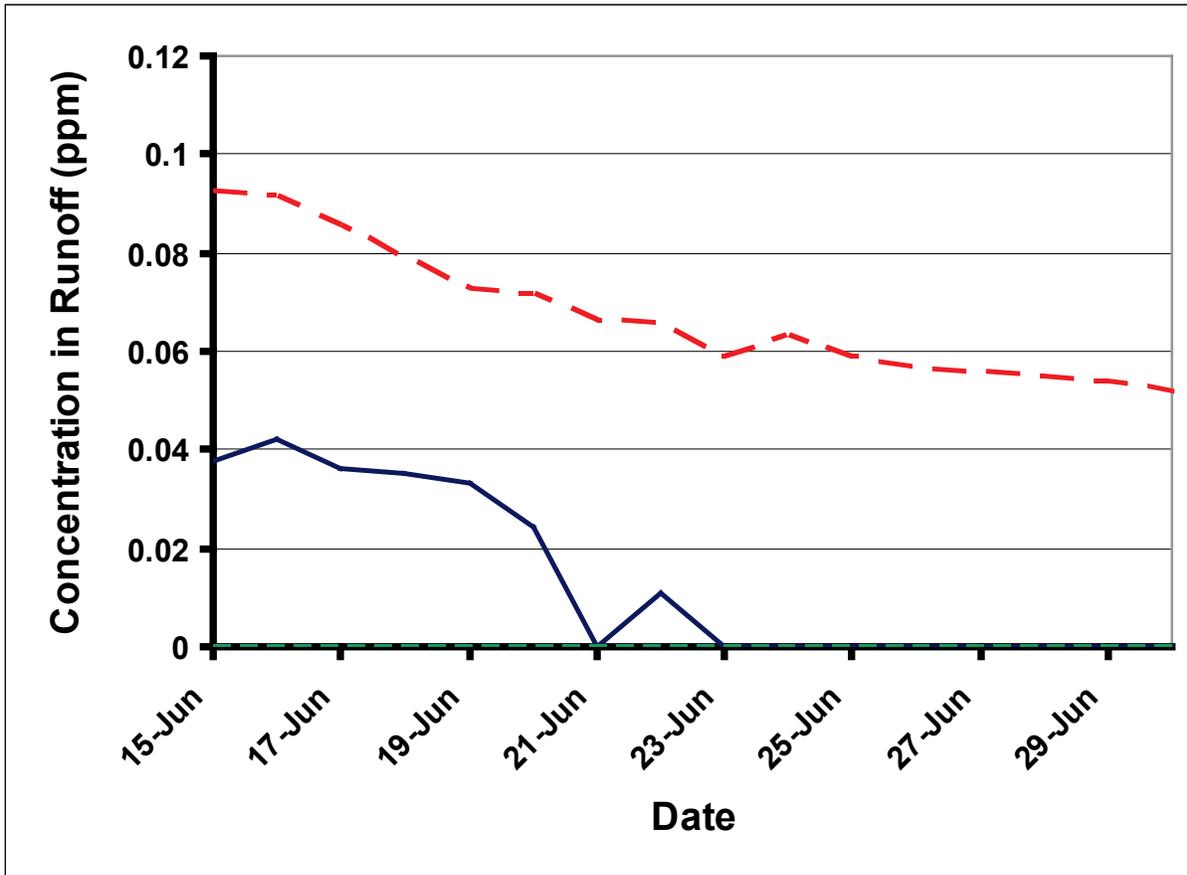


Figure 4: Modeled Concentrations of Strychnine in Runoff

Concentrations in runoff after a surface application of 1 lb a.i./acre. The dashed line is the upper bound. The solid line is the central estimate. See Section 3.2.3.4.5. for discussion.

Parenteral Administration

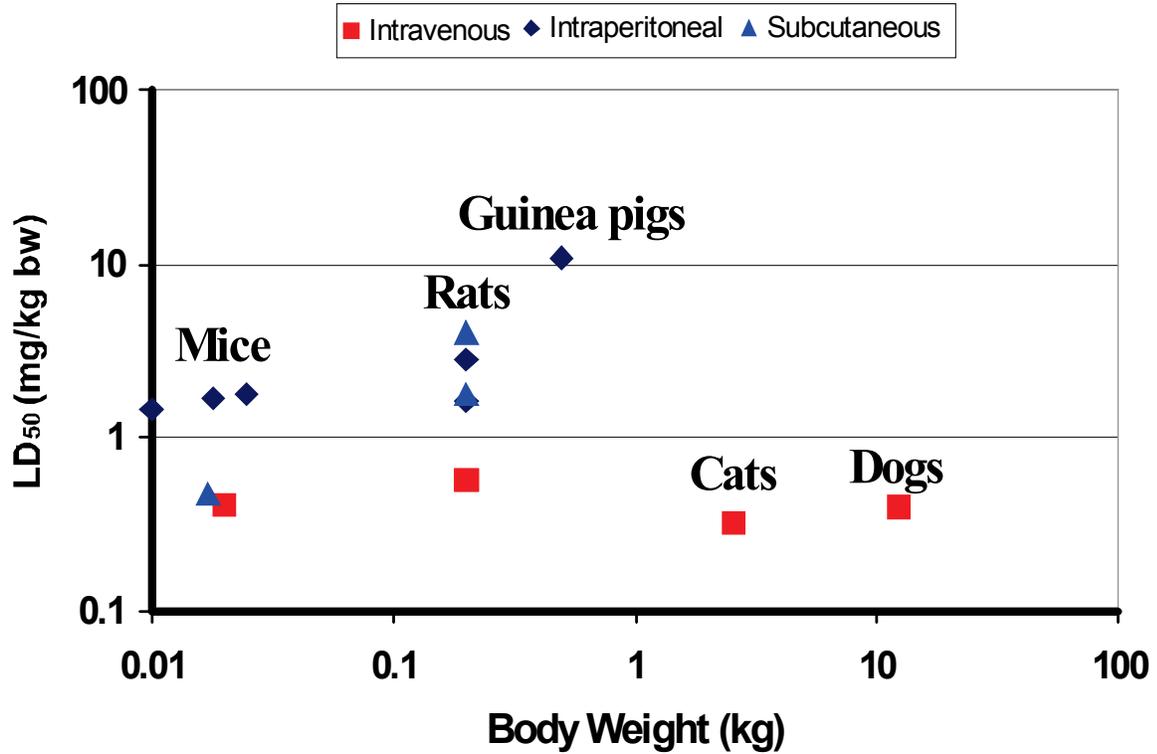


Figure 5: Toxicity of strychnine to mammals following parenteral administration

Data on cats and dogs are approximate lethal doses rather than LD₅₀s.

See Table 13 for data and Section 4.1.2.1 for discussion.

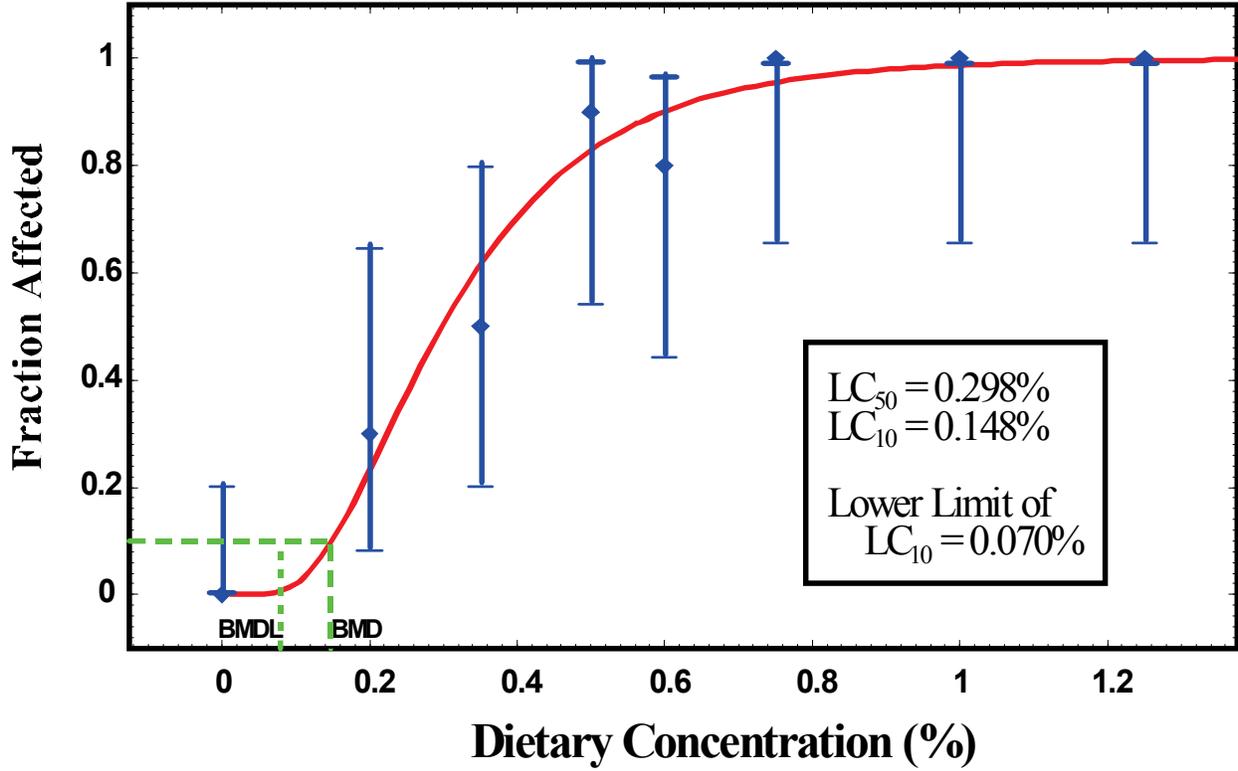


Figure 6: Concentration-Response Analysis for strychnine treated bait to pocket gophers

Data from Evans et al. 1990 as tabulated in Appendix 2.

See Section 4.1.2.1.2 for discussion.

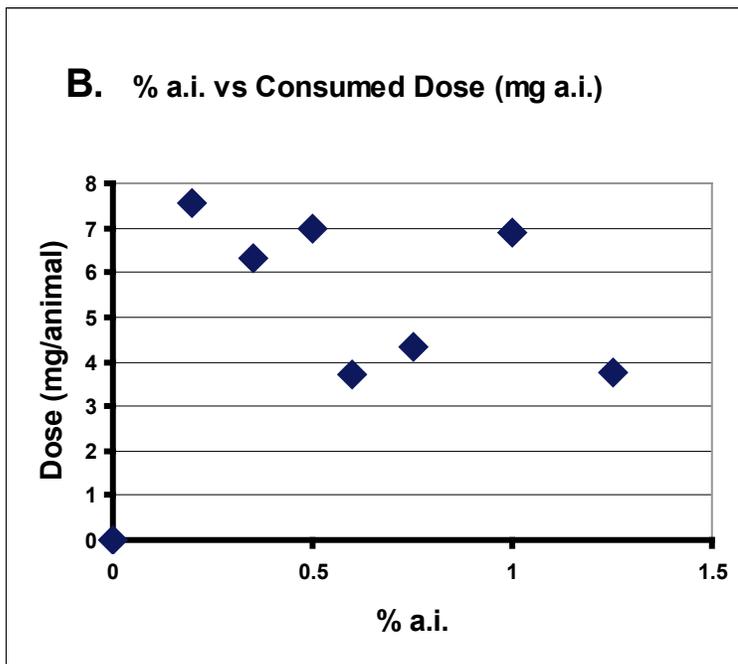
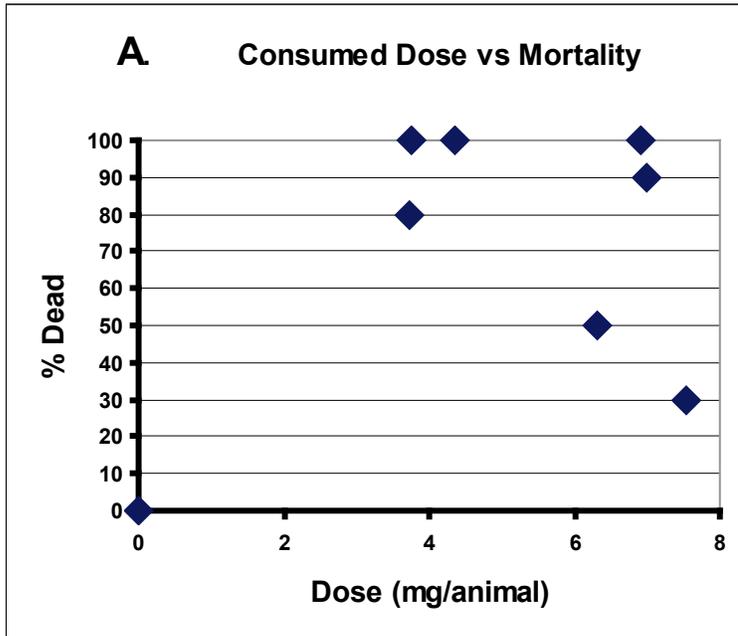


Figure 7: Relationship of strychnine intake and mortality in pocket gophers

Data from Evans et al. 1990 as tabulated in Appendix 2.

See Section 4.1.2.1.2 for discussion.

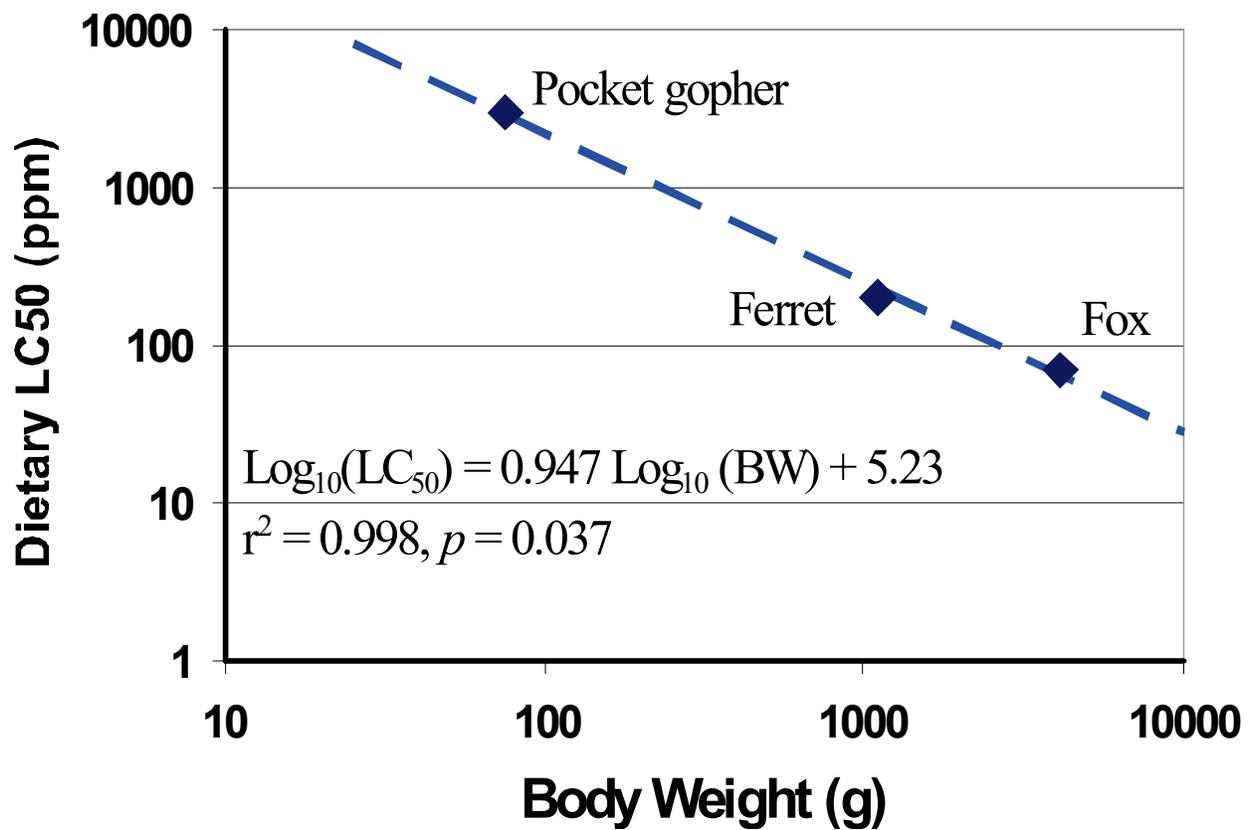


Figure 8: Allometric relationship for dietary exposures in mammals

Based on acute dietary studies by Evans et al. (1990) and Record (1987a,b) as summarized in Appendix 2.

See Section 4.1.2.1.2 for discussion.

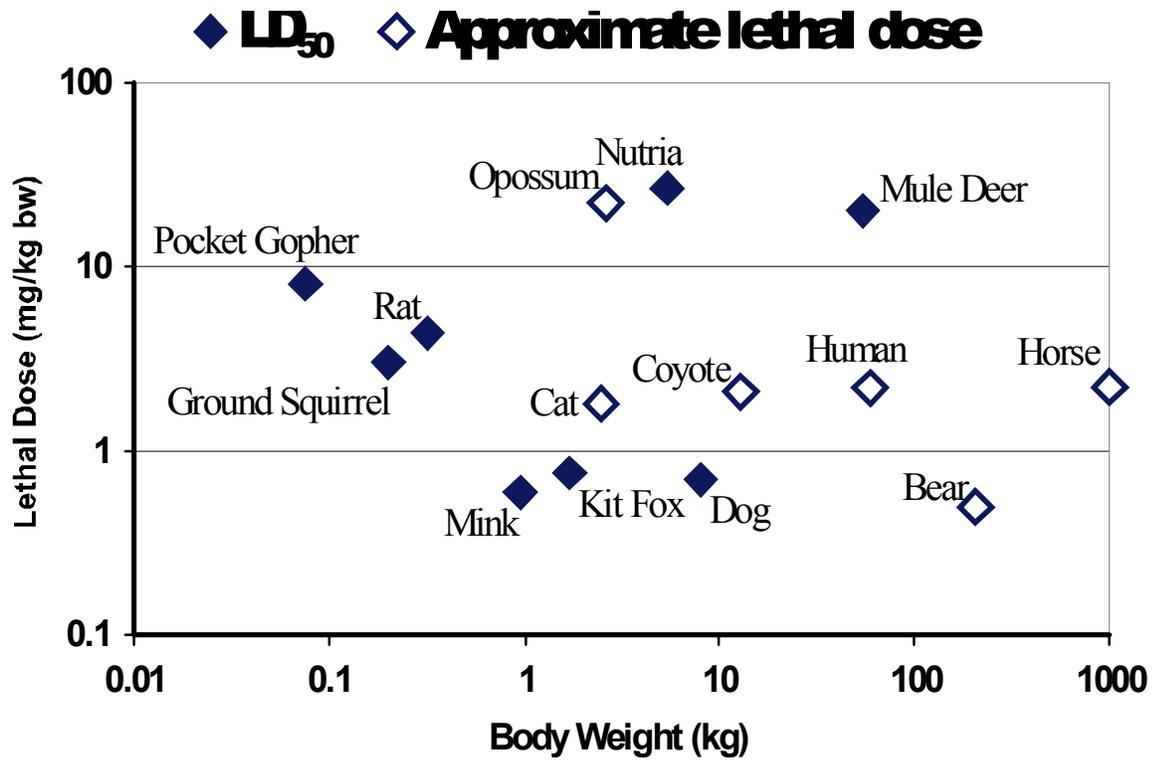


Figure 9: Toxicity of strychnine to mammals

See Table 14 for data and discussion in Section 4.1.2.1.3.

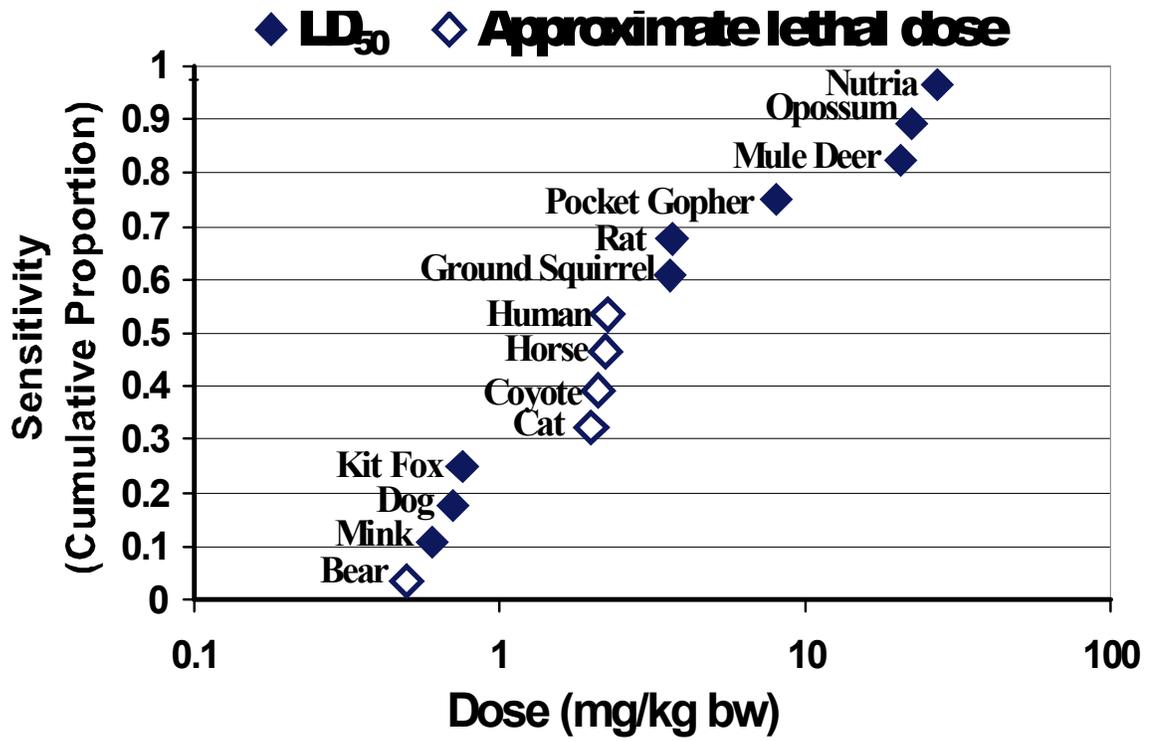


Figure 10: Species sensitivity distribution in mammals (non-dietary)

See Table 14 for data and discussion in Section 4.1.2.1.3.

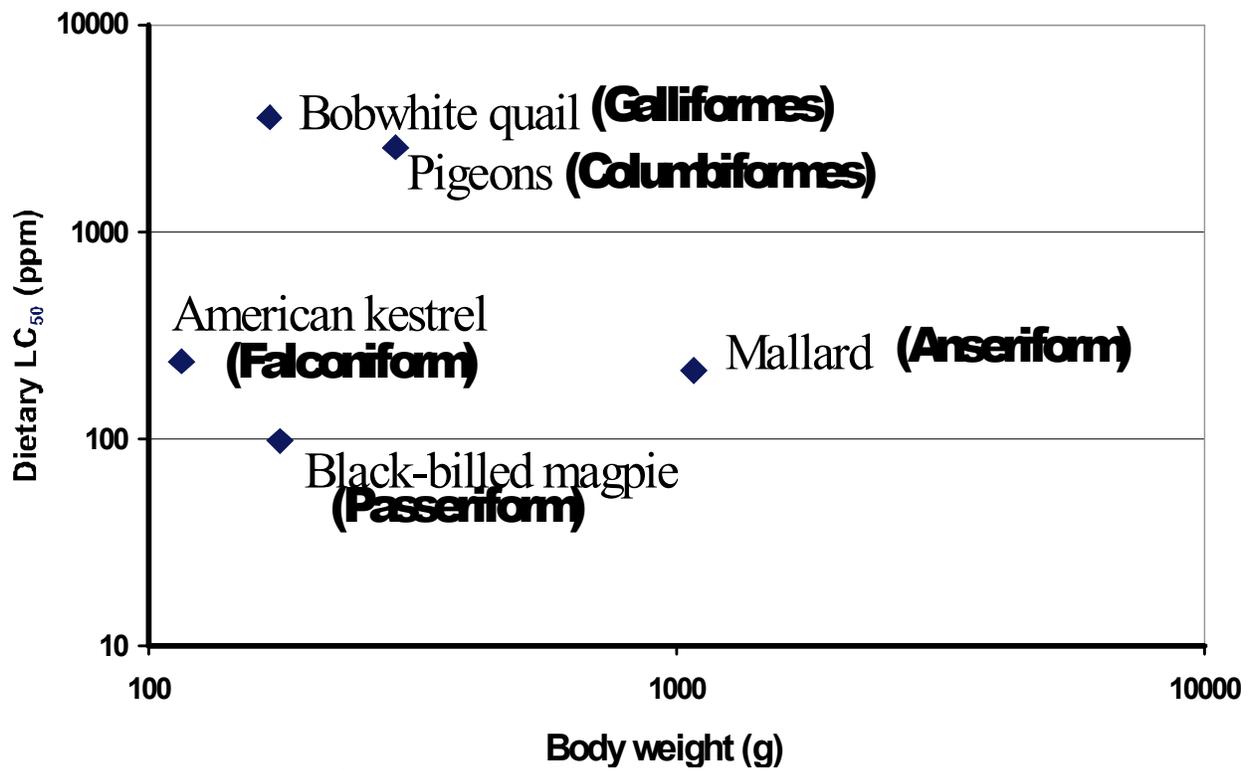


Figure 11: Acute dietary studies in birds

Data summarized in Appendix 4 (Table 2).
See Section 4.1.2.2.1 for discussion.

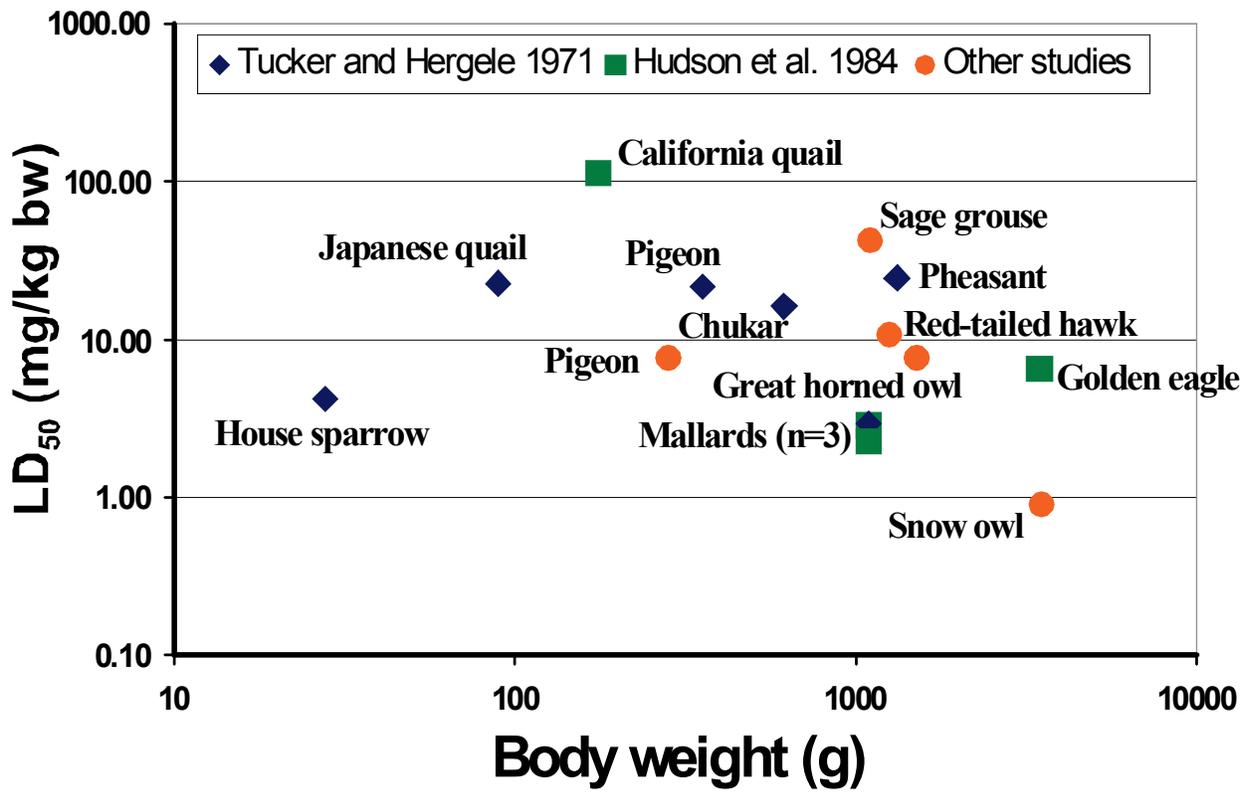


Figure 12: Gavage toxicity studies in birds using strychnine alkaloid

Data summarized in Table 15.
See Section 4.1.2.2.2 for discussion.

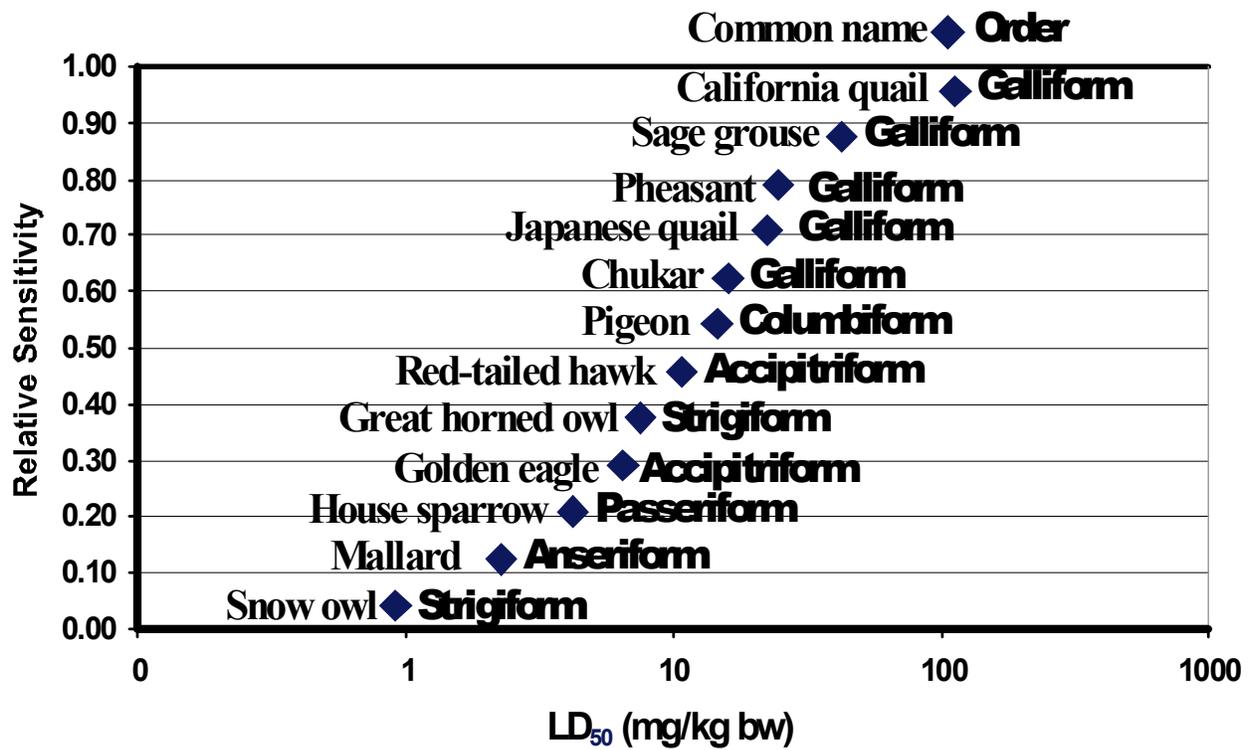


Figure 13: Species sensitivity distribution in birds (gavage LD₅₀s)

Data summarized in Table 15.
 LD₅₀ values for mallards (n=3) and pigeons (n=2) are averaged.
 See Section 4.1.2.2.2 for discussion.

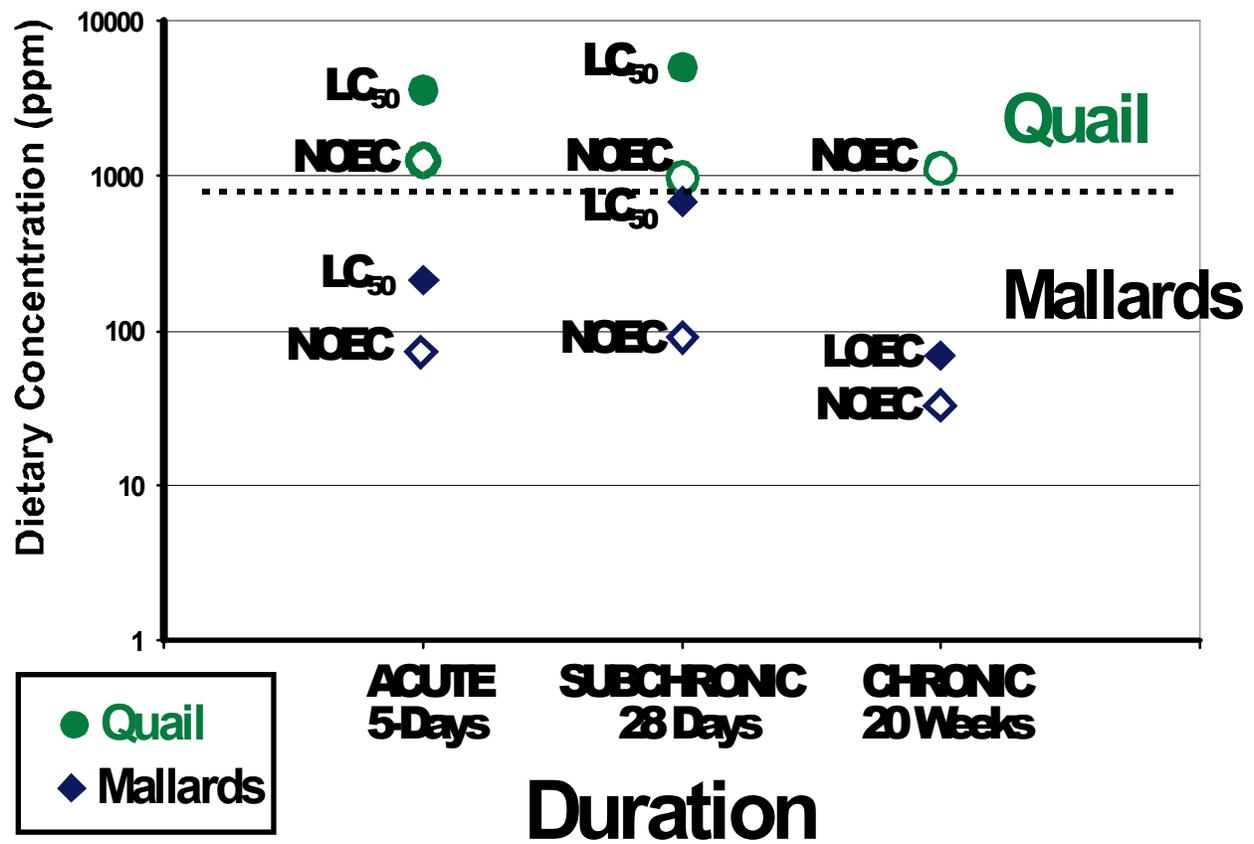


Figure 14: Acute, subchronic, and reproduction studies in quail and mallards

Data summarized in Appendix 4.
See Section 4.1.2.2.3 for discussion.

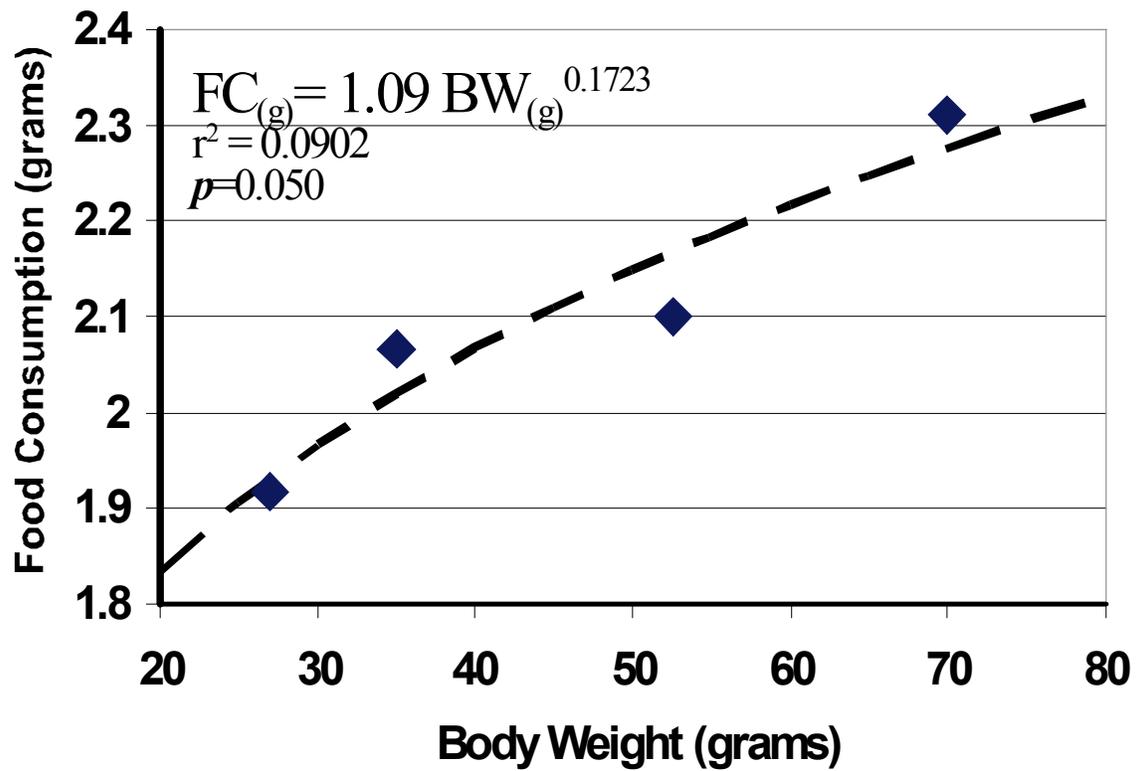


Figure 15: Allometric relationship for food consumption in bullfrogs

Data from U.S. EPA/ORD (1996, p. 457)

Appendix 1: Reports of Poisonings in Humans

Note on Appendix 1: This is a summary of accidental or suicidal exposures.

Most reports involved oral exposures. Other routes of exposure are given in **bold text** at the start of the entry in column 2.

For some reports, doses can be estimated at least crudely. In these cases, the following terms are used for doses in which the individual did or did not survive: **Fatal dose** or **Non-fatal dose**. All cases of non-fatal dosing appear to be dependent on prompt and effective medical treatment.

Most publications do not specify the body weights of the subjects. Unless otherwise specified, a body weight of 70 kg is used for males and 60 kg is used for females.

Some reports from which a dose cannot be estimated have been left in this appendix.

These reports are discussed in Section 3.1.4.1.

Publications arranged in alphabetical order by reference.

Reports of Poisonings in Humans			
Individual	Exposure	Response	Reference
19-year-old male	INTRANASAL "snorted" two lines of a white powder believed to be cocaine. Investigators estimate that "the patient" ingested approximately 120 mg of strychnine.	...rapid onset of severe and uncontrollable muscle spasms, lactic acidosis, body temperature increasing to 43°C, and profound rhabdomyolysis (muscle degeneration consistent with exertion). Complete recovery with normal cerebral, renal, cardiac, and skeletal muscle function. Non-fatal dose: 1.7 mg/kg bw	Boyd et al. 1983
26-year-old female Working note: This paper gives a good discussion the pharmacology and kinetics of strychnine, as well as clinical manifestations in cases of human poisoning and management.	INTRANASAL She "snorted" one "line" of the same white powder ingested by 19-year-old male (described above). Investigators estimate that "the patient" ingested about 60 mg of strychnine (left over from the cutting of cocaine).	Muscle spasms of the extremities, muscle pain and cramps, nausea, vomiting, sweating, blurred vision, and headache. Morning after exposure, headache and severe muscle pain persisted; however, patient was discharge 18 hours after admission and recovered completely within a few days. Non-fatal dose: 1 mg/kg bw	Boyd et al. 1983
32-year old farmer	Oral exposure, dose not characterized.	Source of strychnine not clear. Died after 6 days of hospitalization. Working Note: Diagnosis of strychnine poisoning seems questionable.	Burn et al. 1989
42 year old male	Ingestion of unknown amount	Survived. Peak measured serum of less than 2 mg/L.	Edmunds et al. 1986

Appendix 1: Reports of Poisonings in Humans

Reports of Poisonings in Humans			
Individual	Exposure	Response	Reference
50 year old female, 64 kg bw	Dermal exposure to spilled solution. Author's estimate of 2% concentration of strychnine. Exposure to left palm of hand for about 30 minutes prior to washing hands. Authors' estimate of absorbed dose: 9.375 mg/kg bw. Author's estimate of peak plasma concentration: 0.786 mg/L.	Biomonitoring at 28 hours after exposure: Plasma: 0.196 mg/L, Urine: 6.85 mg/L. Symptoms: Initial tingling of hand but no dermal irritation. After about 12 hours, shaking of arms and legs progressing to spasms. After 24 hours, sought medical attention. Hypersensitive to touch on legs. Non-fatal dose: 9.375 mg/kg bw Sections 3.1.3.2 and 3.1.12 for discussion.	Greene and Meatherall 2001
Suicide. 51-yr old male	Ingestion of tablets containing 4.8 grams (4,800 mg) of strychnine.	Fatal despite aggressive treatment. Peak serum strychnine of about 5 mg/L. Working Note: The authors assumed 100% oral absorption but this is probably wrong. Fatal-dose: 69 mg/kg bw	Heiser et al 1989
Accidental ingestion in 18-yr old woman.	Dose not determined.	Serum strychnine levels of 2.45 mg/L about 6 hours after ingestion. [Similar to peak serum in surviving patient in Edmunds et al. 1996]. Individual survived.	Hernandez et al. 1988
34 year old woman	Consumed 340 mg of strychnine sulfate (equiv. to ≈ 262 mg alkaloid [340 mg sulfate $\times 0.7732 = 262.888$ mg alkaloid, see MW in Table 1])	Seizures without cyanosis. Gastric lavage used. Strychnine found in urine but no values given. No serum assay for strychnine. Non-fatal-dose: 4.3 mg/kg bw	Lambret et al. 1981
56 year old male	Estimated dose of 5.6 g (5,600 mg). The individual was a pharmacist. It is not clear if the strychnine was from a tablet or from a rodenticide.	Found dead. Tissue levels: liver, 125 mg; kidneys, 30 mg; bowel, 4,608 mg.; stomach and contents, 653 mg.; blood, 4 mg/100 mL (Assuming a hematocrit of about 0.5, this would be about 8 mg/100 mL or 0.8 mg/L plasma. This is much lower than other reported fatalities) ; urine, trace Fatal dose: 80 mg/kg bw	Lloyd and Pedley 1953

Appendix 1: Reports of Poisonings in Humans

Reports of Poisonings in Humans																									
Individual	Exposure	Response	Reference																						
34 year old male	½ of a container which had 2.25 g strychnine sulfate, corresponding to about 1,740 mg alkaloid [2,250 mg sulfate x 0.7732 = 1,739.7 mg alkaloid] Assuming 70 kg, dose ≈ 25 mg/kg bw.	Survived poisoning with treatment but subsequently died due to pulmonary embolism. Peak serum concentration of 2.12 mg/L at 3 hours after ingestion. Non-fatal dose: 25 mg/kg bw	Palatnick et al. 1995 (abst) Palatnick et al. 1997 (full paper)																						
54 yr old male, 70 kg bw	<i>Some grains</i> from a can with up to 140 g with 0.35% strychnine sulfate. Dose cannot be determined.	Fatal exposure. <i>61 g of green, thick, mortar-like material in the stomach, of a similar color as the contents of the poison can.</i> <table border="1" data-bbox="841 709 1224 1117"> <thead> <tr> <th>Tissue</th> <th>Concentration (mg/L)</th> </tr> </thead> <tbody> <tr> <td>Stomach contents</td> <td>175</td> </tr> <tr> <td>Stomach</td> <td>14.9</td> </tr> <tr> <td>Bile</td> <td>9.2</td> </tr> <tr> <td>Liver</td> <td>6.2</td> </tr> <tr> <td>Small intestines</td> <td>4.1</td> </tr> <tr> <td>Blood</td> <td>3.3</td> </tr> <tr> <td>Kidney</td> <td>3.2</td> </tr> <tr> <td>Plasma</td> <td>2.6</td> </tr> <tr> <td>Urine</td> <td>1.4</td> </tr> <tr> <td>CSF</td> <td>0.08</td> </tr> </tbody> </table> CSF: cerebrospinal fluid No strychnine detected in brain tissue, vitreous fluid, or colon. Individual died before medical treatment was administered.	Tissue	Concentration (mg/L)	Stomach contents	175	Stomach	14.9	Bile	9.2	Liver	6.2	Small intestines	4.1	Blood	3.3	Kidney	3.2	Plasma	2.6	Urine	1.4	CSF	0.08	Perper 1985
Tissue	Concentration (mg/L)																								
Stomach contents	175																								
Stomach	14.9																								
Bile	9.2																								
Liver	6.2																								
Small intestines	4.1																								
Blood	3.3																								
Kidney	3.2																								
Plasma	2.6																								
Urine	1.4																								
CSF	0.08																								
20 year old woman	Strychnine tables containing 7.5 mg of “N-oxyd-Strychnin”. The individual consumed 18-19 tablets. Estimated dose: 135 to 143 mg of strychnine. Reported dose: 135 to 143 mg	Severe signs of toxicity. Death due to asphyxiation. Fatal-dose: 2.25 to 2.3 mg/kg bw	Salm 1952																						

Appendix 1: Reports of Poisonings in Humans

Reports of Poisonings in Humans			
Individual	Exposure	Response	Reference
21-year old male, 60 kg bw.	Ingested 700 mg of strychnine nitrate. This is equivalent to about 580 mg of strychnine alkaloid [700 mg x 0.8414 = 588.98 mg]. The source of the strychnine is not specified in publication.	Full recovery after 16 days of hospitalization. No detectable concentration in blood (limit of detection not specified). Detectable amounts in urine (\approx 1 mg/L) only in first 24 hours. Gastric lavage fluid contained 79 mg of strychnine. Non-fatal dose: 9.8 mg alkaloid/kg bw.	Sgaragli and Mannaioni 1973
1 year old girl	Estimated dose of 16 mg from strychnine tablets. The dose estimate appears to be based on assays of stomach contents. The stomach, however, had been <i>washed out</i> (probably gastric lavage) and it is not clear how or if this was considered in the dose estimate.	Fatal exposure U.S. EPA/NCEA 2008, body weight for 1 year old child is 11.4 kg. Fatal dose: 1.4 mg/kg bw	Stannard 1969
18 year old male	8 oz. of a 0.2% preparation of strychnine rat poison. About 227 grams of preparations [1 oz. = 28.35 g] or 454 mg.	Muscle tightness and contractions. No measurements of strychnine in serum or urine. Non-fatal dose: 6.5 mg/kg bw	Swissman and Jacoby 1964
Middle aged male	300 mg strychnine (NOS)	Convulsions but survived with treatment. Non-fatal dose: 4.3 mg /kg bw.	Teitelbaum and Ott 1970
29-year old male	240 mg strychnine sulfate	No convulsions. Non-fatal dose: 3.4 mg /kg bw.	Teitelbaum and Ott 1970
56-year old male	2.5 oz. of 0.35% strychnine sulfate.	Seizures and convulsions. Fatal exposure. Note: These data reported in this paper are identical to that reported in Perper 1985. Both studies are from Pittsburgh, PA. Minor differences in study description are incidental.	Winek et al. 1986

Appendix 2: Acute Oral Toxicity to Mammals

Note on Appendix 1: This is a summary of acute toxicity studies in mammals. Most studies involve oral administration but some studies using parenteral routes are included. Some of the publications cited in this appendix also involved field applications.

Observations from field studies are summarized in Appendix 3.

Some studies involve strychnine sulfate and strychnine chloride are included but the text of the risk assessment focuses on strychnine alkaloid.

Studies are listed in alphabetical order by author.

Acute Toxicity in Mammals			
Species	Exposure	Response	Reference
Golden-mantled ground squirrels (<i>Spermophilus lateralis</i>), males and females and mink (<i>Mustela vison</i>), females only	Single gavage administration of pure strychnine alkaloid suspended in propylene glycol with 7-day observation period.	<u>Squirrels</u> LD ₅₀ = 3.6 (2.4-5.4) mg/kg <u>Mink</u> LD ₅₀ = 0.6 mg/kg This was a range-finding procedure for bait bioassays.	Anthony et al. 1984
Golden-mantled ground squirrels (<i>Spermophilus lateralis</i>), n=5 and Western pocket gophers (<i>Thomomys mazama</i>), n=5	Hand baiting with 20 g of 0.5% strychnine-treated oats daily for 3 days. Animals fasted for 4 hours before testing; supplemental food provided after day 1 of test. Controls: untreated oats according to the same testing regime	4/5 squirrels and 4/5 pocket gophers died of bait consumption within 4/12 hours after bait presentation. Mean consumption of bait = 1.03 g (dead squirrels) and 1.02 g (dead gophers); mean consumption of strychnine alkaloid by each species = 5.1 mg. Resistance to strychnine was strongly suggested by surviving squirrel (consumed almost 29 mg of strychnine in 4 consecutive days or about 44 mg/kg/day) and the one surviving pocket gopher (consumed >125 mg of strychnine in 4 consecutive days or about 272 mg/kg/day) with no ill effects.	Anthony et al. 1984

Appendix 2: Acute Oral Toxicity Studies in Mammals (continued)

Acute Toxicity in Mammals			
Species	Exposure	Response	Reference
Domestic mink (<i>Mustela vison</i>), caged	0, 0.5, 1.0, or 3.0 mg of strychnine alkaloid in corn oil after feeding on 100 g of mink feed--the approximate weight of a skinned, decapitated ground squirrel. Strychnine intake (\bar{x}): 0, 0.42, 0.96, or 2.33 mg/kg. Controls received plain corn oil.	0 mg = 0/5 deaths and no effect 0.5 mg = 0/5 deaths and no reaction to strychnine 1.0 mg = 2/5 deaths; two survivors showed no effects of exposure; one survivor had exaggerated response to sound and light for 6 hours 3.0 mg = 5/5 deaths and all deaths occurred within 6 hours. There were no significant changes in food consumption or body weights among survivors.	Anthony et al. 1984
Porcupines (<i>Erethizon dorsatum</i>), 7 males (9.1-11.1 kg) and 8 females (5.7-7.7 kg), individually caged	10 caged porcupines presented with salt blocks containing 5.79% strychnine alkaloid; consumption visually estimated for 3 consecutive days (baits blocks weighed before and after 3-day exposure period). 5 controls received blocks with the nontoxic formulation. Post-exposure 5-day observation period. See Table 2 of the study for detailed consumption information.	None of the animals died or showed any signs of strychnine intoxication despite high strychnine consumption rates. Single dose NOEC: 91.4 mg/kg bw Cumulative NOEC: 177.9 mg/kg bw See Table 2 of study.	Anthony et al. 1986
Cat (NOS)	Strychnine, oral dose (NOS)	Oral lethal dose \approx 2.0 mg/kg	Atkins and Johnson 1975
Most mammals (NOS)	Strychnine, oral dose (NOS)	Oral lethal dose \approx 0.3 to 1 mg/kg	Atkins and Johnson 1975
Dog (NOS)	Strychnine (NOS)	LD ₅₀ = 0.70 mg/kg	Baker et al. 1982
Pigs (NOS)	Strychnine (NOS)	Lethal dose \approx 10 mg/kg bw	Baker et al. 1982
Cow (NOS)	Strychnine (NOS)	Lethal dose \approx 10.0 mg/kg	Baker et al. 1982

Appendix 2: Acute Oral Toxicity Studies in Mammals (continued)

Acute Toxicity in Mammals																																																									
Species	Exposure	Response			Reference																																																				
Opossum (<i>Trichosurus vulpecula</i>), hand caught in New Zealand	Stock solution of strychnine hydrochloride (10 mg strychnine alkaloid/mL distilled water) Single gavage dose of 10, 15, 17, 19, or 20 mg/kg.	Mortality: 10.0 mg/kg – 1/8 at 38 minutes 15.0 mg/kg – 4/9 at 30-38 minutes 17.0 mg/kg – 4/8 at 40-42 minutes 19.0 mg/kg – 6/16 at 45 minutes 20.0 mg/kg – 6/8 at 25 minutes LD ₅₀ = 22.36 (15.23-32.83) mg/kg bw Toxic signs of poisoning included convulsive seizures in the animals while still conscious for approximately 25-45 minutes.			Bell 1972																																																				
Pocket gophers (<i>Thomomys talpoides</i>)	Strychnine in oat bait for 3 days. No other food choice The mg a.i. consumed in each group are given below: <table border="1" data-bbox="539 974 734 1255"> <thead> <tr> <th>% a.i.¹</th> <th>Mg a.i.</th> </tr> </thead> <tbody> <tr><td>0.0</td><td>0</td></tr> <tr><td>0.2</td><td>7.54</td></tr> <tr><td>0.35</td><td>6.3</td></tr> <tr><td>0.50</td><td>7</td></tr> <tr><td>0.60</td><td>3.72</td></tr> <tr><td>0.75</td><td>4.35</td></tr> <tr><td>1.0</td><td>6.9</td></tr> <tr><td>1.25</td><td>3.75</td></tr> </tbody> </table> Working Note: See Evans et al. 1990.xls .	% a.i. ¹	Mg a.i.	0.0	0	0.2	7.54	0.35	6.3	0.50	7	0.60	3.72	0.75	4.35	1.0	6.9	1.25	3.75	<table border="1" data-bbox="841 760 1224 1117"> <thead> <tr> <th>% a.i.¹</th> <th>Bait consumed (g)</th> <th>a.i. mg</th> <th>No. Dead</th> </tr> </thead> <tbody> <tr><td>0.0</td><td>6.46</td><td>0</td><td>0/20</td></tr> <tr><td>0.2</td><td>3.77</td><td>7.54</td><td>3/10</td></tr> <tr><td>0.35</td><td>1.80</td><td>6.3</td><td>5/10</td></tr> <tr><td>0.50</td><td>1.40</td><td>7</td><td>9/10</td></tr> <tr><td>0.60</td><td>0.62</td><td>3.72</td><td>8/10</td></tr> <tr><td>0.75</td><td>0.58</td><td>4.35</td><td>10/10</td></tr> <tr><td>1.0</td><td>0.69</td><td>6.9</td><td>10/10</td></tr> <tr><td>1.25</td><td>0.30</td><td>3.75</td><td>10/10</td></tr> </tbody> </table> ¹ Mean measured concentration. Note: There is no correlation of amount of a.i. consumed and mortality. Higher concentrations sicken animals more rapidly. A similar pattern is seen in field studies. Residues in tissues are not clearly correlated to concentration in bait over ranges of 0.5 to 1.25%. See Table 2 of paper. In fatally exposed animals, tissue residues ranged from 0.2 to 90 mg/kg bw with mean values from about 7.5 mg/kg bw to 19.14 mg/kg bw	% a.i. ¹	Bait consumed (g)	a.i. mg	No. Dead	0.0	6.46	0	0/20	0.2	3.77	7.54	3/10	0.35	1.80	6.3	5/10	0.50	1.40	7	9/10	0.60	0.62	3.72	8/10	0.75	0.58	4.35	10/10	1.0	0.69	6.9	10/10	1.25	0.30	3.75	10/10	Evans et al. 1990
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Dogs	Strychnine (NOS)	Oral toxic dose: 0.1 to 1.2 mg/kg bw Paper is more like a review but is not well-referenced.			Harris 1975																																																				
Dogs	Strychnine (NOS)	Toxic dose: ≈0.45 to 0.75 mg/kg bw			Hatch and Funnel 1968																																																				
Rat	Strychnine (NOSS)	LD ₅₀ : 16.2 mg/kg bw			Hayes 1982																																																				

Appendix 2: Acute Oral Toxicity Studies in Mammals (continued)

Acute Toxicity in Mammals																	
Species	Exposure	Response	Reference														
Bear (<i>Ursus arctos yesoensis</i>)	Strychnine nitrate,	0.25 mg/kg bw: NOEC 0.5 mg/kg bw: death in 13 hours 1 mg/kg bw: death in 30 minutes Detectable amount of strychnine only in the stomach except high dose bear with 11 mg/kg in stomach.	Inukai 1969														
Dogs (40 NOC)	Bear carcass muscle poisoned with strychnine. See above.	No adverse effects	Inukai 1969														
Foxes (2) and raccoon (1)	Bear carcass muscle poisoned with strychnine. See above.	No adverse effects	Inukai 1969														
Mice (NOS)	Strychnine sulfate, intraperitoneal injection	<table border="1"> <thead> <tr> <th rowspan="2">Weight (g)</th> <th colspan="2">LD₅₀ (mg/kg bw)</th> </tr> <tr> <th>Males</th> <th>Females</th> </tr> </thead> <tbody> <tr> <td>10</td> <td>14</td> <td>15</td> </tr> <tr> <td>18</td> <td>31</td> <td>30</td> </tr> <tr> <td>26</td> <td>48</td> <td>41.9</td> </tr> </tbody> </table>	Weight (g)	LD ₅₀ (mg/kg bw)		Males	Females	10	14	15	18	31	30	26	48	41.9	Lamanna and Hart 1968
Weight (g)	LD ₅₀ (mg/kg bw)																
	Males	Females															
10	14	15															
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Coyotes, 10.0 to 16.1 kg	Fed strychnine in squirrel carcasses Low dose: 0.286 to 1.059 mg/kg bw High dose: 1.321 to 2.860 mg/kg bw	Low dose: 0/4 mortality. Signs of toxicity not discussed. High dose: 1/4 mortality. Surviving animals had no signs of toxicity. Coyotes appear to have generally rejected stomach and G.I. tract of squirrels. See Section 4.2.2. of this Forest Service risk assessment.	Marsh et al. 1987														
Coyotes, 10.0 to 16.1 kg (these appear to be same animals used in single dose study)	Fed strychnine in squirrel carcasses at doses of about 1.69 to 7.2 mg/kg bw/day for 5 days.	No mortality or signs of toxicity.	Marsh et al. 1987														
Horses (n=3)	Accidental poisoning incident. 0.025% strychnine in oats. Total consumption of about 1.5 lb – i.e., 0.000375 lb a.i. or about 1700 mg. Not clear how much each horse ate.	Two horse became ill. One (1000 lb) died. Another shivered slightly (1000 lb). The other horse (1200 lb) became severely intoxicated but recovered with treatment. Working Note: While the dose to each horse is not known, the maximum amount that could have been consumed was 1700 mg ÷ 453.6 kg ≈ 3.75 mg/kg bw. If evenly distributed, the average dose is 1.25 mg/kg bw.	Meek and Keatts 1971														

Appendix 2: Acute Oral Toxicity Studies in Mammals (continued)

Acute Toxicity in Mammals			
Species	Exposure	Response	Reference
Nutria (probably <i>Myocastor coypus</i>)	Strychnine NOS	LD ₅₀ : 27 mg/kg bw. Note: This appears to be a secondary citation but no reference is given.	Nolte and Wagner 2001
Rats	Strychnine NOS	LD ₅₀ : 3 mg/kg bw This is the lowest reported LD ₅₀ for rats encountered in the literature but is very similar to the LD ₅₀ s of 2.2 and 6.4 mg/kg bw reported in U.S. EPA/OPP 1996c.	Osweiler 1977
European ferrets (<i>Mustela putorius furo</i>) Body mass of about 1.1 kg from Smith et al. 2000.	5-day dietary exposure to strychnine alkaloid in chow (NOS)	Dietary LC ₅₀ : 198 ppm Working note: For European ferrets, Bleavins and Aulerich (1981) give factors of 0.042 to 0.049. Using 0.05, the dietary LC ₅₀ corresponds to a dose of about 10 mg/kg bw.	Record 1987a, MRID 40296502 in U.S. EPA/OPP 1996d
Red fox (<i>Vulpes fulva</i>)	5-day dietary exposure to strychnine alkaloid in chow (NOS)	Dietary LC ₅₀ : 70 ppm Working note: U.S. EPA/ORD (1993, p. 2-224) gives a food consumption factor of 0.069 (g/g) for a non-breeding red fox (≈4-5 kg). The dietary LC ₅₀ corresponds to a dose of about 4.8 mg/kg bw.	Record 1987b, MRID 40296503 in U.S. EPA/OPP 1996d
Skunk (<i>Mephitis mephitis</i>)	Strychnine alkaloid administered in an egg	31 mg/egg lethal to all animals (number not specified). Taking a body weight of about 2 kg (Smith et al. 2003), the lethal is about 15 mg/kg bw	Record 1987c, MRID 40296501 in U.S. EPA/OPP 1996d
Dogs	Strychnine NOS	Lethal dose: 75 to 300 mg. Note that this is not mg/kg bw.	Rudd 1956
Pigs	Strychnine NOS	Lethal dose: 150 to 750 mg. Note that this is not mg/kg bw.	Rudd 1956
Kit fox (<i>Vulpes macrotis mutica</i>)	strychnine alkaloid	LD ₅₀ : 0.75 (0.33-1.69) mg/kg	Schitoskey 1975
Kit fox (<i>Vulpes macrotis mutica</i>), average size 1.7 kg	Strychnine in rat carcasses	Kangaroo rat dosed with 12.8 mg killed one fox in 30 minutes. Lethal dose: ≈7.5 mg/kg bw. Working note: This is 10x the LD ₅₀ . Not clear why such a high dose was used to assess secondary hazard.	Schitoskey 1975
Mule deer (<i>Odocoileus hemionus</i>)	Strychnine alkaloid Animals 8-11 months old. Vehicle not specified.	LD ₅₀ : 17-24 mg/kg	Tucker and Crabtree 1970; Hudson et al. 1984

Appendix 2: Acute Oral Toxicity Studies in Mammals (continued)

Acute Toxicity in Mammals			
Species	Exposure	Response	Reference
Rat (<i>Rattus norvegicus</i>)	Oral.	LD ₅₀ s Males: 6.4 (5.8-71) mg/kg bw Females: 2.2 (1.9-2.5) mg/kg bw Signs of toxicity included piloerection, tremors, increased breathing rate and difficulty in breathing, and prostration with death occurring within 1 hour.	U.S.EPA/OPP 1996c, p. 4 U.S.EPA/OPP 1996d, p.5

Appendix 3: Field Studies Involving Applications of Strychnine

Note on Appendix 3: This is a summary of field studies involving effects in mammals and birds. Acute toxicity studies in mammals are summarized in Appendix 2 and toxicity studies in birds (acute, subchronic, and reproductive) are summarized in Appendix 4. The field studies are discussed in Section 4.1.2.2.4 of this risk assessment. A summary of incident reports from U.S. EPA/OPP (2009) is given at the end of this appendix.

Application/Site	Response	Reference
<p>Below-ground hand baiting.</p> <p>Distribution of 0.5% strychnine oat bait in pocket gopher burrow s on September 14, 1982 to two 8-ha treated plots (T1 and T2). The treated plots and the one 8-ha control plot (C1) were located in a mixed conifer community dominated by ponderosa pine (<i>Pinus ponderosa</i>) at 1400- to 1500-m elevation on the Sisters Ranger District of the Deschutes National Forest.</p> <p>About 3.5 kg/ha bait was applied (by hand baiting) on plot T1; about 0.8 kg/ha bait was applied at plot T2.</p> <p>N=53 golden-mantled ground squirrels (<i>Spermophilus lateralis</i>) on treated plots</p> <p>N=25 golden-mantled ground squirrels (<i>Spermophilus lateralis</i>) on untreated plots.</p> <p>Squirrels were equipped with 5-6 g 164 MHz radio transmitters. Radio tracking began 5 days prior to baiting and continued daily for 10 or more days after baiting.</p>	<p>Ground squirrel counts decreased by 72% on treated plots (from 3 or 4 pretreatment to 1 post baiting) and increased by 75% (from 8 pretreatment to 14 during the post baiting observation period)</p> <p>There was a significant ($p < 0.05$) decrease in the mean weight of dead squirrels (152.4 g; $CL_{95}, \pm 7.3$ g), compared with survivors (185.5 g; $CL_{95}, \pm 11.6$ g)</p> <p>Mortality accounted for 49% of the squirrels (26/53) on treated plots; furthermore, 88% of the mortalities (23/26) occurred within 5 days after baiting.</p> <p>73% (19/26) of the carcasses of treated squirrels were found above ground. Of the carcasses found below ground, five were in burrow systems of pocket gophers; whereas, only two were found in their own nest. In addition, badgers killed two of the treated squirrels and three others began hibernating prior to treatment.</p> <p>There was no mortality among squirrels on the untreated plot, but two were taken by badgers and three began hibernating prior to treatment. No other animal species were found dead.</p> <p>Strychnine caused mortality in all but one of the recovered animals.</p>	<p>Anthony et al. 1984</p>
<p>Additional note on Anthony et al. 1984</p> <p><u>Body burden in squirrels:</u> mean amount of strychnine in carcasses was 0.35 mg (0.09-1.08 mg, $CL_{95}, \pm 0.10$ mg); 99% of toxicant was found in GI tract.</p> <p>Using average body of 152.4 g, the concentrations in squirrels were ≈ 2.3 (0.6 – 7) mg/kg bw.</p> <p>Of 26 poisoned squirrels, one had 16 kernels of bait (estimated 1.4 mg strychnine) and one had 21 kernels of bait (estimated 1.8 mg of strychnine) in the cheek pouches.</p>		

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Population recovery study performed in 1983 on three widely separated pine plantations (B1, B2, and B3) baited with strychnine for pocket gophers in 1982.</p> <p><i>In 1982, Plots B1 and B2 received 3.5 kg/ha and 0.8 kg/ha, respectively. The lower rate in 1983 was because of lower populations of pocket gophers as a result of baiting in 1982</i></p> <p>Three plantations with similar habit characteristics but no recent history of baiting were used as control areas (C1, C2, and C3).</p> <p>Golden-mantled ground squirrels were trapped during three 5-day periods in early June, mid-July, and late August. Peanuts were used to bait the squirrels.</p>	<p>Population levels of squirrels appeared to be <i>considerably lower</i> than levels on unbaited plots; due to variations between plots within treatments, there were no significant differences between population means in July and August.</p> <p>[See Table 1 of study for estimated squirrel populations and standard errors in June, July, and August 1983 on plots baited for pocket gophers.]</p>	<p>Anthony et al. 1984</p>
<p><u>Effect of rebaiting in 1983:</u> <i>about 0.4 kg/ha of bait was applied to Plot B2 (4.7 g/set with 93 sets/ha); and about 0.2 kg/ha of bait was applied on Plot B3 (4.7 g/set with 467 sets/ha).</i></p>	<p>None of the squirrels (24 on baited plots and 40 on unbaited plots) died as a result of strychnine treated bait; furthermore, no bait was found in nine excavated ground squirrel nests.</p> <p>Raptors took 5/6 preyed upon squirrels; a badger consumed one squirrel; and five squirrels escaped exposure by hibernating.</p>	<p>Anthony et al. 1984</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Strychnine salt blocks placed in trees and in cubbies (covered bait stations on the ground) in pine forests in Oregon (Fremont National Forest) and California (Modoc National Forest).</p> <p>Target species: Porcupines (<i>Erethizon dorsatum</i>), n=40</p> <p>Bait: pine blocks containing 5.79% strychnine alkaloid in sodium chloride. <i>To maximize exposure, bait blocks were placed in trees or in cubbies at the base of trees occupied by radio-equipped porcupines.</i></p>	<p>Only 4/32 marked porcupines were poisoned (2/4 died at tree sets and 2/4 died at cubby sets). The exact dates of the deaths are unknown; however, none died immediately after exposure, which is contrary to expectation for acute toxic bait.</p> <p>The other 36/40 porcupines (28 treated and 8 controls) survived with no apparent signs of toxicity.</p> <p>Nine unmarked porcupines were found dead at bait stations: five on the Modoc site and four on the Fremont site.</p> <p><u>Nontarget Mortality:</u> yellow-pine chipmunks (<i>Tamias amoenus</i>) (n=9) northern flying squirrel (<i>Glaucomys sabrinus</i>) (n=1) Nuttall's cottontails (<i>Sylvilagus nuttallii</i>) (n=5) deer mice (<i>Peromyscus maniculatus</i>) (n=4) golden-mantled ground squirrels (<i>Spermophilus lateralis</i>) (n=3) Douglas' squirrel (<i>Tamiasciurus douglasii</i>) (n=1)</p> <p>All nontarget species were found under cubbies or next to bait blocks and all exhibited muscular tetanus, a characteristic of strychnine poisoning. No residue data in nontargets.</p>	<p>Anthony et al. 1986.</p>
<p>Above ground applications: ...at edges of prairie dog mounds.</p> <p>Strychnine with pre-bait (4 g high-quality, untreated, steam-rolled oats), and strychnine without pre-bait (8 g 0.5% strychnine alkaloid steam-rolled oats) were applied to black-tailed prairie dog (<i>Cynomys ludovicianus</i>) colonies in west central South Dakota.</p>	<p><u>Short-term (4 days post treatment) effects:</u> strychnine reduced Horned Larks relative densities 66% with strychnine only and 55% with pre-baited strychnine.</p> <p><u>Long-term (1 year post treatment) effects:</u> no direct impact on Horned Larks.</p> <p>There were no short-term or long-term effects on granivorous seed-eating birds.</p>	<p>Apa et al. 1991</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Field study conducted in 1998-1999 at four sites on the Rogue River National Forest in Oregon (sites typical of recent reforestation areas normally targeted for pocket gopher population reduction) to assess the fate of above ground carcasses of pocket gophers, house mice, deer mice, and voles.</p> <p>Furthermore, the same sites were used in Aug 1999 to analyze strychnine residue in several general categories of insects: Diptera adults (flies), Diptera larva, Hymenoptera-Formicidae (ants), Hymenoptera-Vespidae (hornets and yellow jackets), Hymenoptera-other, Coleoptera (beetles), and other species. Insects included in the "other" category included Lepidoptera ($n = 4$), Hemiptera ($n = 1$), and Orthoptera ($n = 1$).</p>	<p>In the field study regarding carcass fate of four species, there was no difference among species or the type of carcass damage (i.e., scavenging damage or insect) during the four trials; however; in two of the trials there were fewer pocket gopher carcasses, relative to the carcasses of the three other species.</p> <p>The numbers of insects collected at the sites of treated and control carcasses were similar, suggesting that strychnine is neither a repellent nor attractant to insects. Strychnine concentrations were consistently higher in fly larvae ($0.37 \pm 0.12 \mu\text{g/g SE}$) and ants ($0.19 \pm 0.05 \mu\text{g/g SE}$) collected from treated carcasses, relative to hornets and yellow jackets ($0.03 \pm 0.02 \mu\text{g/g SE}$), adult flies ($0.14 \pm 0.07 \mu\text{g/g SE}$), and beetles (concentration not specified).</p>	<p>Arjo et al. 2005</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Below-ground hand baiting.</p> <p>Field study of alkaloid residues of underground-baited strychnine (steam-rolled oats containing 0.5% strychnine alkaloid) for pocket gopher control in forest plantations (West Bitch Creek [WBC] and South Antelope Flat [SAF] management units of the Ashton Ranger District, Targhee National Forest in eastern Idaho) in July 1979. Application rates of 1 to 2 lb formulation/acre.</p>	<p><u>Recovery of carcasses:</u> 40-radio-equipped and 5 unmarked carcasses were recovered (two in one nest, three in another nest, and four found singly). 30 carcasses were located >40 cm below ground; 22 were ≤10 cm from a nest. Carcass locations ranged from 10 to 152 cm below ground, and there were no significant differences in depths between study areas (p>0.10).</p> <p><u>Mean strychnine residues in carcasses (SAF):</u> Pocket gopher (n=18) – 0.23 mg (0.05-0.39) Deer mouse (n= 2) – 0.20 (0.14-0.26)</p> <p>Working note: Assuming a 75 g gopher, the above residues correspond to 3 (0.6-5.2) mg/kg bw. Assuming a 20 g mouse, the above residues correspond to 10 (7-13) mg/kg bw.</p> <p><u>Mean strychnine residues in carcasses (WBC):</u> Pocket gopher (n=23) – 0.11 mg (0.01-1.34) Yellow pine chipmunk (n=2) – 0.01 mg for both.</p> <p>Strychnine residue in pocket gopher carcasses was relatively low, with the greatest residue detected in a gopher with 0.4 g of bait and 1.3 mg of strychnine in a cheek pouch; five other gophers had lesser amounts of strychnine in their cheek pouches. Residual strychnine was concentrated (69%) in the GI tract. Baiting has no adverse effects on small animal populations and there was no evidence of poisoned animals available to predators or scavengers.</p> <p>The investigators conclude that strychnine treated baiting for gopher control on forest plantations poses a low risk to grizzly bears.</p>	<p>Barnes et al. 1985</p>
<p>Western South Dakota, Strychnine alkaloid, 0.5% for the control of the prairie dog (<i>Cynomys zudovicianus</i>).</p>	<p>Deer mice: No immediate impact on deer mice. Longer-term increase in deer mice populations associated with a decrease in prairie dog populations.</p> <p>Invertebrates: Variable effects attributed to changes in habitat but not to strychnine toxicity.</p>	<p>Deisch 1986; Deish et al. 1990</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Below ground: NOS</p> <p>Southwest Oregon, Rogue River National Forest, 2.8 ha plots. Two applications of 0.5% strychnine oat bait: Aug. 28 at 0.45 kg/ha and Sept. 4 at 0.05 kg/ha and Sept. 30 at 0.4 kg/ha. All applications below ground. Application method not described in detail.</p>	<p>The first 2 applications did not reduce pocket gophers by 80%. Most pocket gophers died below ground. None of the collared gophers appear to have been eaten by predators. Golden mantled ground squirrel and yellow pine chipmunk were the only species present in sufficient numbers to adequately assess population changes. Decline in squirrel populations but not in chipmunks. Squirrel and chipmunk carcasses found above ground <i>but few animals had strychnine treated bait in their cheek pouches</i>. Carcasses consumed by insects within 48 hours. Some potential for secondary exposure of predators but this appears to be reduced by rapid consumption of carcasses by insects.</p> <p>Residue values in nontargets not reported.</p>	<p>El Hani et al. 2002</p> <p>Note: Also discussed in Nolte and Wagner 2001.</p>
<p>Below ground hand baiting and burrow builder applications.</p> <p>Below-ground hand baiting Efficacy study of applications of 0.5 to 1.25% formulations.</p>	<p>Strychnine residues in tissues of pocket gophers assayed from 1.05 to 90 mg/kg bw. See Table 2 of publication.</p> <p>Nontarget Effects: Mortality in 7 mice noted in areas with hand-baiting. Residue analysis done on one mouse but value not reported.</p> <p>Further details of this study are in Appendix 2.</p>	<p>Evans et al. 1990</p>
<p>Below ground hand baiting.</p> <p>Targhee National Forest, Idaho. Two 8 ha treatment sites. Two 2 ha control sites. Hand baiting of gopher burrows with 0.5% bait on steam-rolled oats at about 1 kg/ha.</p>	<p>No differences in small mammal populations (See Table 1 of paper).</p> <p>30 chipmunks and one flying squirrel fitted with radio transmitters.</p> <p>2 chipmunks died with strychnine residues in body. One chipmunk had 0.29 ppm in the body and 0.1 ppm in GI tract. Another had 0.35 ppm in body but no assay of GI tract was possible.</p> <p>1 chipmunks killed by kestrel.</p> <p>27 chipmunks survived as did squirrel.</p> <p>Carcass search found two dead deer mice. One body had residues of 36 ppm in GI tract and 2.6 ppm in rest of body. The second had 18 ppm in GI tract and 5.4 ppm in body.</p> <p>No indication of secondary poisoning.</p>	<p>Fagerstone et al. 1980</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Above ground for squirrel control</p> <p>9 sites (2.3 to 20.5 acres) in Montana. Surface broadcast and hand baiting of burrow area with 0.44% strychnine for the control of ground squirrels. Application rates of 1.0 to 5.7 lb formulation per acre (0.0044 to 0.025 lb a.i./acre).</p>	<p>Crows, magpies, and golden eagles seen feeding on poisoned ground squirrel carcasses. No dead carnivores (mammals or birds) were found – i.e., no indication of secondary poisoning. Detailed observations on eagles given in Appendix 1 of paper.</p> <p>Observed nontarget effects from primary exposures: one meadowlark and one pigeon, both with detectable levels of strychnine. Residues of strychnine not specified. One deer mouse carcass found but strychnine poisoning could not be confirmed.</p>	<p>Graham 1977</p>
<p>Below-ground burrow builder applications</p> <p>Wildlife refuge, Minnesota, 662 ha with 0.5% bait with burrow builder at a rate of about 1.25 lb/acre. Radio transmitters used on groups of 36 raptors (hawks, kestrels, and owls) and mammalian predators (badgers, skunks, fox, and coyotes). Additional observations on red-winged blackbirds.</p>	<p>About a 90% decline in pocket gopher populations as well as a decline in small rodents.</p> <p>No effects documented in avian or mammalian predators but transmitters on most raptors failed. Four raptors – a kestrel, an owl, and two hawks – were monitored in the treatment area and not adverse effects were noted over a 3 week post-application period. Of the mammalian predators, 3 fox and 1 skunk died prior to treatment. At 3 weeks after treatment, 1 badger found dead 2 miles from the treated area. Two skunks, 3 badgers, 2 fox, and one coyote monitored over 3 weeks with no apparent adverse effects.</p> <p>In a search of about 0.3% of the treatment area, one mouse and one ground squirrel found dead with strychnine residues in stomach. See Table 2 of paper for small rodent population data.</p> <p>No adverse effects on a population of red-winged blackbirds.</p> <p>Death in one mourning dove (<i>Zenaida macroura</i>) with strychnine residues.</p> <p>One dead snake (western hognose) was found but no strychnine was detected. This species does not consume rodents.</p> <p>Carcass monitoring was done but residues in carcasses are not reported.</p>	<p>Hegdal and Gatz 1976</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference												
<p>Prairie dog control (above ground)</p> <p>Nebraska, baiting for prairie dog control. 0.5% strychnine alkaloid.</p>	<p>Two rabbits found dead. Timing and proximity suggest death due to bait ingestion.</p> <p>Three horned larks, a cottontail rabbit, and a jackrabbit found dead on strychnine treated plots. Timing and proximity suggest death due to bait ingestion. No carcass monitoring.</p>	<p>Holbrook and Timm 1985</p>												
<p>Kangaroo rat, above ground.</p> <p>New Mexico, for kangaroo rat control, 0.15% or 0.5% strychnine. 2% zinc phosphide used in some sites. Baits applied on either side of mounds – i.e., above ground.</p>	<p>Few nontarget deaths. One mouse and one horned lark on 0.16% strychnine treated plot. One mouse on a 0.5% strychnine treated plot.</p> <p>No monitoring of carcass residues.</p>	<p>Howard and Bodenchuk 1984</p>												
<p>Hand baiting, below-ground for ground squirrel control</p> <p>Saskatchewan, 8 treated pastures with 27 pairs of owls and 7 control pastures with 28 pairs of owls. Strychnine in wheat at 2500 ppm (0.25%) placed into ground squirrel holes. Pastures monitored and dead squirrels collected each evening.</p>	<p>Effects on owls assayed relative to a control pastures.</p> <p>No loss of breeding pairs of owls. Adult mass is reported as significantly (<0.05) decreased using a t-test:</p> <table border="1" data-bbox="613 911 1138 1010"> <thead> <tr> <th></th> <th>Mean</th> <th>SD</th> <th>N</th> </tr> </thead> <tbody> <tr> <td>Treated</td> <td>160</td> <td>11.5</td> <td>29</td> </tr> <tr> <td>Control</td> <td>168</td> <td>16.2</td> <td>37</td> </tr> </tbody> </table> <p>The author's suggest that this could indicate ... <i>a possible sublethal effect.</i></p> <p>Working note: The test for the above data was repeated. The p-value for a one-tailed test of the differences between the two means is about 0.0096.</p> <p>Statistically insignificant effects in: Breeding success: -16% No. chicks/nest attempt: -20% No. chicks/success: -4%</p> <p>No effect on chick mass.</p> <p>Working note: Of the 5 sublethal endpoints, 4 qualitatively suggest an effect. Assuming all differences are random, the probability of this occurring is $0.5^4 = 0.0625$. Note further, however, that the statistics on chicks are likely to be correlated.</p> <p>No overt effects noted on birds attempting to feed on dead squirrels. No carcass monitoring.</p>		Mean	SD	N	Treated	160	11.5	29	Control	168	16.2	37	<p>James et al. 1990</p>
	Mean	SD	N											
Treated	160	11.5	29											
Control	168	16.2	37											

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
<p>Below-ground applications</p> <p>Texas, Pleasanton. Efficacy study with 0, .35%, 0.75%, and 1.3% bait at rates of 0.335, 0.370, 0.465, and 0.435 kg/ha, respectively.</p>	<p>No substantial differences in efficacy among concentrations of strychnine in baits. Possible indication of aversion at 1.3% bait. No non-target mortality above ground observations. Residue data for gophers but not for nontargets. Gopher residues of about 0.9 mg/kg bw in a surviving gopher. Residues of 5.03 to 9.47 mg/kg bw in fatally poisoned gophers.</p>	<p>Ramey et al. 2002</p>
<p>Presumably above ground for pigeon control.</p> <p>Strychnine used for pigeon control in Minnesota. Appears to be 1% (10,000 ppm) bait but this is not specified.</p>	<p>Mortality in snowy owls, mallards, and herring gulls. Residues in crops of pigeons: 312-13,700 ppm.</p>	<p>Redig et al. 1982</p>
<p>Hand baiting, loose grain or paraffin pellets.</p> <p>Pocket gopher control in forests of Northern California. 0.5% grain applied to 50 clearcuts (124 ha).</p>	<p>Efficacy: Initial reduction in gopher populations followed by recovery within about 1 year.</p>	<p>Smallwood 1999</p>
<p>Burrow builder</p> <p>Pocket gopher control in forests of Northern California. 0.5% grain applied to 4 clearcuts (124 ha) at 3.4 kg/ha (eq. 3 lb/acre or 0.015 lb a.i./acre). This exceeds current label rates.</p>	<p>Below is a quotation: <i>far more hazardous to nontarget animal species, because they failed to conceal the poison baits within the artificial tunnels. Soil collapsed into the tunnels along the tracks of the burrow builder, and the baits were readily visible from above-ground. Many non-target animals perished when they consumed the exposed bait.</i></p> <p>This is a summary of an activity that was not a part of the Smallwood (1999) study. No other details are provided and there is not monitoring data on strychnine in nontarget species.</p>	<p>Smallwood 1999</p>
<p>Prairie dog (above ground)</p> <p>West-central South Dakota, 18 sites with prairie dog colonies, 12 ha to 283 ha. 3 control and 3 treated sites. Strychnine, 0.5% bait. Application rate in lb/acre not specified</p>	<p>No significant effect on deer mice or cottontail rabbits.</p> <p>Significant reductions in horned larks with and without pre-baiting.</p> <p>No significant effect on mixed species of ground-feeding birds.</p>	<p>Uresk et al. 1988</p>

Appendix 3: Field Studies Involving Applications of Strychnine (continued)

Application/Site	Response	Reference
Six application methods including den treatment (below ground). New Mexico, grasslands for control of kangaroo rat. Some applications were above ground. Other applications to dens. These, however, involved ... <i>about one heaping teaspoonful of poison grain deposited directly on top of each kangaroo rat den.</i>	<i>Mortality of animals other than rodents was noted. Within the study area two gray foxes and two coyotes were found dead. The cause of death was not known, but it may have been from eating poisoned rodents.</i> No measurements of strychnine were made in the dead animals. Decrease in dear mouse densities.	Wood 1965

Supplemental Table: Summary of Incident Reports from U.S. EPA/OPP (2009).

Incident Number	Year	Application Area	Species (Number)	Probability of Association
B0000-300-88	1982	Agricultural	Bald eagle (1)	Highly probable
B0000-300-88	1982	Agricultural	Bald eagle (1)	Highly probable
B0000-503-01	1980	Not recorded	Peregrine falcon (1)	Highly probable
B0000-503-02	1984	Not recorded	Bald eagle (1)	Highly probable
B0000-503-03	1982	Not recorded	Bald eagle (1)	Highly probable
B0000-503-05	1983	Terrestrial (NOS)	Bald eagle (2)	Probable
B0000-503-08	1980	Grain elevator	Peregrine falcon (2)	Probable
B0000-503-09	1977	Agricultural	Bald eagle (1)	Probable
B0000-503-09	1977	Agricultural	Bald eagle (1)	Probable
B0000-503-10	1972	Rangeland	Bald eagle	Highly probable
B0000-503-11	1984	Rangeland	Bald eagle	Highly probable
B0000-503-15	1983	Field	Eagle (1)	Highly probable
B0000-503-32	1981	Home/lawn	American kestrel (1)	Highly probable
B0000-503-36	1978	Bait, grain/seed	Owl (1) and rough legged hawk (1)	Highly probable
B0000-503-39	1981	Agricultural	Golden eagle (1)	Highly probable
B0000-503-43	1983	Field	Red-tailed hawk (1)	Highly probable *
B0000-503-44	1985	Field	Red-tailed hawk (3)	Highly probable
B0000-503-45	1974	Field	Ring-billed gull (11)	Highly probable *
I001566-002	1994	Granary	Owl (2)	Probable

*Specifically notes secondary poisoning

Source: U.S. EPA/OPP 2009, Appendix E
See Section See Section 4.1.2.2.4 for discussion.

Appendix 4: Toxicity Studies in Birds

Note on Appendix 4: This appendix is organized into tables as listed below. Field studies involving observations in birds are summarized in Appendix 3.

Some studies involve strychnine sulfate and strychnine chloride are included but the text of the risk assessment focuses on strychnine alkaloid.

Within each table, studies are listed alphabetically by author.

A4 Table 1: Acute Oral Toxicity to Birds by Gavage, Capsule, or Prey..... 198
 A4 Table 2: Acute Dietary Toxicity to Birds..... 202
 A4 Table 3: Subchronic Toxicity to Birds 203
 A4 Table 4: Reproductive Toxicity to Birds..... 204

A4 Table 1: Acute Oral Toxicity to Birds by Gavage, Capsule, or Prey			
Species	Exposure	Response	Reference
Great horned owls (<i>Bubo virginianus</i>), 2/dose group Body weights estimated from data on mg administered and corresponding mg/kg doses: 1.2 to 1.8 kg See Table 3 in paper Mg ÷ mg/kg = kg	3, 6, 9, 12, or 15 mg strychnine or 0, 2.1-2.5, 3.8-3.9, 5.0-5.1, 7.5-7.7, or 10.5-11.8 mg/kg strychnine (equal to 1, 2, 3, 4, or 5 time the 3-mg maximum level found in field-killed golden-mantled ground squirrels during 1982. <i>To insure ingestion of these exorbitant dose levels, the appropriate amount of strychnine was injected into the body of a dead deer mouse and, along with an untreated mouse, immediately force-fed to a test bird. Control birds each received two mice without strychnine. Following force feeding, all birds received normal food rations.</i>	0.0 mg/kg – no visible toxic effect 2.1 mg/kg – convulsions, inability to perch 2.5 mg/kg - convulsions, inability to perch 3.8 mg/kg – emesis, inability to perch 3.9 mg/kg - convulsions, inability to perch 5.0 mg/kg - emesis, inability to perch 5.1 mg/kg – emesis only 7.5 mg/kg – emesis only 7.7 mg/kg – death within 24 hours 10.5 mg/kg - death within 24 hours 11.8 mg/kg - death within 24 hours Approximate lethal dose: 7.6 mg/kg bw. FEL: 2.1 mg/kg bw	Anthony et al. 1984

Appendix 4: Toxicity Studies in Birds (continued)

A4 Table 1: Acute Oral Toxicity to Birds by Gavage, Capsule, or Prey			
Species	Exposure	Response	Reference
Red-tailed hawks (<i>Buteo jamaicensis</i>), 2/dose group Body weights estimated from data on mg administered and corresponding mg/kg doses: 1.0 to 1.5 kg See Table 3 in paper mg ÷ mg/kg = kg	3, 6, 9, 12, or 15 mg strychnine or 0, 2.0-2.9, 4.5-4.6, 6.2-6.9, 9.2-12.3, or 10.2-11.2 mg/kg strychnine (equal to 1, 2, 3, 4, or 5 time the 3-mg maximum level found in field-killed golden-mantled ground squirrels during 1982) <i>To insure ingestion of these exorbitant dose levels, the appropriate amount of strychnine was injected into the body of a dead deer mouse and, along with an untreated mouse, immediately force-fed to a test bird. Control birds each received two mice without strychnine. Following force feeding, all birds received normal food rations.</i>	0.0 mg/kg – no visible toxic effect 2.0 mg/kg – no visible toxic effect 2.9 mg/kg - no visible toxic effect 4.6 mg/kg – convulsions, inability to perch 4.5 mg/kg - convulsions, inability to perch 6.2 mg/kg - convulsions, inability to perch 6.9 mg/kg – convulsions, inability to perch 9.2 mg/kg – convulsions, inability to perch 12.3 mg/kg – death within 24 hours 10.2 mg/kg - death within 24 hours 11.2 mg/kg - death within 24 hours Approximate lethal dose: 10.75 mg/kg bw. NOEC: 2.9 mg/kg bw LOEC: 4.6 mg/kg bw Approximate lethal dose: 10.75 mg/kg bw	Anthony et al. 1984
Great horned owl (<i>Bubo virginianus</i>)	Two birds fed mice injected with strychnine in increasing doses.	NOEC: 0.5 to 1.0 mg/kg bw LOEC (slight loss of coordination): 1.5 mg/kg bw (1 bird) FEL (significant loss of coordination): 1 to 1.8 mg/kg bw.	Cheney et al. 1987
Red-tailed hawk (<i>Buteo jamaicensis</i>)	Fed mice injected with strychnine in increasing doses.	NOEC: 2.0 mg/kg bw LOEC: 2.3 mg/kg bw, incoordination. FEL: 2.5 mg/kg bw	Cheney et al. 1987
Mallard (<i>Anas platyrhynchos</i>), 36 h old	Strychnine alkaloid	LD ₅₀ : 2.62 (1.94-3.55) mg/kg	Hudson et al. 1984
Mallard, 1 wk old	Strychnine alkaloid	LD ₅₀ : 2.00 (1.51-2.65) mg/kg	Hudson et al. 1984
Mallard, 1 month old	Strychnine alkaloid	LD ₅₀ : 5.88 (3.23-10.7) mg/kg	Hudson et al. 1984

Appendix 4: Toxicity Studies in Birds (continued)

Species	Exposure	Response	Reference										
Mallard, male and female, 6 months old	Strychnine sulfate	LD ₅₀ : 2.83 (2.00-4.00) mg/kg	Hudson et al. 1984										
Mallard male and female, 6 months old	Strychnine alkaloid	LD ₅₀ : 2.27 (1.26-4.11) mg/kg	Hudson et al. 1984										
Golden eagle, M (<i>Aquila chrysaetos</i>), N=3	Strychnine alkaloid	LD ₅₀ : 4.8-8.1 mg/kg	Hudson et al. 1984										
Golden eagle, N=2	Strychnine sulfate	LD ₅₀ : 5.0-10.0 mg/kg	Hudson et al. 1984										
California quail, M (<i>Callipepla californica</i>)	Strychnine alkaloid	LD ₅₀ : 112 (51.6-243) mg/kg	Hudson et al. 1984										
Japanese quail, F (<i>Coturnix japonica</i>)	Strychnine alkaloid	LD ₅₀ : 22.6 (11.9-42.9) mg/kg	Hudson et al. 1984										
Ring-necked pheasant (<i>Phasianus colchicus</i>)	Strychnine alkaloid in water	LD ₅₀ : 24.7 (14.4-42.2) mg/kg	Hudson et al. 1984										
Ring-necked pheasant	Strychnine sulfate	LD ₅₀ : 8.48 (4.41-16.3) mg/kg	Hudson et al. 1984										
Chukar partridge, m&f, N=8	Strychnine alkaloid	LD ₅₀ : 16 (8-32) mg/kg	Hudson et al. 1984										
Rock dove. M/F (<i>Columba livia</i>)	Strychnine alkaloid, in water	LD ₅₀ : 21.3 (16.9-26.9) mg/kg	Hudson et al. 1984										
House sparrow, M, N=20	Strychnine alkaloid in water	LD ₅₀ : 4.18 (3.18-5.50) mg/kg	Hudson et al. 1984										
House sparrow, F N=6	Strychnine sulfate in water	LD ₅₀ : 4-8 mg/kg	Hudson et al. 1984										
House sparrow (<i>Passer domesticus</i>), 19.66 g M/ 19.3 g F	Intubation with strychnine chloride in either water or one of three grains.	<table border="1"> <thead> <tr> <th>Vehicle</th> <th>LD₅₀</th> </tr> </thead> <tbody> <tr> <td>Water</td> <td>0.68 (0.54-0.88)</td> </tr> <tr> <td>Millet</td> <td>13.15 (6.41-20.69)</td> </tr> <tr> <td>Sorghum</td> <td>10.17 (2.57-14.95)</td> </tr> <tr> <td>Wheat</td> <td>9.92 (6.03-13.23)</td> </tr> </tbody> </table> <p>For millet, sorghum, and wheat, the lowest dose tested (5 mg/kg bw) was a LOAEL: transient signs of toxicity.</p> <p>The paper (Table II, p. 125) gives separate results for males and females but no clear pattern of sensitivity is apparent. Note: strychnine chloride is much more toxic in water. May be due to slower release from grains and/or more rapid absorption from water.</p>	Vehicle	LD₅₀	Water	0.68 (0.54-0.88)	Millet	13.15 (6.41-20.69)	Sorghum	10.17 (2.57-14.95)	Wheat	9.92 (6.03-13.23)	Hussain et al. 1993
Vehicle	LD₅₀												
Water	0.68 (0.54-0.88)												
Millet	13.15 (6.41-20.69)												
Sorghum	10.17 (2.57-14.95)												
Wheat	9.92 (6.03-13.23)												

Appendix 4: Toxicity Studies in Birds (continued)

A4 Table 1: Acute Oral Toxicity to Birds by Gavage, Capsule, or Prey			
Species	Exposure	Response	Reference
Snowy owls (<i>Bubo scandiacus</i>) (3-4 kg), n=2	Strychnine from consuming poisoned pigeons.	Lethal dose \approx 2.7-3.6 mg or \approx 0.675 to 1.2 mg/kg bw. Average of range: 0.9375 mg/kg bw. This is a secondary reference to a 1975 text on veterinary toxicology. Cannot locate text.	Redig et al. 1982
Pigeons (<i>Columba livia</i>), bw \approx 285 g	Strychnine alkaloid in propylene glycol	LD ₅₀ : 7.73 (6.75-8.85)mg/kg bw LD ₉₀ : 11.0 (8.79-13.7)mg/kg bw See more detailed entry in Table 2	Schafer and Eschen 1986
Mallards, m&f (<i>Anas platyrhynchos</i>)	Strychnine alkaloid	LD ₅₀ : 2.9 mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
Ring-necked pheasants (<i>Phasianus colchicus</i>), m, 10-23 mo.	Strychnine alkaloid in gelatin capsule	LD ₅₀ : 24.7 (14.4-42.2) mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
Pheasants, m, 2 mo.	Strychnine sulfate	LD ₅₀ : 8.48 (4.41-16.3)mg/kg	Tucker and Crabtree 1970
Chukar partridge (<i>Alectoris graeca</i>), m&f, 5-7 mo.	Strychnine alkaloid, in gelatin capsule	LD ₅₀ : 16 (8-32)mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
Japanese quail (<i>Coturnix japonica</i>), f, 2 mo.	Strychnine alkaloid, in gelatin capsule	LD ₅₀ : 22.6 (11.9-42.9) mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
Pigeons (<i>Columba livia</i>), m&f	Strychnine alkaloid, in gelatin capsule	LD ₅₀ : 21.3 (16.9-26.9) mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
Mourning doves (<i>Zenaida macroura</i>), m&f	Strychnine sulfate	LD ₅₀ : >5.12 mg/kg	Tucker and Crabtree 1970
House sparrows (<i>Passer domesticus</i>), f	Strychnine alkaloid, in gelatin capsule	LD ₅₀ : 4.18 (3.18-5.50)mg/kg	Tucker and Crabtree 1970; Tucker and Haegele 1971
House sparrows	Strychnine sulfate	LD ₅₀ : 4.0-8.0mg/kg	Tucker and Crabtree 1970
Golden eagles (<i>Aquila chrysaetos</i>)	Strychnine alkaloid	LD ₅₀ : \approx 5 mg/kg	Tucker and Crabtree 1970
Golden eagles	Strychnine sulfate	LD ₅₀ : >5 mg/kg	Tucker and Crabtree 1970
Sage grouse, 0.85 to 1.1 kg (<i>Centrocercus urophasianus</i>)	Strychnine alkaloid in grain	5 bird survived gavage doses of 25-50 mg/kg bw. Two others died at 20.6 or 46.2 mg/kg, the former possibly due to handling.	Ward et al. 1942
Sage grouse, 1.076 to 1.22 kg	Strychnine alkaloid in 1% solution (vehicle not specified).	15 to 35 mg/kg bw: survival 50 or 100 mg/kg bw: death	Ward et al. 1942
Sage grouse	Strychnine alkaloid, i.p. injection	5 mg/kg: survived 10 to 50 mg/kg died	Ward et al. 1942

Appendix 4: Toxicity Studies in Birds (continued)

A4 Table 2: Acute Dietary Toxicity to Birds																		
Species	Exposure	Response	Reference															
<p>Pigeons (<i>Columba livia</i>), groups of 24 birds per dose. Each group consisted of 4 cages with 6 pigeons per cage.</p> <p>NOTE: No concurrent control groups appear to have been used in this dietary study.</p> <p>Body weights are not explicitly reported. On p. 279 of the study, the authors note that 28 to 29 grams of bait is about 10% of the birds average body weight. Thus, the body weights can be estimated at 285 grams.</p>	<p>Strychnine in corn bait at 0, 0.2%, 0.4%, and 0.6%. Birds fasted for 12 to 16 hours and groups of 6 pigeons offered 150 kernels ($\approx 6x$ normal consumption). Exposure period: 1 hour (at heavy feeding time).</p> <p>Working Note: The weight of 91 to 94 kernels is given as 28 to 29 g – i.e., ≈ 0.3 g/kernel.</p>	<p>Two studies, AM feeding and PM feeding.</p> <table border="1"> <thead> <tr> <th colspan="3">Mortality</th> </tr> <tr> <th>Conc.</th> <th>A.M.</th> <th>P.M.</th> </tr> </thead> <tbody> <tr> <td>0.2%</td> <td>33%</td> <td>17%</td> </tr> <tr> <td>0.4%</td> <td>58%</td> <td>63%</td> </tr> <tr> <td>0.6%</td> <td>71%</td> <td>42%</td> </tr> </tbody> </table> <p>Authors suggest that birds feeding in the PM test were under less stress than birds feeding in the AM test.</p> <p>Authors state that ingestion of 2x gavage LD₉₀ (11 mg/kg bw) caused mortality but ingestion of 1x gavage LD₉₀ caused only sublethal effects (neurotoxicity). See gavage component of this study in Table 1 of this appendix.</p>	Mortality			Conc.	A.M.	P.M.	0.2%	33%	17%	0.4%	58%	63%	0.6%	71%	42%	<p>Schafer and Eschen 1986</p>
Mortality																		
Conc.	A.M.	P.M.																
0.2%	33%	17%																
0.4%	58%	63%																
0.6%	71%	42%																
<p><i>Additional Notes on Schafer and Eschen 1986</i></p> <p>Based on the data in Table 4 of study, the author's statement is correct. Average lethal doses in the dietary study appear to be about 27 to 95 mg/kg bw – i.e., factors of ≈ 2 to 9 above the gavage LD₉₀ of 11 mg/kg bw. In the 0.2% dose group, surviving birds consumed about 13 mg/kg strychnine. Authors do not give LC₅₀. Based on Table 4, the LC₅₀ is about 0.3% or 3000 ppm, similar to quail.</p>																		
Bobwhite quail (<i>Colinus virginianus</i>)	5-day exposure, 3 day recovery	LC ₅₀ : 3536 ppm NOEC: 1250 ppm	U.S. EPA/OPP 1996d, MRID 41322602, cited to Pedersen 1989															
Mallard ducks (<i>Anas platyrhynchos</i>),	5-day exposure, 3 day recovery	LC ₅₀ : 212 ppm NOEC: 78 ppm	U.S. EPA/OPP 1996d, MRID 41322602, cited to Pedersen 1989															
Black-billed magpie (<i>Pica pica</i>)	Exposures not detailed.	LC ₅₀ : 99 (65-130) ppm	U.S. EPA/OPP 1996d, cited to File No. 56228-16.															
American kestrel (<i>Falco sparverius</i>)	Exposures not detailed.	LC ₅₀ : 234 ppm	U.S. EPA/OPP 1996d, cited to File No. 56228-16.															

Appendix 4: Toxicity Studies in Birds (continued)

A4 Table 3: Subchronic Toxicity to Birds			
Species	Exposure	Response	Reference
Mallard ducks (<i>Anas platyrhynchos</i>), 27 week old, 5 M and 5 F/dose	Strychnine alkaloid. Dietary concentrations of 0, 18.8, 91.1, 235.0, 484.2, and 972.6 ppm strychnine for 28 days	<p>Author NOEC: 91.1 ppm LC₅₀: 679.8 ppm</p> <p>Mortality of 4/10 at 484 ppm and 7/10 at 973 ppm Concentration related pathological changes in all dosed groups. At 20 ppm, damage to testes noted in both males examined. See Table 5 of publication.</p> <p>No overt signs of toxicity at two lower doses.</p> <p>Tremors, incoordination, and other signs of neurotoxicity at higher concentrations.</p> <p>Food consumption: at 484 ppm and higher, 50%-75% decrease in food consumption in week 1. At 235 ppm and less, no marked change in food consumption. See Figure 2 of paper. At lower doses, food consumption ranged from about 80 to 140 g/bird.</p>	Sterner et al. 1998
Bobwhite quail (<i>Colinus virginianus</i>), 29 week old, 5 M and 5 F/dose	Strychnine alkaloid. Dietary concentrations of 0, 484.2, 972.6, 1870.8, 3516.7, and 6083.3 ppm strychnine for 28 days	<p>Author NOEC: 972.6 ppm LC₅₀: 4,973.6 ppm</p> <p>No gross signs of toxicity at two lower doses.</p> <p>Mortality of 5/10 at two higher doses.</p> <p>Intestinal hemorrhage in 1 animal at 972.6 ppm.</p> <p>Weight loss at doses above 1870 ppm.</p> <p>Food consumption: Marked reduction in food consumption in high dose group. Approximate food consumption of 15 to 20 g/day per bird in other groups. See Figure 1 of paper.</p>	Sterner et al. 1998

Appendix 4: Toxicity Studies in Birds (continued)

A4 Table 4: Reproductive Toxicity to Birds			
Species	Exposure	Response	Reference
Mallard ducks (<i>Anas platyrhynchos</i>)	Strychnine alkaloid. Dietary concentrations of 33.2, 68.9, and 140.9 ppm strychnine for 20 weeks	<p>NOEC: 33.2 ppm LOEC: 68.9 ppm decreased body weights in chicks. Signs of neurotoxicity in some adult birds. LOEC: 140.9 ppm based on decreased egg production and decreased hatching success, and mortality in F1 hatchling. Also, decreased body weight and signs of neurotoxicity in adult females.</p> <p>Using a standard food consumption factor of 0.07 for mallards, the NOEC is about 2.3 mg/kg bw.</p> <p>NB: U.S. EPA/OPP 1996d classifies 33.2 ppm as a LOEC based on reduced testes weight. This is based on small testes in 1 male. This may be an incidental finding.</p>	<p>Pedersen et al. 2000</p> <p>Summarized in U.S. EPA/OPP 1996d as Pedersen 1993, MRID 42716802</p>
Bobwhite quail (<i>Colinus virginianus</i>)	Strychnine alkaloid. Dietary concentrations of 279.2, 557.4, and 1,113.6 ppm strychnine for 20 weeks	<p>NOEC: 1113.6 ppm Based on measured food consumption (\approx19 g/day per bird) and reported body weights of about 200 g/bird, the estimated dose is \approx105 mg/kg bw.</p>	<p>Pedersen et al. 2000</p> <p>Summarized in U.S. EPA/OPP 1996d as Pedersen 1993, MRID 42716801</p>

Appendix 5: Toxicity Studies in Fish and Aquatic Invertebrates

Species	Exposure	Response	Reference
FISH			
Rainbow trout, 600-900 g, n=4, spinally transected	Strychnine hemisulfate (98%, from Sigma Chemical Co.) in <i>pecially designed flow-through exposure unit that provided automated data acquisition and measurement control.</i>	Lethal aqueous concentration = 4.7 ± 0.46 mg/L Mean survival time = 12.8 ± 6.6 hours Reaction to strychnine exposure was rapid with increased coughing and whole body spasms, including tail arching observed by 10% survival time	Baradbury et al. 1991
Japanese medaka (<i>Oryzias latipes</i>), 21-32 days old	Strychnine hemisulfate, static bioassays.	48-h LC ₅₀ : > 2 mg/L At 2 mg/L, loss of equilibrium, convulsions and spasms.	Carlson et al. 1998
Bluegill sunfish (<i>Lepomis macrochirus</i>)	Strychnine (NOS), static	96-h LC ₅₀ : 0.87 mg/L NOEC (mortality): 0.5 mg/L, slight effects not otherwise described.	Dawson et al. 1977
Tidewater silversides (<i>Menidia beryllina</i>)	Strychnine (NOS), static	96-h LC ₅₀ : 0.95 mg/L NOEC (mortality): 0.5 mg/L	Dawson et al. 1977
Japanese medaka (<i>Oryzias latipes</i>), 30 days old	hemisulfate salt	48-h LC ₅₀ : 5.7 (4.7-6.2) mg/L 1 mg/L: behavioral effects in 24 hours and some mortality (>10%) in 48 hours.	Rice et al. 1997
Rainbow trout (<i>Oncorhynchus mykiss</i>)	Strychnine, NOS	96-h LC ₅₀ : 2.3 (1.7-3.2) mg/L	U.S. EPA/OPP 1996d, MRID 41126502
Bluegill sunfish (<i>Lepomis macrochirus</i>)	Strychnine, NOS	96-h LC ₅₀ : 0.76 (0.61-0.96) mg/L	U.S. EPA/OPP 1996d, MRID 41126501
AQUATIC INVERTEBRATES			
<i>Daphnia magna</i>	Strychnine, NOS	48-h LC ₅₀ : 8 (10-12) mg/L	U.S. EPA/OPP 1996d, MRID 41126503

Appendix 6: Summary of Gleams-Driver Simulations

Table 1: Effective Offsite Application Rate (lb/acre)

Site	Clay	Loam	Sand
Dry and Warm Location	0.00078 (0 - 0.0206)	0 (0 - 0.00219)	0 (0 - 0.00141)
Dry and Temperate Location	0.00046 (0 - 0.0068)	0 (0 - 0.000297)	0 (0 - 0.000058)
Dry and Cold Location	0.000184 (1.52E-06 - 0.00164)	0 (0 - 0)	0 (0 - 0)
Average Rainfall and Warm Location	0.0255 (0.0092 - 0.069)	0.00312 (0.00034 - 0.0281)	0.00123 (2.88E-06 - 0.0112)
Average Rainfall and Temperate Location	0.0134 (0.0048 - 0.049)	0.00146 (1.61E-06 - 0.0154)	0.000282 (0 - 0.011)
Average Rainfall and Cool Location	0.0065 (0.00169 - 0.034)	0.000124 (0 - 0.0037)	0 (0 - 0.00295)
Wet and Warm Location	0.041 (0.0157 - 0.098)	0.0081 (0.00204 - 0.062)	0.0039 (0.0005 - 0.046)
Wet and Temperate Location	0.0281 (0.0084 - 0.065)	0.0041 (0.00097 - 0.0198)	0.00129 (0.000148 - 0.0078)
Wet and Cool Location	0.098 (0.048 - 0.183)	0.0086 (0.00223 - 0.053)	0.0028 (0.00033 - 0.0284)
		Average of Central Values:	0.00922
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.183
		Summary of Values:	0.0092 (0 - 0.183)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 2: Concentration in Top 12 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.288 (0.263 - 0.33)	0.257 (0.233 - 0.283)	0.254 (0.233 - 0.288)
Dry and Temperate Location	0.282 (0.264 - 0.32)	0.248 (0.233 - 0.289)	0.252 (0.235 - 0.289)
Dry and Cold Location	0.277 (0.263 - 0.31)	0.241 (0.232 - 0.275)	0.241 (0.231 - 0.264)
Average Rainfall and Warm Location	0.279 (0.263 - 0.32)	0.246 (0.232 - 0.278)	0.242 (0.232 - 0.269)
Average Rainfall and Temperate Location	0.199 (0.189 - 0.225)	0.184 (0.175 - 0.204)	0.183 (0.175 - 0.203)
Average Rainfall and Cool Location	0.2 (0.189 - 0.224)	0.185 (0.174 - 0.204)	0.183 (0.174 - 0.203)
Wet and Warm Location	0.271 (0.263 - 0.294)	0.24 (0.231 - 0.26)	0.239 (0.231 - 0.261)
Wet and Temperate Location	0.27 (0.262 - 0.294)	0.24 (0.232 - 0.263)	0.24 (0.232 - 0.267)
Wet and Cool Location	0.269 (0.261 - 0.299)	0.24 (0.232 - 0.265)	0.24 (0.232 - 0.269)
		Average of Central Values:	0.2404
		25th Percentile of Lower Bounds:	0.231
		Maximum Value:	0.33
		Summary of Values:	0.24 (0.231 - 0.33)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 3: Concentration in Top 60 Inches of Soil (ppm)

Site	Clay	Loam	Sand
Dry and Warm Location	0.058 (0.053 - 0.066)	0.051 (0.047 - 0.057)	0.051 (0.047 - 0.058)
Dry and Temperate Location	0.056 (0.053 - 0.064)	0.05 (0.047 - 0.058)	0.05 (0.047 - 0.058)
Dry and Cold Location	0.055 (0.053 - 0.062)	0.048 (0.046 - 0.055)	0.048 (0.046 - 0.053)
Average Rainfall and Warm Location	0.056 (0.053 - 0.065)	0.049 (0.046 - 0.056)	0.048 (0.046 - 0.054)
Average Rainfall and Temperate Location	0.04 (0.038 - 0.045)	0.037 (0.035 - 0.041)	0.037 (0.035 - 0.041)
Average Rainfall and Cool Location	0.04 (0.038 - 0.045)	0.037 (0.035 - 0.041)	0.037 (0.035 - 0.041)
Wet and Warm Location	0.054 (0.053 - 0.059)	0.048 (0.046 - 0.052)	0.048 (0.046 - 0.052)
Wet and Temperate Location	0.054 (0.052 - 0.059)	0.048 (0.046 - 0.053)	0.048 (0.046 - 0.053)
Wet and Cool Location	0.054 (0.052 - 0.06)	0.048 (0.046 - 0.053)	0.048 (0.046 - 0.054)
		Average of Central Values:	0.0481
		25th Percentile of Lower Bounds:	0.046
		Maximum Value:	0.066
		Summary of Values:	0.048 (0.046 - 0.066)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 4: Maximum Penetration into Soil Column (inches)

Site	Clay	Loam	Sand
Dry and Warm Location	8 (8 - 8)	8 (8 - 12)	8 (8 - 12)
Dry and Temperate Location	8 (4 - 8)	8 (4 - 8)	8 (8 - 12)
Dry and Cold Location	8 (8 - 8)	8 (8 - 8)	8 (8 - 12)
Average Rainfall and Warm Location	8 (8 - 12)	12 (8 - 18)	12 (12 - 18)
Average Rainfall and Temperate Location	8 (8 - 12)	8 (8 - 12)	12 (12 - 18)
Average Rainfall and Cool Location	8 (8 - 12)	8 (8 - 12)	12 (8 - 12)
Wet and Warm Location	12 (8 - 12)	12 (8 - 18)	18 (12 - 24)
Wet and Temperate Location	8 (8 - 12)	12 (8 - 18)	18 (12 - 24)
Wet and Cool Location	12 (8 - 12)	12 (12 - 18)	18 (12 - 30)
		Average of Central Values:	10.4
		25th Percentile of Lower Bounds:	8
		Maximum Value:	30
		Summary of Values:	10.4 (8 - 30)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 5: Stream, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	1.5 (0 - 10.9)	0 (0 - 1.91)	0 (0 - 1.43)
Dry and Temperate Location	0.7 (0 - 3.7)	0 (0 - 0.29)	0 (0 - 0.04)
Dry and Cold Location	0.29 (0.005 - 2.99)	0 (0 - 0)	0 (0 - 0)
Average Rainfall and Warm Location	6.9 (2.71 - 18.3)	1.38 (0.26 - 5.7)	0.5 (0.0023 - 3.8)
Average Rainfall and Temperate Location	4.9 (2.18 - 10.9)	0.7 (0.0012 - 4.4)	0.13 (0 - 3.9)
Average Rainfall and Cool Location	3.2 (1.21 - 9.2)	0.07 (0 - 1.88)	0 (0 - 1.06)
Wet and Warm Location	7.4 (3.4 - 13.6)	1.8 (0.7 - 7.5)	1.16 (0.13 - 8.2)
Wet and Temperate Location	4.9 (2 - 11)	0.9 (0.22 - 2.81)	0.4 (0.05 - 1.99)
Wet and Cool Location	9.4 (5.3 - 25.2)	1.95 (0.6 - 6.5)	1.04 (0.14 - 4.7)
		Average of Central Values:	1.82
		25th Percentile of Lower Bounds:	0
		Maximum Value:	25.2
		Summary of Values:	1.82 (0 - 25.2)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 6: Stream, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.005 (0 - 0.06)	0 (0 - 0.006)	0 (0 - 0.004)
Dry and Temperate Location	0.003 (0 - 0.029)	0 (0 - 0.0008)	0 (0 - 0.00012)
Dry and Cold Location	0.0014 (0.000012 - 0.013)	0 (0 - 0)	0 (0 - 0)
Average Rainfall and Warm Location	0.11 (0.05 - 0.22)	0.007 (0.0011 - 0.032)	0.0019 (0.000006 - 0.011)
Average Rainfall and Temperate Location	0.06 (0.026 - 0.14)	0.0026 (0.000003 - 0.023)	0.0006 (0 - 0.013)
Average Rainfall and Cool Location	0.04 (0.012 - 0.12)	0.00025 (0 - 0.006)	0 (0 - 0.0029)
Wet and Warm Location	0.16 (0.07 - 0.27)	0.015 (0.006 - 0.05)	0.006 (0.001 - 0.029)
Wet and Temperate Location	0.13 (0.05 - 0.25)	0.009 (0.0028 - 0.024)	0.0022 (0.0003 - 0.01)
Wet and Cool Location	0.3 (0.18 - 0.6)	0.018 (0.007 - 0.06)	0.005 (0.0008 - 0.031)
		Average of Central Values:	0.0325
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.6
		Summary of Values:	0.032 (0 - 0.6)

Appendix 6: Summary of Gleams-Driver Simulations (continued)

Table 7: Pond, Maximum Peak Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.28 (0 - 6.1)	0 (0 - 0.7)	0 (0 - 0.4)
Dry and Temperate Location	0.16 (0 - 1.34)	0 (0 - 0.11)	0 (0 - 0.024)
Dry and Cold Location	0.06 (0.0006 - 0.6)	0 (0 - 0)	0 (0 - 0)
Average Rainfall and Warm Location	3.9 (1.42 - 12.9)	0.9 (0.11 - 5)	0.31 (0.0013 - 2.87)
Average Rainfall and Temperate Location	2.67 (0.7 - 8.8)	0.4 (0.0004 - 3.7)	0.09 (0 - 2.52)
Average Rainfall and Cool Location	1.36 (0.3 - 4.8)	0.03 (0 - 1.5)	0 (0 - 0.7)
Wet and Warm Location	4.6 (2.14 - 14.1)	1.32 (0.4 - 7.3)	0.7 (0.08 - 7)
Wet and Temperate Location	2.37 (1 - 6.9)	0.5 (0.11 - 2.13)	0.19 (0.018 - 1.42)
Wet and Cool Location	4.9 (2.31 - 11.5)	0.8 (0.23 - 3.8)	0.4 (0.07 - 2.73)
		Average of Central Values:	0.961
		25th Percentile of Lower Bounds:	0
		Maximum Value:	14.1
		Summary of Values:	0.96 (0 - 14.1)

Appendix 6: Summary of Gleams-Driver Simulations *(continued)*

Table 8: Pond, Annual Average Concentration in Surface Water (ug/L or ppb)

Site	Clay	Loam	Sand
Dry and Warm Location	0.0018 (0 - 0.04)	0 (0 - 0.004)	0 (0 - 0.0021)
Dry and Temperate Location	0.0012 (0 - 0.015)	0 (0 - 0.0006)	0 (0 - 0.00012)
Dry and Cold Location	0.0004 (3.1E-06 - 0.004)	0 (0 - 0)	0 (0 - 0)
Average Rainfall and Warm Location	0.09 (0.03 - 0.22)	0.009 (0.0009 - 0.05)	0.0029 (0.000007 - 0.021)
Average Rainfall and Temperate Location	0.04 (0.014 - 0.14)	0.004 (1.8E-06 - 0.04)	0.0007 (0 - 0.022)
Average Rainfall and Cool Location	0.024 (0.008 - 0.09)	0.00023 (0 - 0.01)	0 (0 - 0.005)
Wet and Warm Location	0.15 (0.06 - 0.29)	0.022 (0.008 - 0.09)	0.009 (0.0013 - 0.07)
Wet and Temperate Location	0.09 (0.03 - 0.2)	0.01 (0.0027 - 0.04)	0.0026 (0.0004 - 0.015)
Wet and Cool Location	0.22 (0.13 - 0.4)	0.017 (0.005 - 0.07)	0.005 (0.0008 - 0.03)
		Average of Central Values:	0.02592
		25th Percentile of Lower Bounds:	0
		Maximum Value:	0.4
		Summary of Values:	0.0259 (0 - 0.4)