

**Risks of Cholecalciferol Use to
the Federally Endangered
Salt Marsh Harvest Mouse
(*Reithrodontomys raviventris*)**

**Pesticide Effects Determination
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List of Commonly Used Abbreviations and Nomenclature

µg/kg	Symbol for “micrograms per kilogram”
µg/L	Symbol for “micrograms per liter”
°C	Symbol for “degrees Celsius”
AAPCO	Association of American Pesticide Control Officials
a.i.	Active Ingredient
AIMS	Avian Monitoring Information System
Acc#	Accession Number
BCF	Bioconcentration Factor
BEAD	Biological and Economic Analysis Division
bw	Body Weight
CAM	Chemical Application Method
CARB	California Air Resources Board
CBD	Center for Biological Diversity
CDPR	California Department of Pesticide Regulation
CDPR-PUR	California Department of Pesticide Regulation Pesticide Use Reporting Database
CI	Confidence Interval
CL	Confidence Limit
EC ₀₅	5% Effect Concentration
EC ₂₅	25% Effect Concentration
EC ₅₀	50% (or Median) Effect Concentration
ECOTOX	EPA managed database of Ecotoxicology data
EEC	Estimated Environmental Concentration
EFED	Environmental Fate and Effects Division
<i>e.g.</i>	Latin <i>exempli gratia</i> (“for example”)
EPI	Estimation Programs Interface
ESA	Endangered Species Act
ESU	Evolutionarily significant unit
<i>et al.</i>	Latin <i>et alii</i> (“and others”)
<i>etc.</i>	Latin <i>et cetera</i> (“and the rest” or “and so forth”)
EXAMS	Exposure Analysis Modeling System
FIFRA	Federal Insecticide Fungicide and Rodenticide Act
FQPA	Food Quality Protection Act
ft	Feet

GENEEC	Generic Estimated Exposure Concentration model
IC ₀₅	5% Inhibition Concentration
IC ₅₀	50% (or median) Inhibition Concentration
<i>i.e.</i>	Latin for <i>id est</i> (“that is”)
IECV1.1	Individual Effect Chance Model Version 1.1
kg	Kilogram(s)
kJ/mole	Kilojoules per mole
km	Kilometer(s)
K _{AW}	Air-water Partition Coefficient
K _d	Solid-water Distribution Coefficient
K _{OC}	Organic-carbon Partition Coefficient
K _{OW}	Octanol–water Partition Coefficient
LAA	Likely to Adversely Affect
lb a.i./A	Pound(s) of active ingredient per acre
LC ₅₀	50% (or Median) Lethal Concentration
LD ₅₀	50% (or Median) Lethal Dose
LOAEC	Lowest Observable Adverse Effect Concentration
LOAEL	Lowest Observable Adverse Effect Level
LOC	Level of Concern
LOD	Level of Detection
LOEC	Lowest Observable Effect Concentration
LOQ	Level of Quantitation
m	Meter(s)
MA	May Affect
MATC	Maximum Acceptable Toxicant Concentration
m ² /day	Square Meters per Day
mg	Milligram(s)
mg/kg	Milligrams per kilogram (equivalent to ppm)
mg/L	Milligrams per liter (equivalent to ppm)
mi	Mile(s)
mmHg	Millimeters of mercury
MRID	Master Record Identification Number
MW	Molecular Weight
n/a	Not applicable
NASS	National Agricultural Statistics Service
NAWQA	National Water Quality Assessment

NCOD	National Contaminant Occurrence Database
NE	No Effect
NLAA	Not Likely to Adversely Affect
NLCD	National Land Cover Dataset
NMFS	National Marine Fisheries Service
NOAA	National Oceanic and Atmospheric Administration
NOAEC	No Observable Adverse Effect Concentration
NOAEL	No Observable Adverse Effect Level
NOEC	No Observable Effect Concentration
NRCS	Natural Resources Conservation Service
OPP	Office of Pesticide Programs
OPPTS	Office of Prevention, Pesticides and Toxic Substances
ORD	Office of Research and Development
PCE	Primary Constituent Element
pH	Symbol for the negative logarithm of the hydrogen ion activity in an aqueous solution, dimensionless
pKa	Symbol for the negative logarithm of the acid dissociation constant, dimensionless
ppb	Parts per Billion (equivalent to $\mu\text{g/L}$ or $\mu\text{g/kg}$)
ppm	Parts per Million (equivalent to mg/L or mg/kg)
PCO	Pest Control Operator
PRD	Pesticide Re-Evaluation Division
PRZM	Pesticide Root Zone Model
PUR	Pesticide Use Reporting
RMD	Risk Mitigation Decision
RQ	Risk Quotient
SLN	Special Local Need
SMHM	Salt Marsh Harvest Mouse
T-REX	Terrestrial Residue Exposure Model
UCL	Upper Confidence Limit
USDA	United States Department of Agriculture
USEPA	United States Environmental Protection Agency
USFWS	United States Fish and Wildlife Service
USGS	United States Geological Survey
wt	Weight

1. Executive Summary

1.1. Purpose of Assessment

The purpose of this assessment is to evaluate potential direct and indirect effects on the federally-listed endangered salt marsh harvest mouse (SMHM) arising from FIFRA regulatory actions regarding use of the rodenticide cholecalciferol on agricultural and non-agricultural sites. This assessment was completed in accordance with the U.S. Fish and Wildlife Service (USFWS) and National Marine Fisheries Service (NMFS) *Endangered Species Consultation Handbook* (USFWS/NMFS, 1998), procedures outlined in the Agency's Overview Document (USEPA, 2004a), and consistent with a suit in which cholecalciferol was alleged to be of concern to the SMHM (*Center for Biological Diversity (CBD) vs. EPA et al.*, Case No. 07-2794-JCS).

In this assessment, direct and indirect effects of the use of cholecalciferol as a rodenticide to the SMHM are evaluated in accordance with the methods described in the Agency's Overview Document (USEPA, 2004a). The SMHM was listed by the USFWS as an endangered species in 1970. The species is found in tidal and non-tidal salt marshes along the San Francisco, San Pablo, and Suisun Bays in California. Critical habitat has not been designated for the SMHM; therefore, primary constituent elements (PCEs) have not been defined for the species.

1.2. Scope of Assessment

1.2.1. Uses Assessed

Cholecalciferol is a sterol (vitamin D₃). Its ingestion results in hypercalcemia from mobilization of calcium from bone matrix into blood plasma (Pelfrene, 1991) leading to metastatic calcification of soft tissues (Frazer 1995). Cholecalciferol is used to control Norway rats (*Rattus norvegicus*), roof rats (*Rattus rattus*), and house mice (*Mus musculus*) in and around homes, industrial buildings and similar man-made structures; in and around agricultural buildings, including swine, poultry, cattle and dairy facilities, warehouses and food storage areas; in transport vehicles (ships, trains and aircraft) and in and around related port and terminal buildings; and in alleys. Formulation types include pellets and blocks. All formulations contain 0.075% cholecalciferol. All bait products used outdoors must be placed inside tamper-resistant bait stations and these bait stations must be placed within 50 feet of buildings.

Cholecalciferol has both indoor and outdoor use sites. Indoor use of cholecalciferol is not expected to result in primary exposure to the SMHM. However, many label uses classified as "indoor" actually refer to uses that may take place indoors and/or outdoors within 50 feet of residences or other structures. Therefore, all of the use sites listed above are considered part of the Federal action evaluated in this assessment.

1.2.2. Environmental Fate Properties of Cholecalciferol

The environmental fate of cholecalciferol is not well described because no environmental fate data have been submitted to the Agency for this pesticide. In this assessment, many of the

physical/chemical properties of cholecalciferol were obtained using the quantitative structure-activity relationship (QSAR) estimation software EPISuite (USEPA 2011).

Cholecalciferol is a nonvolatile compound that is essentially insoluble in water. Based on the estimated soil organic carbon-normalized partition coefficient (K_{oc}) of 1.5×10^6 mL/g, cholecalciferol is expected to be immobile in soil as classified using the Food and Agriculture Organization (FAO) mobility classification scheme (the EPISuite software cannot generate a K_d value). Information on biotic and abiotic degradation is not available. Although the compound has an estimated logarithm octanol-water partition coefficient ($\log K_{ow}$) of 10.24, the compound is not expected to bioconcentrate since it is metabolized in mammals¹ (it is not clear whether there is potential for cholecalciferol to bioconcentrate in other taxa).

1.2.3. Evaluation of Degradates and Stressors of Concern

The stressor of concern (*i.e.*, the compound introduced into the environment) for this assessment is defined as the parent compound only (*i.e.*, cholecalciferol). While the environmental fate database is nonexistent, and estimations of the physical/chemical properties of the parent compound have been made, there are no data on potential environmental degradates. While cholecalciferol is metabolized in rodents to form other compounds that are more active than the parent, the stressor of concern is the compound that is present in the environment, not in the target organisms following metabolism.

1.3. Assessment Procedures

A description of routine procedures for evaluating risk to the San Francisco Bay Species is provided in **Attachment I**.

1.3.1. Exposure Assessment

1.3.1.a. Aquatic Exposures

The only aquatic taxon relevant to this assessment is aquatic plants since direct effects to aquatic plants could result in indirect effects to the SMHM; however, no aquatic plant toxicity data are available. Given that cholecalciferol is used in very small quantities and must be placed in tamper-resistant bait stations, the likelihood that it will come into contact with water and/or plants is low. Therefore, concentrations of cholecalciferol in both freshwater and saltwater marshes are expected to be negligible and are not expected to impact aquatic vegetation. Consequently, models that estimate concentrations in surface water or calculate spray drift deposition of cholecalciferol to aquatic habitats were not needed. No surface water monitoring data were available for cholecalciferol, as it was not a monitored analyte.

1.3.1.b. Terrestrial Exposures

For this assessment, it was assumed that terrestrial animals could be exposed by directly consuming cholecalciferol bait (*i.e.*, primary exposure). An assessment for primary exposure

¹ Marshall, 1984

was conducted for the SMHM and for other rodents of various sizes because other rodents provide nesting sites for the SMHM, and effects to other rodents may result in an indirect effect to the SMHM. A secondary exposure assessment was not conducted for the SMHM because the SMHM's diet consists primarily of plants, taxa for which uptake or ingestion of cholecalciferol is unlikely.

Direct or indirect risk to the SMHM mediated through exposure to birds, plants and invertebrates was not assessed. Birds were not evaluated because the only indirect effect to the SMHM from bird exposure to cholecalciferol would result in potentially reducing the availability of bird nests (as nesting sites for the SMHM). Further, it is assumed that bird species that would build nests which could be used by the SMHM for shelter (i.e., are non-cavity-nesting species) are not likely to enter tamper-resistant bait stations.

Since cholecalciferol is not applied directly onto plants, and because cholecalciferol is not expected to leach from the bait and be available for plant uptake, exposure to plants is expected to be minimal. Exposure to terrestrial invertebrates is not expected to impact the SMHM. While exposure to terrestrial invertebrates can occur through ingestion and contact with bait and exposed individuals could be adversely affected and be available for consumption by the SMHM, indirect effects to the SMHM mediated through exposure of terrestrial invertebrates are expected to be negligible given that 1) use of cholecalciferol is restricted to areas within 50' of buildings and therefore will not affect overall terrestrial invertebrate populations, and 2) invertebrates represent only a small component of the diet of the SMHM, which is mainly herbivorous (Massicot, 2005). Therefore, no terrestrial invertebrate exposure assessment was conducted.

Acute, primary exposure of the SMHM to cholecalciferol was considered in this risk assessment. Potential indirect effects to the SMHM resulting from exposure of other rodents to cholecalciferol were also considered because the SMHM may nest in abandoned rodent burrows. Exposure to the SMHM and other rodents was evaluated using a dose-based approach that is dependent on body weight and food consumption rates and a dietary approach that compares the amount of cholecalciferol bait needed to consume the LD₅₀ dose. On a dosage basis, estimated environmental concentrations (EECs) were calculated based on food intake, the concentration of cholecalciferol in the bait and the body size of the consumer. On a dietary basis, the bait concentration of 750 mg a.i./kg-bait was used to estimate the amount of bait consumed in order to reach a lethal dose for acute risk assessment.

The endpoints used in this assessment include direct toxic effects on survival, reproduction, and growth of individuals. The Agency evaluated registrant-submitted studies and data from the open literature to characterize cholecalciferol toxicity. The most sensitive toxicity value available from acceptable or supplemental mammalian studies was used.

Section 4 summarizes available cholecalciferol ecotoxicity data that are pertinent to the effects determination calls for the SMHM. Cholecalciferol is slightly toxic to birds on an acute oral exposure basis, and highly toxic to mammals on an acute oral exposure basis. Chronic toxicity data for birds and mammals were not available; also, no cholecalciferol toxicity data were available for aquatic and terrestrial plants or terrestrial invertebrates. In the absence of chronic

toxicity data, chronic risk to mammals was assumed, based on the high acute toxicity of this chemical. **Appendix B** tabulates all the ecotoxicity data available for cholecalciferol.

1.3.2. Measures of Risk

Acute and chronic risk quotients (RQs) are compared to the Agency's Levels of Concern (LOCs) to identify instances where cholecalciferol use has the potential to adversely affect the assessed species. When RQs for a particular type of effect are below LOCs, the pesticide is considered to have "no effect" on the species. Where RQs exceed LOCs, a potential to cause adverse effects or habitat modification is identified, leading to a conclusion of "may affect." If cholecalciferol use "may affect" the assessed species, the best available additional information is considered to refine the potential for exposure and effects, and distinguish actions that are Not Likely to Adversely Affect (NLAA) from those that are Likely to Adversely Affect (LAA).

1.4. Summary of Conclusions

Based on the best available information, the Agency makes a May Affect, Likely to Adversely Affect (LAA) determination for the SMHM. A summary of the risk conclusions and effects determinations for the SMHM is presented in **Table 1-1**. Use-specific determinations are provided in **Table 1-2**. Further information on the results of the effects determination is included as part of the Risk Description in **Section 5.2**. Given the LAA determinations, a description of the baseline status and cumulative effects for the SMHM is provided in **Attachment III**.

Table 1-1. Effects Determination Summary for Effects of Cholecalciferol on the SMHM

Species	Effects Determination	Basis for Determination
Salt Marsh Harvest Mouse (SMHM) (<i>Reithrodontomys raviventris</i>)	<i>May Affect, and Likely to Adversely Affect (LAA)</i>	Potential for Direct Effects
		Risk assessment indicates that the use of cholecalciferol may result in direct effects to the SMHM from acute and chronic toxicity. Dose-based exposure estimates and data on acute toxicity to small mammals result in acute RQs that exceed the LOC for primary exposure. This species is predicted to be susceptible to primary exposure through direct contact with cholecalciferol bait products. This contact may result in ingestion of the bait which would likely result in acute and/or chronic toxic effects.
		Potential for Indirect Effects
		Habitat modifications Risk assessment indicates the use of cholecalciferol may adversely modify the habitat of this species by reducing the availability of nest sites. This conclusion is based on acute RQs for mammals that exceed the LOC. Adverse effects to mammals may result in a reduction of abandoned mammal nests, which are used as nest sites by the SMHM.

Table 1-2. Use-Specific Summary of the Potential for Adverse Effects to Taxa

Use Pattern	Potential for Effects to Identified Taxa:						
	SMHM and Small Mammals ¹		Birds		Terrestrial Invertebrates	Terrestrial Plants	Aquatic Plants
	Acute	Chronic ²					
Bait for rat and mouse control in and around buildings and in alleys and transport vehicles	Yes	Yes	No	No	No	No	No

¹Yes in this column indicates a potential for direct and indirect effects to the SMHM.

²Chronic toxicity data are not available to assess these taxa, but risk may be assumed based upon the high acute risks.

Based on the conclusions of this assessment, a formal consultation with the U. S. Fish and Wildlife Service under Section 7 of the Endangered Species Act should be initiated.

When evaluating the significance of this risk assessment's direct/indirect and adverse habitat modification effects determinations, it is important to note that pesticide exposures and predicted risks to the listed species and its resources (*i.e.*, habitat) are not expected to be uniform across the action area. Exposure to cholecalciferol and associated risks to the SMHM and its resources are expected to decrease rapidly with increasing distance away from the sites of bait placement. Evaluation of the implication of this non-uniform distribution of risk to the species would require information and assessment techniques that are not currently available. Examples of such information and methodology required for this type of analysis would include the following:

- Enhanced information on the density and distribution of SMHM life stages within the action area. This information would allow for quantitative extrapolation of the present risk assessment's predictions of individual effects to the proportion of the population extant within geographical areas where those effects are predicted. Furthermore, such population information would allow for a more comprehensive evaluation of the significance of potential resource impairment to individuals of the assessed species.

2. Problem Formulation

Problem formulation provides a strategic framework for the risk assessment. By identifying the important components of the problem, it focuses the assessment on the most relevant life history stages, habitat components, chemical properties, exposure routes, and endpoints. The structure of this risk assessment is based on guidance contained in U.S. EPA's *Guidance for Ecological Risk Assessment* (USEPA, 1998) and the Services' *Endangered Species Consultation Handbook* (USFWS/NMFS, 1998), and is consistent with procedures and methodology outlined in the Overview Document (USEPA, 2004a) and reviewed by the U.S. Fish and Wildlife Service and National Marine Fisheries Service (USFWS/NMFS/NOAA, 2004).

2.1. Purpose

The purpose of this endangered species assessment is to evaluate potential direct and indirect effects on individuals of the federally endangered salt marsh harvest mouse (SMHM) arising from FIFRA regulatory actions regarding use of cholecalciferol on all sites. This ecological risk assessment has been prepared consistent with a stipulated injunction in the case *Center for Biological Diversity (CBD) vs. EPA et al.* (Case No. 07-2794-JCS) entered in Federal District Court for the Northern District of California on May 17, 2010.

In this assessment, direct and indirect effects of the use of cholecalciferol as a rodenticide to the SMHM are evaluated in accordance with the methods described in the Agency's Overview Document (USEPA, 2004a). The SMHM was listed by the USFWS as an endangered species in 1970. The species is found in tidal and non-tidal salt marshes along the San Francisco, San Pablo, and Suisun Bays in California.

In accordance with the Overview Document, provisions of the ESA, and the Services' *Endangered Species Consultation Handbook*, the assessment of effects associated with registrations of cholecalciferol is based on an action area. The action area is the area directly or indirectly affected by the federal action, as indicated by the exceedance of the Agency's Levels of Concern (LOCs). It is acknowledged that the action area for a national-level FIFRA regulatory decision associated with a use of cholecalciferol may potentially involve numerous areas throughout the United States and its Territories. However, for the purposes of this assessment, attention will be focused on relevant sections of the action area including those geographic areas associated with locations of the SMHM and its designated critical habitat within the state of California. As part of the "effects determination", one of the following three conclusions will be reached separately for each of the assessed species in the lawsuits regarding the potential use of cholecalciferol in accordance with current labels:

- "No effect";
- "May affect, but not likely to adversely affect"; or
- "May affect and likely to adversely affect".

A description of routine procedures for evaluating risk to the San Francisco Bay Species is provided in **Attachment I**.

2.2. Scope

The end result of the EPA pesticide registration process (*i.e.*, the FIFRA regulatory action) is an approved product label. The label is a legal document that stipulates how and where a given pesticide may be used. Product labels (also known as end-use labels) describe the formulation type (*e.g.*, liquid or granular), acceptable methods of application, approved use sites, and any restrictions on how applications may be conducted. Thus, the use or potential use of cholecalciferol in accordance with the approved product labels for California is "the action" relevant to this ecological risk assessment.

Cholecalciferol (3 β ,5Z,7E)-9,10-secocholesta-5,7,10(19)-trien-3-ol) is a sterol (Vitamin D₃) rodenticide. It is registered for use in bait, pellets and blocks to control Norway rats (*Rattus*

norvegicus), roof rats (*Rattus rattus*), and house mice (*Mus musculus*) in and around homes, industrial buildings and similar man-made structures; in and around agricultural buildings, including swine, poultry, cattle and dairy facilities, warehouses and food storage areas; in transport vehicles (ships, trains and aircraft) and in and around related port and terminal buildings; and in alleys. All formulations contain 0.075% cholecalciferol. All cholecalciferol bait products used outdoors must be placed inside tamper-resistant bait stations and these bait stations must be placed within 50 feet of buildings.

Cholecalciferol has both indoor and outdoor use sites. Indoor use sites are classified as: **indoor food** (agricultural/farm structures/buildings and equipment); **indoor non-food** (commercial/institutional/industrial premises/equipment; commercial transportation facilities; public buildings/structures; food processing plant premises - nonfood contact; ships and boats); and **indoor residential** (household/domestic dwellings). Outdoor use sites are classified as: **outdoor residential** (household/domestic dwellings); **terrestrial non-food** (agricultural/farm structures/buildings and equipment; commercial/institutional/industrial premises/equipment; nonagricultural outdoor buildings/structures; food processing plant premises – nonfood contact); **terrestrial non-food + outdoor residential** (urban areas).

Although current registrations of cholecalciferol allow for use nationwide, this ecological risk assessment and effects determination addressed currently registered uses of cholecalciferol in portions of the action area that are reasonably assumed to be biologically relevant to the SMHM. Further discussion of the action area for the SMHM is provided in **Section 2.7**.

Because of the properties of cholecalciferol and since all products used outdoors must be placed in tamper-resistant bait stations, risk to all terrestrial and aquatic organisms other than rodents is expected to have an insignificant impact on the SMHM. Therefore, this assessment focuses on direct risk to the SMHM and indirect risk to the SMHM from effects to other rodents which may provide habitat (nesting sites) for the SMHM.

2.2.1. Evaluation of Degradates

In mammals, cholecalciferol is metabolized (hydroxylated) in the liver to 25-hydroxycholecalciferol and is further metabolized (hydroxylated) in the kidney to form 1, 25-dihydroxycholecalciferol which is the most hormonally active form of the compound (Fraser 1995)². At this time, there are insufficient data to describe the extent to which this metabolic pathway is conserved in other non-target species and the extent to which the hydroxylated forms of cholecalciferol are formed in the environmental media. For the purposes of this assessment, the assumption is made that all of the cholecalciferol is present as 1, 25-dihydroxycholecalciferol, the most active form of the compound.

2.2.2. Evaluation of Mixtures

Cholecalciferol does not have registered products that contain multiple active ingredients.

² Fraser, D. R. 1995. Vitamin D. *The Lancet* 345: 104 – 107.

2.3. Previous Assessments

Cholecalciferol was first issued a conditional registration as a rodenticide in November of 1984 under the “public interest” clause of FIFRA Section 3 (c)(7)(C). Cholecalciferol baits were approved as an alternative for control of anti-coagulant-resistant baits.

In 1993, the Health Effects Division (HED) reviewed a package containing information on “numerous” poisonings in dogs³ (this was prior to the requirement for tamper-proof bait stations). The conclusions of the review highlighted the severe, irreversible toxicity of cholecalciferol to mammals (for which there is no known antidote). HED stated that the possibility of non-target animals finding and consuming bait warranted strong restrictions on use of cholecalciferol such as tamper-proof bait stations.

Also in 1993, a Biological Opinion (BO) was issued by the U.S. Fish and Wildlife Service (USFWS) for several listed species, including the SMHM.

In 1999, EFED reviewed a request for use of cholecalciferol in New Mexico to control rock squirrels (*Spermophilus variegatus*). In 2004, cholecalciferol was included in a comparative risk assessment conducted by EPA for nine rodenticides to evaluate the potential for rodenticide bait products to pose ecological risks to non-target birds and mammals. In 2007, EFED evaluated an experimental use permit for cholecalciferol to control the rodent nutria (*Myocastor caoypus*) in Louisiana. These assessments are described below.

1993 Biological Opinion on Cholecalciferol

The USFWS addressed the risk of cholecalciferol use on endangered species in a BO issued in March of 1993 (USFWS, 1993). The USFWS produced the BO in response to a request by the EPA in 1991 for formal Section 7 consultation on 31 registered chemicals, including 16 vertebrate control agents. The USFWS did not specify application rates evaluated in their BO. The BO included an evaluation of the use of cholecalciferol for control of Norway rats, roof rats, and house mice in and around homes (*i.e.*, commensal uses), industrial, commercial, agricultural and poultry buildings and similar man-made structures.

The BO concluded that normal use of cholecalciferol is not likely to harm aquatic fauna due to the virtual insolubility of Vitamin D3 (solubility <1 ppm) and the fact that for the bait application patterns, the pesticide will not be subject to runoff into aquatic systems. For terrestrial animals, the BO discussed concerns for primary and secondary poisoning of listed scavengers and predators. The USFWS issued a jeopardy call for species listed in **Table 2-1**. Furthermore, the BO contained the following Reasonable and Prudent Alternatives (RPAs):

- Prohibit use of cholecalciferol within 100 yards of occupied habitat of the Choctawhatchee beach mouse, Alabama beach mouse, and Perdido Key beach mouse.
- Prohibit use of cholecalciferol within 100 yards of occupied habitat of the Anastasia Island beach mouse and the Southeastern beach mouse.

³ U.S. EPA, 1993a

- Prohibit the outdoor use of cholecalciferol within the occupied habitat of the Carolina northern flying squirrel.
- Prohibit the use of cholecalciferol within 100 yards of the landward edge of the Florida salt marsh vole's salt marsh habitat in Levy County, Florida.
- Prohibit outdoor use of cholecalciferol within 100 yards of all occupied salt marsh harvest mouse habitats.
- Prohibit use of cholecalciferol within 100 yards of the occupied habitat of the Morro Bay kangaroo rat.

The BO also contained the following Reasonable and Prudent Measure (RPM) for cholecalciferol: to minimize anticipated incidental take, EPA must establish a monitoring enforcement program. The terms and conditions of such a program were outlined in the BO. Further detail on individual species is provided in the BO

(http://www.fws.gov/sacramento/es/programmatic_consultations.htm).

Table 2-1. Jeopardy Calls for Species Evaluated in the 1993 FWS Biological Opinion on Cholecalciferol Use

Species	N/NJ ¹	Species	N/NJ ¹
Alabama beach mouse (<i>Peromyscus polionotus ammobates</i>)	J	Morro Bay kangaroo rat (<i>Dipodomys heermanni morroensis</i>)	J
Anastasia Island beach mouse (<i>Peromyscus polionotus phasma</i>)	J	Perdido Key beach mouse (<i>Peromyscus polionotus trissyllepsis</i>)	J
Carolina northern flying squirrel <i>Glaucomys sabrinus coloratus</i>	J	Point Arena mountain beaver (<i>Aplodontia rufa nigra</i>)	NJ
Choctawhatchee beach mouse (<i>Peromyscus polionotus allophrys</i>)	J	Salt marsh harvest mouse (<i>Reithrodontomys raviventris</i>)	J
Florida salt marsh vole <i>Microtus pennsylvanicus dukecampbelli</i>	J	Southeastern beach mouse (<i>Peromyscus polionotus niveiventris</i>)	J
Fresno kangaroo rat (<i>Dipodomys nitratoideis exilis</i>)	J	Stephen's kangaroo rat (<i>Dipodomys stephensi</i>)	NJ
Giant kangaroo rat <i>Dipodomys ingens</i>	NJ	Tipton kangaroo rat (<i>Dipodomys nitratoideis nitratoideis</i>)	NJ

¹J= Jeopardy ; NJ = No Jeopardy

1999 Rock Squirrel Control in New Mexico

EFED concluded that no risk to endangered species would result from the proposed use to control rock squirrel in New Mexico, citing the 1995 BO which determined jeopardy for 10 species of small rodents, since none of the species occur in the state of New Mexico (U.S. EPA, 1999).

EPA's 2004 Comparative Assessment

The OPP document entitled “*Potential Risks of Nine Rodenticides to Birds and Non-target Mammals: a Comparative Approach*” (USEPA, 2004b), evaluated primary and secondary exposure of birds and mammals to cholecalciferol and eight other rodenticides. The document was developed to provide further guidance in developing mitigations for all rodenticides. The assessment determined that primary risks of cholecalciferol to non-target mammals are high and that primary risks to birds are low to moderate. On the other hand, the assessment determined that there were insufficient data to determine the secondary risks to birds and mammals from

non-anticoagulant rodenticides such as cholecalciferol. The assessment also specified a number of factors contributing to uncertainty in assessing non-anticoagulant rodenticides. Those factors that contributed the most uncertainty were: (1) missing data, including acute, chronic, and secondary toxicity as well as data regarding retention of some active ingredients in the liver, blood, and other body tissues; (2) the variable quality and quantity of existing data on metabolism and retention times in rodents and non-target species; (3) specific use information by formulation, including typical amounts applied by use site, seasonally, and annually; distances applied from buildings; amounts used in rural versus urban areas; use by Certified Applicators versus homeowners and other non-certified applicators; and other such relevant information; (4) information on the number and species of birds and non-target mammals frequenting baited areas and the likelihood of their finding and consuming bait or poisoned primary consumers in the various use areas; (5) methods to determine liver concentration(s) and total body burdens of rodenticide that would corroborate death or even if such a cause-effect relationship is appropriate (e.g., the “threshold of toxicity” concentration); (6) not accounting for the impacts of sub-lethal effects on reproduction and non-target mortality; (7) not accounting for bioaccumulation of repeated sublethal exposures to bait or poisoned rodents utilized as food by predators and scavengers; and (8) lack of incident reporting. All of the above issues remain as uncertainties for this assessment.

2007 Experimental Use Permit to Control Nutria in Louisiana

In its evaluation of an Experimental Use Permit (EUP) under FIFRA Section 5 for the control of the rodent nutria in Louisiana with cholecalciferol, EFED concluded that since cholecalciferol is highly toxic to mammals on an acute oral exposure basis, mammals that consume the poisoned bait could be injured or killed. Also, it was concluded that experimental use of cholecalciferol in Louisiana could pose a threat to the Louisiana black bear (*Ursus americanus luteolus*) due to an overlap in the proposed study area and the habitat of the Louisiana black bear (at the time of the assessment, tamper-resistant bait stations were not required) (U.S. EPA, 2007).

EPA's 2008 Risk Mitigation Decision

In 2008, the Agency issued a Risk Mitigation Decision (RMD) for Ten Rodenticides (USEPA, 2008). The RMD was a summary of the risk mitigation measures for each of the ten rodenticide products representing first- and second-generation anticoagulants and non-anticoagulants, including cholecalciferol. The decision also reflected the Agency's final action in response to the remand order in *West Harlem Environmental Action and Natural Resources Defense Council v. U.S. Environmental Protection Agency*, 380 F.Supp.2d 289 (S.D.N.Y. 2005). The 2008 RMD considered only commensal rodent control uses in and around buildings and underground manual application to pocket gopher and mole burrows. The two major mitigation components of the RMD included minimizing the exposure of children to rodenticide products used in homes and reduction of wildlife exposure and ecological risks from these products. Mitigations measures relevant to this assessment include the following conditions of registration for rodenticides:

“Consumer Size” Products (Products containing ≤ 1 pound of bait)

- Loose bait forms such as pellets are prohibited.
- Each retail unit must include a bait station.
- Bait refills may be sold with bait stations in a single retail unit.

- All outdoor above ground use must be in a bait station and be applied within 50 feet of buildings.

First Generation Anticoagulant and Non-Anticoagulant Products for Professional Users (Agricultural and PCO)

- Products must contain at least four pounds of bait.
- Bait stations are required for all outdoor, above-ground placements of first-generation anticoagulant and non-anticoagulant products.
- Bait stations are required indoors if exposure to children, pets, or non-target animals is possible.
- Distribution to and sales in “consumer” stores including grocery stores, drug stores, hardware stores, club stores will be prohibited.
- All outdoor above ground use must be in a bait station and be applied within 50 feet of buildings.

EPA requires all outdoor, above-ground placements of bait products with non-anticoagulants be contained in bait stations, in order to limit non-target animal access to the rodenticide bait. Most formulated rodent baits are grain-based and are therefore attractive to many birds and non-target mammals. Tamper-resistant bait stations are required if the bait placement would be within reach of pets, domestic animals, non-target wildlife or children under six years-of-age. Other types of bait stations may be constructed and used in settings, such as around livestock production buildings, where exposure to children and non-target wildlife is unlikely (USEPA, 2008)

At the writing of this risk assessment, all active cholecalciferol labels are compliant with the risk mitigations for non-anticoagulants as described in the 2008 RMD⁴.

2.4. Environmental Fate Characterization

2.4.1. Environmental Fate Characterization

The environmental fate of cholecalciferol [(3 β ,5Z,7E)-9,10-secocholesta-5,7,10(19)-trien-3-ol] (**Figure 2-1**) is not well described based on current environmental fate data because no environmental fate data have been submitted to the Agency for this pesticide. The physical/chemical properties of cholecalciferol were estimated using the quantitative structure-activity relationship (QSAR) estimation software EPISuite (U.S. EPA, 2011). These properties are presented in **Table 2-2**.

Cholecalciferol is a nonvolatile compound that is essentially insoluble in water. Based on the estimated soil organic carbon-normalized partition coefficient (K_{oc}) of 1.5×10^6 mL/g, it is expected to be immobile in soil when classified using the Food and Agriculture Organization (FAO) mobility classification scheme. Information on potential environmental degradates from biotic or abiotic degradation is not available, as there are no submitted environmental fate data, and other sources of such data could not be located.

⁴ <http://www.epa.gov/oppsrrd1/reregistration/rodenticides/finalriskdecision.htm>

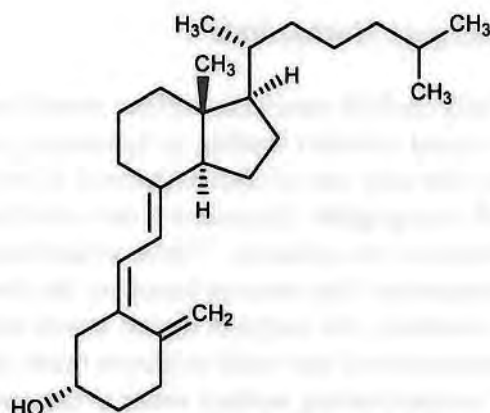


Figure 2-1. Cholecalciferol Chemical Structure

Table 2-2. Physical-Chemical Properties of Cholecalciferol

Physical/Chemical Property	Value (unit)	Source	Comments
CAS Number	67-97-0		
CAS	(5- <i>Z</i> ,7 <i>E</i>)-(3 <i>S</i>)-cholesta-5,7,10(19)-trien-3-ol		
IUPAC	(3β,5 <i>Z</i> ,7 <i>E</i>)-9,10-secocholesta-5,7,10(19)-trien-3-ol		
Molecular Formula	C ₂₇ H ₄₄ O	U.S. EPA, 2004b	
Molecular Weight	384.64 g/mole	U.S. EPA, 2004b	
Physical State	Solid (crystals)	U.S. EPA, 2004b	
Vapor Pressure (@25°C; estimated)	2.4X10 ⁻⁹ Torr	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10.
Water Solubility (@25°C; estimated)	2.2X10 ⁻⁵ mg/L	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10. Practically insoluble in water.
Soil Organic Carbon-Normalized Partition Coefficient (K _{oc})	1.5X10 ⁶ mL/g	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10.
Log Octanol-Water Partition Coefficient (K _{ow})	10.2	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10.
Henry's Law Constant (@25°C)	2.3X10 ⁻⁴ atm·m ³ /mole	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10.
Log Octanol-Air Partition Coefficient (K _{oa})	12.3	Estimated	Estimated using EPI-Suite ¹ . Ver.4.10.
Bioconcentration Factor	30	Estimated (Arnot-Gobas method)	Estimated using EPI-Suite ¹ . Ver.4.10.

¹ Available at <http://www.epa.gov/oppt/exposure/pubs/episuite.html>. See Appendix C for EPI-Suite output for cholecalciferol.

2.4.2. Environmental Transport Mechanisms

Potential transport mechanisms typically include pesticide surface water runoff, spray drift, and secondary drift of volatilized or soil-bound residues leading to deposition onto nearby or more distant ecosystems. However, because the only use of cholecalciferol is in bait for rodent control, the potential for runoff and spray drift is negligible. Exposure from volatilization (vapor pressure = 2.4×10^{-9} Torr) from dry soil is expected to be minimal. While volatilization from moist soil or water surfaces could be a relatively important fate process based on the Henry's Law Constant of 2.3×10^{-4} atm-cu m/mole, the high tendency for sorption to soil would make this route of transport unlikely. Additionally, cholecalciferol bait used outdoors must be placed in bait stations. Therefore, the potential for contaminating surface water is assumed to be insignificant. Furthermore, since the active ingredient is often placed in highly hydrophobic, weather-resistant blocks, overall volatilization from the bait is also expected to be insignificant.

Secondary exposure to the SMHM through environmental transport mechanisms is not a concern because the SMHM's diet consists primarily of plants, taxa for which uptake or ingestion of cholecalciferol is unlikely.

2.4.3. Mechanism of Action

Cholecalciferol ingestion results in hypercalcemia from mobilization of calcium from bone matrix into blood plasma (Pelfrene, 1991) resulting in metastatic calcification of soft tissues (Frazer 1995) and a generalized disruption of calcium homeostasis. It has been hypothesized that ingestion of cholecalciferol results in increased hepatic metabolism of the compound to 25-hydroxycalciferol which is in turn activated to 1,25-dihydroxycholecalciferol in the mammalian kidney. The plasma protein binding efficiency of the precursor 25-hydroxycholecalciferol is higher and displaces the active dihydroxycholecalciferol making the active compound more available for cellular uptake from the blood (Frazer 1995).

2.4.4. Use Characterization

Analysis of labeled use information is the critical first step in evaluating the federal action. The current labels for cholecalciferol represent the FIFRA regulatory action; therefore, labeled use and application rates specified on the label form the basis of this assessment. The assessment of use information is critical to the development of the action area and selection of appropriate modeling scenarios and inputs.

Nationwide, cholecalciferol is registered for use in pellets and blocks to control three commensal rodents: the Norway rat, the roof rat, and the house mouse. Baits containing cholecalciferol are registered for use in and around homes, industrial buildings and similar man-made structures and in and around agricultural buildings including swine, poultry, cattle, and dairy facilities, warehouses and food storage areas, in transport vehicles (ships, trains, aircraft) and in and around related port and terminal buildings and in alleyways. All baits are to be placed not farther than 50 feet from buildings. Thus, cholecalciferol has both indoor and outdoor uses with outdoor uses requiring that bait be placed in tamper-resistant bait stations. Indoor use sites are classified as: **indoor food**, **indoor non-food**, and **indoor residential**. Outdoor use sites are classified as:

outdoor residential, and terrestrial non-food, terrestrial non-food + outdoor residential (urban areas).

Uses that occur indoors would not be expected to result in any primary exposure to the SMHM. Many label uses classified as “indoor” actually refer to uses that may take place indoors and/or outdoors within 50 ft of residences or other structures. Therefore, all of the uses listed above (both indoor and outdoor) are considered as part of the federal action evaluated in this assessment. Therefore, all registered products of cholecalciferol could be used in the area inhabited by the assessed species.

Labels of cholecalciferol products do not limit the amount of product or active ingredient that may be applied per unit area, the number of applications that can be made per unit time, or the minimal time interval between applications. Labels generally state the number of bait stations or bait blocks that may be placed in one location as well as the linear interval between placements. The linear interval is generally 15 to 30 feet for rats and 8 to 12 feet for mice. The concentration of cholecalciferol in bait is 0.075% for all rodent-control products.

The amount of active ingredient per placement or the amount of active ingredient per linear foot can be calculated for cholecalciferol products. The maximum amount of active ingredient per placement for any product is 170 mg for rats and 21.3 mg for mice. The maximum amount of active ingredient per linear foot is 11.3 mg/ft for controlling rats and 2.66 mg/ft for controlling mice. Use information for applications considered in this assessment is summarized in **Table 2-3**.

Table 2-3. Cholecalciferol Uses Assessed for California

Use (Application Method)	Formulation	% a.i.	mg a.i./kg bait	Maximum Application Rate per Bait Placement (mg a.i./placement) ¹	Bait Placement Interval
Bait for rat and mouse control in and around buildings, in alleys and transport vehicles, in agricultural settings, food storage areas (bait stations)	Pellets and bait blocks	0.075	750	8 oz. bait (170 mg a.i.) (rats) 1 oz. bait (21.3 mg a.i.) (mice)	15-30 ft (rats) 8-12 ft (mice)

¹ 1 oz bait=28,350 mg*0.00075= 21.3 mg a.i.

2.4.5. Reported Usage Data

The Agency’s Biological and Economic Analysis Division (BEAD) provides an analysis of both national- and county-level usage information using state-level usage data obtained from USDA-NASS⁵, Doane (www.doane.com; the full dataset is not provided due to its proprietary nature) and the California’s Department of Pesticide Regulation Pesticide Use Reporting (CDPR PUR)

⁵ United States Department of Agriculture (USDA), National Agricultural Statistics Service (NASS) Chemical Use Reports provide summary pesticide usage statistics for select agricultural use sites by chemical, crop and state. See http://www.pestmanagement.info/nass/app_usage.cfm.

database⁶. CDPR PUR is considered a more comprehensive source of usage data than USDA-NASS or EPA proprietary databases, and thus the usage data reported for cholecalciferol by county in this California-specific assessment were generated using CDPR PUR data. It should be noted that the CDPR PUR database does not include data on homeowner uses. Eleven years (1999-2009) of usage data were included in this analysis. Data from CDPR PUR were obtained for every agricultural pesticide application made on every use site at the section level (approximately one square mile) of the public land survey system⁷. BEAD summarized these data to the county level by site, pesticide, and unit treated. Calculating county-level usage involved summarizing across all applications made within a section and then across all sections within a county for each use site and for each pesticide. The county-level usage data that were calculated include average annual pounds applied and average and maximum application rate across all 11 years.

CDPR PUR data from 1999 to 2009 show that cholecalciferol was used in all of the counties in California where the SMHM may occur (**Table 2-5**) except Yolo, Madera and San Luis Obispo Counties. The counties of Fresno, Alameda and Santa Barbara had the three highest average pounds applied per county with 0.88, 0.37, and 0.36 lbs. a.i. per year, respectively. Average annual and maximum application rates and average annual area treated were not summarized below because these values were reported in various units of area (*e.g.*, acres, square feet) or not reported at all (*e.g.*, “miscellaneous”). A summary of cholecalciferol usage for California counties is provided below in **Table 2-4**.

Table 2-4. Summary of California Department of Pesticide Registration (CDPR) Pesticide Use Reporting (PUR) Data from 1999 to 2009¹

County	Average Annual Pounds Applied	County	Average Annual Pounds Applied
Alameda	0.37	San Benito	0.01
Contra Costa	0.17	San Joaquin	0.01
Fresno	0.88	San Luis Obispo	0.00
Kern	0.14	San Mateo	0.09
Kings	0.01	Santa Barbara	0.36
Madera	0.00	Santa Clara	0.21
Marin	0.02	Solano	0.06
Merced	0.04	Sonoma	0.07
Monterey	0.11	Stanislaus	0.09
Napa	0.02	Tulare	0.01

¹ Based on data supplied by BEAD.

² **Bolded numbers** indicate the highest average county usage in California.

⁶ The California Department of Pesticide Regulation’s Pesticide Use Reporting database provides a census of pesticide applications in the state. See <http://www.cdpr.ca.gov/docs/pur/purmain.htm>.

⁷ Most pesticide applications to parks, golf courses, cemeteries, rangeland, pastures, and along roadside and railroad rights of way, and postharvest treatments of agricultural commodities are reported in the database. The primary exceptions to the reporting requirement are home-and-garden use and most industrial and institutional uses (<http://www.cdpr.ca.gov/docs/pur/purmain.htm>).

2.5. Assessed Species

Table 2-5 provides a summary of the current distribution, habitat requirements, and life history parameters for the listed species being assessed. More detailed life-history and distribution information can be found in **Attachment II**. See **Figure 2.2** for a map of the current range of the SMHM. The SMHM was listed by the USFWS as an endangered species in 1970. The species is found in tidal and non-tidal salt marshes along the San Francisco, San Pablo, and Suisun Bays in California.

Table 2-5. Summary of Current Distribution, Habitat Requirements, and Life History Information for the Salt Marsh Harvest Mouse¹

Assessed Species	Size	Current Range	Habitat Type	Designated Critical Habitat?	Reproductive Cycle	Diet
Salt Marsh Harvest Mouse (SMHM) (<i>Reithrodontomys raviventris</i>)	Adult 8 – 14 g	Northern subspecies can be found in Marin, Sonoma, Napa, Solano, and northern Contra Costa counties. The southern subspecies occurs in San Mateo, Alameda, and Santa Clara counties with some isolation populations in Marin and Contra Costa counties.	Dense, perennial cover with preference for habitat in the middle and upper parts of the marsh dominated by pickleweed and peripheral halophytes as well as similar vegetation in diked wetlands adjacent to the Bay.	No	<u>Breeding:</u> March – November <u>Gestation period:</u> 21 – 24 days	Leaves, seeds, and plant stems; may occasionally eat insects; prefers “fresh green grasses” in the winter and pickleweed and saltgrass during the rest of the year; drinks both salt and fresh water.

¹For more detailed information on the distribution, habitat requirements, and life history information of the assessed listed species, see Attachment II.

Salt Marsh Harvest Mouse Habitat

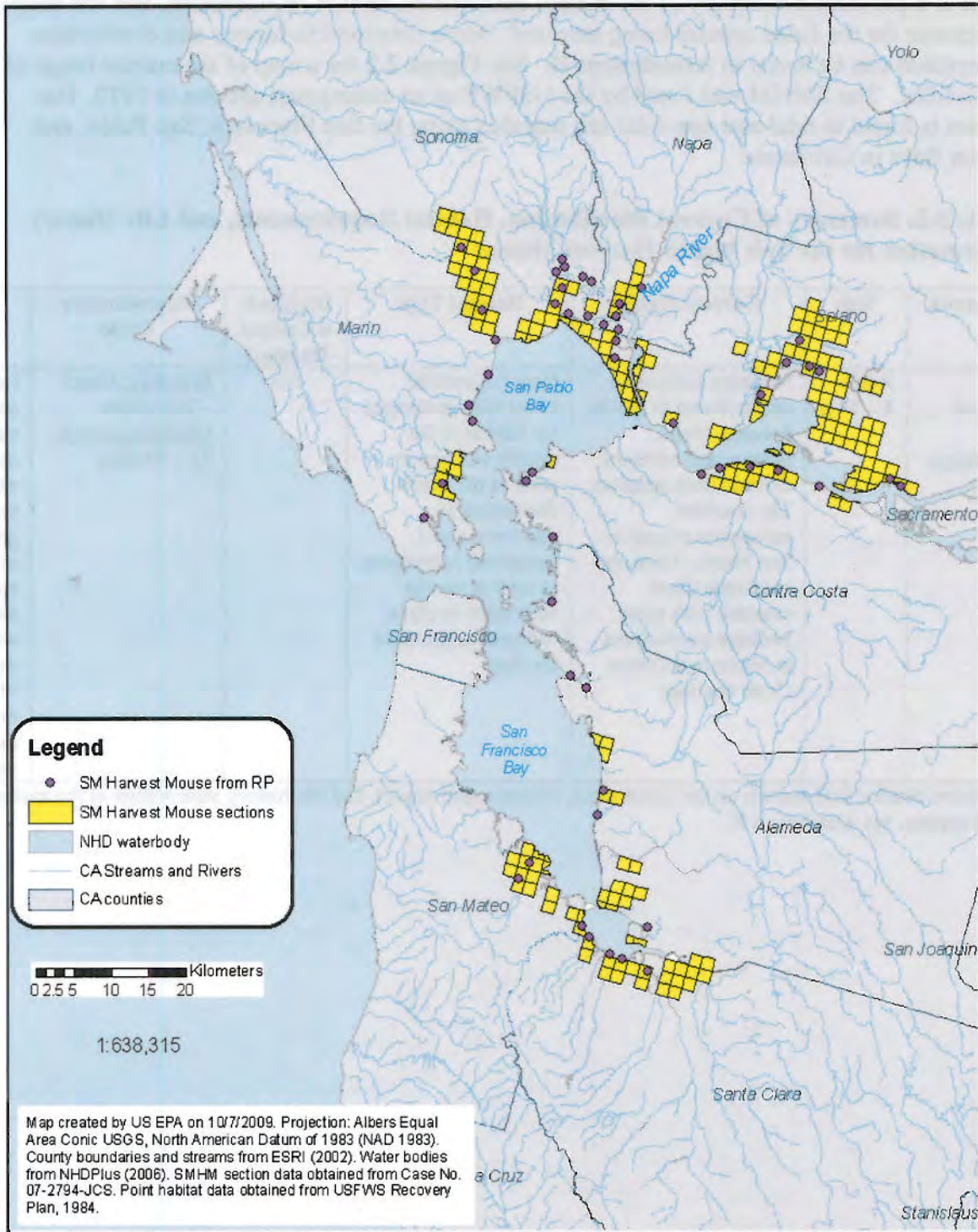


Figure 2-2. Occurrences and occurrence sections of the Salt Marsh Harvest Mouse, as identified in Case No. 07-2794-JCS

2.6. Designated Critical Habitat

Critical habitat has been not been designated for the SMHM.

2.7. Action Area and LAA Effects Determination Area

2.7.1. Action Area

The action area is used to identify areas that could be affected by the Federal action. The Federal action is the authorization or registration of pesticide use or uses as described on the label(s) of pesticide products containing a particular active ingredient. The action area is defined by the Endangered Species Act as, “all areas to be affected directly or indirectly by the Federal action and not merely the immediate are involved in the action” (50 CFR §402.2). Based on an analysis of the Federal action, the action area is defined by the actual and potential use of the pesticide and areas where that use could result in effects. Specific measures of ecological effect for the assessed species that define the action area include any direct and indirect toxic effect to the assessed species and any potential modification of its critical habitat, including reduction in survival, growth, and fecundity as well as the full suite of sublethal effects available in the effects literature. It is recognized that the overall action area for the national registration of cholecalciferol is likely to encompass considerable portions of the United States based on its widespread use for rodent control. However, the scope of this assessment limits consideration of the overall action area to those portions that may be applicable to the protection of the SMHM within the state of California. For this assessment, the entire state of California is considered the action area. The purpose of defining the action area as the entire state of California is to ensure that the initial area of consideration encompasses all areas where the pesticide may be used now and in the future that could influence the San Francisco Bay Species. Additionally, the concept of a state-wide action area takes into account the potential for direct and indirect effects and any potential modification to critical habitat based on ecological effect measures associated with reduction in survival, growth, and reproduction, as well as the full suite of sublethal effects available in the effects literature.

2.7.2. LAA Effects Determination Area

Typically, when assessing the potential for use of a pesticide to affect threatened or endangered species, the Agency determines a Likely to Adversely Affect (LAA) Effects Determination Area. This is the area where the pesticide’s use is expected to directly or indirectly affect the species and/or modify its designated critical habitat, as determined by applying EFED’s standard assessment procedures (see **Attachment I**) based on effects endpoints related to survival, growth, and reproduction. The LAA Effects Determination Area is typically designated as the area where the land use corresponds with land use on which the pesticide is likely to be used (*e.g.*, row crops or orchards), plus the area outside this use area which could receive exposure via spray drift and/or downstream transport at levels that are potentially toxic for the species of concern. In the case of this assessment, however, the area of potential use of cholecalciferol is not restricted spatially. Considering the use pattern of rodent control baits, cholecalciferol potentially could be used in any terrestrial land use type. Thus, any area of the state of California is considered an area of potential use of cholecalciferol bait, and thus the assessed species

potentially could be exposed to cholecalciferol wherever they occur. Based on CDPR Pesticide Usage Reporting data, cholecalciferol has been used within the years 1999-2009 in 18 of 20 of the California counties in which occurrences or occurrence sections were identified for the SMHM in Case No. 07-2794-JCS.

2.8. Assessment Endpoints and Measures of Ecological Effect

For more information on the assessment endpoints, measures of ecological effect, see **Attachment I**.

2.8.1. Assessment Endpoints

A complete discussion of all the toxicity data available for this risk assessment, including resulting measures of ecological effect selected for the taxonomic group of concern, is included in **Section 4** of this document. **Table 2-8** identifies the taxa used to assess the potential for direct and indirect effects from the uses of cholecalciferol for each listed species assessed here.

Mammals are assessed for direct and indirect effects. Birds, terrestrial plants, aquatic plants and terrestrial invertebrates are considered for indirect effects to the SMHM. Terrestrial and aquatic plants provide food for the SMHM and also play a role as important habitat requirements of the SMHM. In addition to plants, birds and mammals are considered as habitat requirements because this species is known to build its nests over bird nests (USFWS, 2011a+b) and in abandoned nests built by shrews (Goals Project, 2000).

However, birds that provide rearing sites to the SMHM (*e.g.*, passerine species) are not likely to be at risk from cholecalciferol use because all cholecalciferol must be formed as bait and must be placed in bait stations, making it inaccessible to most birds. While some birds may be able to access the bait within the bait station, these birds are generally ground-nesting birds and are unlikely to create habitat for the SMHM. Indirect effects to the SMHM mediated through plants were also assumed to have negligible contributions to overall risk since the use of cholecalciferol, which is only available within bait boxes, is unlikely to affect plants. Finally, indirect effects resulting from terrestrial invertebrates were assumed to be negligible given the restriction that use of cholecalciferol must be used within 50' of buildings and the diverse array of (mostly plant) food items that make up the diet of the SMHM. The specific assessment endpoints used to assess the potential for direct and indirect effects to each listed species are provided in **Table 2-9**.

Table 2-6. Taxa Used in the Analyses of Direct and Indirect Effects for the Assessed Listed Species

Listed Species	Birds	Mammals	Terrestrial Invertebrates	Terrestrial Plants And Aquatic Plants
Salt Marsh Harvest Mouse	Not Assessed- Negligible Exposure to birds providing rearing sites	Direct and Indirect (rearing sites)	Not Assessed- Low exposure and not a critical food source	Not Assessed- Negligible Exposure

Table 2-7. Taxa and Assessment Endpoints Used to Evaluate the Potential for Use of Cholecalciferol to Result in Direct and Indirect Effects to the SMHM

Taxa	Assessed Listed Species	Assessment Endpoints	Measures of Ecological Effects
Mammals	<u>Direct Effects</u> -SMHM	Survival, growth, and reproduction of individuals via direct effects.	<u>Acute</u> : Most sensitive laboratory mammalian acute LC ₅₀ or LD ₅₀ .
	<u>Indirect Effects</u> -SMHM (burrows/rearing sites)	Survival, growth, and reproduction of individuals via indirect effects on other small mammals that provide habitat.	<u>Chronic</u> : No data available.

2.8.2. Assessment Endpoints for Designated Critical Habitat

As previously discussed, designated critical habitat has not been identified for the SMHM. Therefore, an assessment of the critical habitat is not necessary.

2.9. Conceptual Model

2.9.1. Risk Hypotheses

Risk hypotheses are specific assumptions about potential adverse effects (*i.e.*, changes in assessment endpoints) and may be based on theory and logic, empirical data, mathematical models, or probability models (USEPA, 1998). For this assessment, the risk is stressor-linked, where the stressor is the release of cholecalciferol into the environment. The following risk hypotheses are presumed in this assessment.

The labeled use of cholecalciferol within the action area may:

- directly affect the SMHM by causing mortality or by adversely affecting growth or fecundity;
- indirectly affect the SMHM by reducing or changing the terrestrial habitat in their current range (via reduction in availability of small burrowing mammal nests used by the SMHM as nest sites).

2.9.2. Diagram

The conceptual model is a graphic representation of the structure of the risk assessment. It specifies cholecalciferol release mechanisms, biological receptor types, and effects endpoints of potential concern. The conceptual model for the possible effects of cholecalciferol on the SMHM is shown in **Figure 2-3**. Typically a separate diagram is created for terrestrial and aquatic exposure and effects. However, for this assessment, only a single diagram of terrestrial exposure and effects is depicted because use of cholecalciferol bait is not expected to result in any significant exposure or effects to the assessed species through aquatic pathways. Although

the conceptual models for direct/indirect effects are shown on the same diagrams, the potential for direct/indirect effects are evaluated separately in this assessment. Exposure routes shown in dashed lines are not quantitatively considered because the contribution of those potential exposure routes to potential risks to the SMHM is expected to be negligible.

As shown in the diagram, exposure through direct consumption of intact bait (*i.e.*, primary exposure) is considered to be the main route of exposure to the SMHM. Therefore, the quantitative risk assessment focuses on this route of exposure. Indirect effects to the SMHM mediated through plants and terrestrial invertebrates are possible but were assumed to have negligible contributions to overall risk to the SMHM (See **Section 2.8.1**). These presumed negligible exposure routes and indirect effects include:

- Consumption of terrestrial invertebrates which consume intact bait;
- Consumption of terrestrial invertebrates which ingest soil contaminated by dislodgement of cholecalciferol from the intact bait;
- Consumption of plants which have taken up cholecalciferol from residues dislodged from the bait into soil;
- Indirect food chain effects resulting from cholecalciferol reducing the abundance of plants and terrestrial invertebrates.

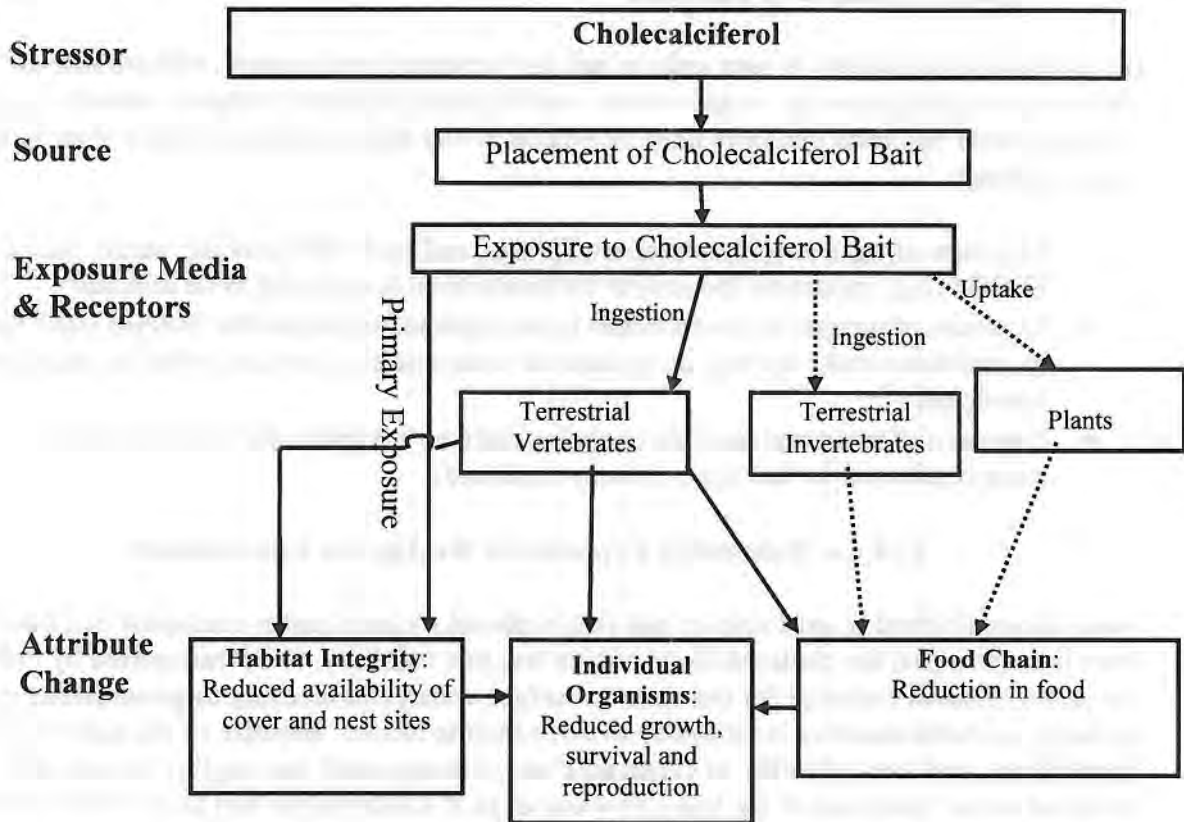


Figure 2-3. Conceptual Model Depicting Stressors, Exposure Pathways, and Potential Effects to Terrestrial Organisms from the Use of Cholecalciferol (Dotted lines indicate exposure pathways that have a low likelihood of contributing to ecological risk)

2.10. Analysis Plan

In order to address the risk hypothesis, the potential for direct and indirect effects to the SMHM is estimated based on a taxon-level approach. In the following sections, the use, environmental fate, and ecological effects of cholecalciferol are characterized and integrated to assess the risks. This is accomplished using a risk quotient (RQ; the ratio of estimated exposure concentration to the effects concentration) approach. Although ecological risk is often defined as the likelihood and magnitude of adverse ecological effects, the risk quotient-based approach does not provide a quantitative estimate of likelihood and/or magnitude of an adverse effect. However, as outlined in the Overview Document (U.S. EPA, 2004a), the likelihood of effects to individual organisms from particular uses of cholecalciferol is estimated using the probit dose-response slope and either the level of concern (discussed below) or actual calculated risk quotient value.

Descriptions of routine procedures for evaluating risk to the San Francisco Bay Species are provided in **Attachment I**.

2.10.1. Measures of Exposure

Given that cholecalciferol is used only in bait for vertebrate pest control, outdoor uses of cholecalciferol are limited to in and around buildings and in alleys, transport vehicles, and cholecalciferol bait used outdoors must be placed in bait stations and not farther than 50 feet from buildings:

- Exposure of aquatic plants, terrestrial plants, and birds that provide rearing sites to the SMHM (*e.g.*, passerine species) to cholecalciferol is expected to be minimal;
- Exposure of terrestrial invertebrates is not expected to impact the SMHM since terrestrial invertebrates make up only an occasional component of the diet, which is mainly plant-based; and
- Exposure of terrestrial animals to cholecalciferol is expected to occur via direct consumption of the bait (*i.e.*, primary exposure).

2.10.1.a. Estimating Exposure in the Aquatic Environment

Since cholecalciferol is used only in bait that is placed by hand and is contained in a bait station, there is no potential for cholecalciferol, which has low volatility, to be transported by drift. The use poses minimal potential for transport to surface water, and leaching to groundwater is unlikely, as cholecalciferol is estimated to be immobile in soil. Because of the high binding, lipophilicity, and low solubility of cholecalciferol, it is expected that negligible amounts of the chemical would leach out of the bait into water even if it were to get wet (*e.g.* if rainwater would leak into a bait station). The bait is designed to be weather-resistant. Thus, aquatic exposure is not a concern.

The only aquatic taxon relevant to this assessment is aquatic plants for indirect effects to the SMHM. Concentrations of cholecalciferol in saltwater marshes are also expected to be negligible and not impact aquatic vegetation. Therefore, models that estimate concentrations of cholecalciferol in surface water or calculate spray drift deposition of cholecalciferol on aquatic habitats were not needed for this assessment. In addition, no surface water monitoring data were available for cholecalciferol, as it is not a monitored analyte.

2.10.1.b. Estimating Exposure in the Terrestrial Environment

The SMHM is likely to consume cholecalciferol bait if encountered. Therefore, the terrestrial exposure for this species was based on dietary exposure to the bait itself. The concentration of cholecalciferol in the diet of this species was assumed to be equal to the maximum concentration of active ingredient in bait products registered for rodent control uses. Indirect risk to the SMHM was also addressed by assessing risk to other small mammals that may consume the bait.

The Agency typically uses T-REX to calculate estimated environmental concentrations (EECs) for dietary exposure of terrestrial wildlife to pesticides. However, this model only calculates EECs (and risk quotients based on the EECs) for natural wildlife food items such as plants, seeds, and insects that are exposed from foliar application of pesticides. These models are not appropriate for calculating EECs for animals that directly consume bait products (*i.e.*, primary

exposure). These models also calculate risk quotients (RQs) for application of granular pesticides and seed treatment uses but cannot be used to calculate RQs for bait products. Therefore, terrestrial animal exposure to cholecalciferol was calculated without the use of T-REX.

For animals that directly consume cholecalciferol bait, (i.e., primary exposure), the assessment was based on the maximum concentration of cholecalciferol in bait products used for rodent control. The maximum concentration is 0.075% (750 ppm). For dose-based risk assessments, the cholecalciferol concentrations in bait had to first be converted to a daily ingestion rate. This was done using the allometric equations of Nagy (1987) as provided in U.S. EPA's *Wildlife Exposure Factor Handbook* (U.S. EPA, 1993). Ingested doses of cholecalciferol (mg ai/kg-bw) were calculated for mammals of various assumed body weights (see **Table 3-1**). While dietary risk was not calculated (due to a lack of a dietary toxicity study), the amount of bait that an animal would have to consume to reach the LD₅₀ dose was compared to the daily food intake.

2.10.2. Measures of Effect

Data identified in **Section 2.8** were used as measures of effect for direct and indirect effects. Data were obtained from registrant submitted studies or from literature studies identified by ECOTOX. More information on the ECOTOXicology (ECOTOX) database and how toxicological data are used in assessments is available in **Attachment I**.

2.10.3. Integration of Exposure and Effects

Risk characterization is the integration of exposure and ecological effects characterization to determine the potential ecological risk from agricultural and non-agricultural uses of cholecalciferol, and the likelihood of direct and indirect effects to the assessed species in aquatic and terrestrial habitats. The exposure and toxicity effects data are integrated in order to evaluate the risks of adverse ecological effects on non-target species. The risk quotient (RQ) method is used to compare exposure and measured toxicity values. EECs are divided by acute and chronic toxicity values. The resulting RQs are then compared to the Agency's levels of concern (LOCs) (USEPA, 2004a) (see **Appendix A**). More information on standard assessment procedures is available in **Attachment I**.

2.10.4. Data Gaps

The environmental fate and ecological effects data requirements for cholecalciferol have changed since the issuance of the first risk assessment (U.S. EPA, 1999). The data requirements are now consistent with the 40 CFR Part 158 guideline requirements for terrestrial, aquatic, and outdoor residential use patterns (Federal Register: October 26, 2007 (Volume 72, Number 207)).

Data from the following guideline studies are considered to have low potential to add value to the ecological risk assessment because exposure of the associated taxa to cholecalciferol is expected to be insignificant (Series 850 Ecological Effects Test Guidelines) or the environmental fate of cholecalciferol is limited by placement of bait in bait stations for outdoor uses (Series 835 Fate, Transport and Transformation Test Guidelines):

- Avian Acute Oral Toxicity (850.2100).
- Avian Reproduction (850.2300).
- Algal Toxicity, Tier I (850.5400)
- Aquatic Plant Toxicity Test using *Lemna* spp., Tier I (850.4400)
- Seedling Emergence, Tier I (850.4100)
- Vegetative Vigor, Tier I (850.4150)
- Honey Bee Acute Contact Toxicity (850.3020)
- Freshwater Invertebrate Acute Toxicity (850.1010)
- Freshwater Fish Acute Toxicity, warm water species (850.1075)
- Freshwater Invertebrates Life Cycle (850.1300)
- Early Life Stage Toxicity of Freshwater fish (850.1400)
- Estuarine/Marine Acute Toxicity (850.1025, 850.1035, 850.1045, 850.1055, 850.1075)
- Adsorption/Desorption and Leaching (835.1230)
- Hydrolysis (835.2120)
- Photolysis in Water (835.2240)
- Photolysis in Soil (835.2410)
- Aerobic Soil Metabolism (835.4100)
- Anaerobic Soil Metabolism (835.4200)
- Aerobic Aquatic Metabolism (835.4300)
- Anaerobic Aquatic Metabolism (835.4400)
- Terrestrial Field Dissipation (835.6100)
- Bioconcentration in Fish (850.1730)

Although not an ecological effects data requirement under CFR40 Part 158, a chronic rodent study (e.g., 870.4100) was not available to assess chronic risk to mammals.

3. Exposure Assessment

Cholecalciferol is formulated as pellets and blocks. Baits are placed by hand; they may not be broadcasted. Since there is no potential for spray drift and/or runoff, these routes of exposure were not considered in this assessment.

3.1. Label Application Rates and Intervals

Labels of cholecalciferol products do not limit the amount of product or active ingredient that may be applied per unit area, the number of applications that can be made per unit time, or the minimal time interval between applications. However, labels state that cholecalciferol bait must be applied within 50 feet of buildings and that, for outdoor uses, bait must be placed in bait stations. Labels generally state the number of bait stations, bait blocks, or bait packages that may be placed in one location as well as the linear interval between placements. The linear interval is 15 to 30 feet for rats and 8 to 12 feet for mice. The concentration of cholecalciferol in bait is 0.075% (750 mg/kg bait) for all products. The amount of active ingredient per placement or the amount of active ingredient per linear foot can be calculated for cholecalciferol products. The maximum amount of active ingredient per placement for any product is 170 mg for rats and

21.3 mg for mice. The maximum amount of active ingredient per linear foot is 11.4 mg/ft for controlling rats and 2.7 mg/ft for controlling mice. Use information for applications considered in this assessment is summarized in **Table 2-4**.

3.2. Aquatic Exposure Assessment

3.2.1. Modeling Approach

Aquatic exposure from use of cholecalciferol was assumed to be negligible (see **Section 2.10.1.a**). Therefore, aquatic exposures were not assessed.

3.2.2. Existing Monitoring Data

No monitoring data in surface water, groundwater, and/or air were found from the USGS National Water-Quality Assessment Program (NAWQA) program (<http://water.usgs.gov/nawqa>), the California Department of Pesticide Regulation (CDPR) (<http://www.cdpr.ca.gov/docs/emon/surfwttr/surfcont.htm>), or from the USEPA STORET program. Water monitoring programs such as these generally monitor for agricultural pesticides and typically do not include analysis for vertebrate control agents such as cholecalciferol. Additionally, cholecalciferol is also used as a medication, so any detections of it in the environment could not be solely attributed to its use as a rodenticide.

3.3. Terrestrial Animal Exposure Assessment

For this assessment, exposure to terrestrial animals was assessed for a single pathway, animals that directly consume bait (*i.e.*, primary exposure). Primary exposure was evaluated using two methodologies, when possible:

- a dose-based approach that is dependent on body weight and food consumption rates resulting in an estimate of cholecalciferol intake as mg a.i./kg-bw/day, where kg-bw is the kilograms of the consuming individual; and
- a dietary approach using the amount of cholecalciferol bait needed to be consumed to reach the LD₅₀ dose which can then be compared to the daily food intake.

Both approaches and the expected exposure levels are detailed below.

3.3.1. Primary Exposure of Terrestrial Wildlife

Primary exposure was evaluated for assessing direct risk to the SMHM and other mammals that may indirectly affect the SMHM. An assessment for primary exposure of the birds that may indirectly affect the SMHM was not conducted because all outdoor uses of cholecalciferol require that bait be placed in bait stations. The use of bait stations should prevent access to bait by non-ground nesting birds that could indirectly support the SMHM by providing habitat. Thus exposure to birds is not a concern.

Primary exposure through cholecalciferol bait consumption was calculated using two methodologies. For the first method, cholecalciferol exposure was calculated as mg a.i./kg-bw/day, where kg-bw is the kilograms of the consuming individual for three standard weight classes of mammals and for a typical weight of the SMHM. Exposure (food dry weight consumption) estimates were derived using allometric equations from USEPA's *Wildlife Exposure Factor Handbook* (1993). The allometric equation for rodents was used as this would best approximate those individuals with a high potential for consuming grain and thus give the most conservative exposure estimates. Formulas for calculation of intake estimates are provided in **Table 3-1**, and cholecalciferol exposure estimates (on a dose basis) are provided in **Table 3-2**.

The EEC for direct effects to the SMHM was calculated based on an estimated average body weight of 10 g. EFED default weight classes for mammals (e.g., rodents) are usually small (15 g), medium (35 g), and large (1000 g). However, the large weight class for mammals (i.e., 1000 g) may exceed the size of a rodent capable of entering a bait station to consume bait as reported body weights of house mice, roof rats, and Norway rats, the three target rodent species for cholecalciferol bait, are 18-23 g (Whitaker, 1996), 142-283 g (ICWDM, online)⁸, and 195-485 g (Whitaker, 1996), respectively. Therefore, the upper-bound weight (i.e., 485 g) for the largest target rodent species (i.e., the Norway rat) was used as the large weight class for this analysis.

Acute and chronic RQs, presented in the Risk Estimation section, are generated by dividing these estimates of cholecalciferol exposure (mg a.i./kg-bw/day) for a given weight class by the most conservative toxicity endpoint for the SMHM adjusted for the default body weights.

Table 3-1. Formulas for Calculating Cholecalciferol Intake Based on Consumption of Bait

Rodent food intake (kg wt/day) $\text{Food Intake (kg wt/day)} = 0.621 * \text{Wt (kg)}^{0.564}$	
Cholecalciferol intake (mg a.i./kg-bw/day) $\text{Cholecalciferol Intake} = (\text{FI (kg wt/day)} * \text{C (mg a.i./kg-bait)}) / \text{Wt (kg)}$	
Where: Wt (kg) = weight (in kilograms) of the rodent consumer C (mg a.i./kg-bait) = concentration of cholecalciferol in bait	
FI = Food intake Rodent food intake equation is from the <i>Wildlife Exposure Factors Handbook</i> (U.S. EPA, 1993b)	

⁸ <http://icwdm.org/handbook/rodents/RoofRats.asp>

Table 3-2. Expected Cholecalciferol Intake for SMHM and Generic Rodents Weights Based on Primary Consumption of Bait

Species or Taxa	% a.i. in bait	Cholecalciferol Concentration in Bait (mg a.i./kg-bait)	Weight (g)	Food Intake (g/day)	Cholecalciferol Intake (mg a.i./kg-bw/day)*
SMHM	0.075	750	10	46	3469
Rodents			15	58	2907
	0.075		35	94	2009
			485	413	640

*See Table 3-1 for derivation

A second method for assessing primary exposure involves the concentration of cholecalciferol in the formulated bait itself. An acute dietary toxicity study (in which an LC₅₀ was calculated) was not available for use in this assessment. However, the amount of bait that a SMHM would have to consume to reach the LD₅₀ of 11.8 mg a.i./kg can be calculated. This value, in comparison to the daily food intake, allows one to view the proportionately small amount of bait a SMHM or non-target mammal could consume to reach a lethal dose.

3.3.2. Secondary Exposure of Terrestrial Wildlife

An assessment for secondary exposure of the SMHM was not conducted because the SMHM's diet consists primarily of plants, taxa for which uptake or ingestion of cholecalciferol by plants is considered unlikely.

3.3.3. Exposure of Terrestrial Invertebrates

As described in **Section 2.9**, indirect effects to the SMHM mediated through exposure of terrestrial invertebrates is expected to be negligible. According to NatureServe, both the adults and young of this species are herbivorous and would eat very few if any terrestrial insects.⁹ It is possible that some terrestrial invertebrates could directly consume cholecalciferol bait and that the cholecalciferol exposure could cause some mortality of such invertebrates. However, given the outdoor use of cholecalciferol within 50 feet of buildings, any mortality of invertebrates would be localized. The impact to the invertebrate abundance throughout the range of the assessed species is expected to be negligible. Therefore, no exposure assessment was conducted for terrestrial invertebrates.

3.4. Terrestrial Plant Exposure Assessment

As described in **Section 2.9**, indirect effects to the SMHM mediated through exposure of terrestrial plants are expected to be negligible because the use pattern of cholecalciferol is unlikely to affect terrestrial plants. Treated bait is contained within bait stations. Therefore no terrestrial plant exposure assessment was conducted.

⁹ <http://www.natureserve.org/explorer/>

4. Effects Assessment

This assessment evaluates the potential for cholecalciferol to directly or indirectly affect the SMHM. Assessment endpoints for the effects determination for each assessed species include direct toxic effects on the survival, reproduction, and growth, as well as indirect effects, such as reduction of food sources.

As described in the Agency's Overview Document (USEPA, 2004a), the most sensitive endpoint for each taxon is used for risk estimation. For this assessment, evaluated taxa include the SMHM and other mammals which may provide nesting sites for the SMHM. Birds, terrestrial invertebrates, terrestrial and aquatic plants are not evaluated because exposure to cholecalciferol is precluded based on the use pattern. Acute (short-term) and chronic (long-term) toxicity information is characterized based on registrant-submitted studies and a comprehensive review of the open literature on cholecalciferol.

4.1. Ecotoxicity Study Data Sources

Toxicity endpoints are established based on data generated from guideline studies submitted by the registrant, and from open literature studies that meet the criteria for inclusion into the ECOTOX database maintained by EPA/Office of Research and Development (ORD) (USEPA, 2004a). Open literature studies presented in this assessment were obtained from citations in previous risk assessments as well as ECOTOX information obtained on 15 March 2011. In order to be included in the ECOTOX database, papers must meet the following minimum criteria:

- (1) the toxic effects are related to single chemical exposure;
- (2) the toxic effects are on an aquatic or terrestrial plant or animal species;
- (3) there is a biological effect on live, whole organisms;
- (4) a concurrent environmental chemical concentration/dose or application rate is reported; and
- (5) there is an explicit duration of exposure.

Open literature toxicity data on the acute oral or dietary effects of cholecalciferol to "target" rodent species (the house mouse, the Norway rat, and the roof rat), which include efficacy studies, were not considered in deriving the most sensitive endpoint for terrestrial mammals. In the case of rodenticides, adequate data on the toxicity to rats and mice are already provided by acute mammalian toxicity studies that the rodenticide registrants are required to submit for product registration. Therefore, toxicological data on target species of rats and mice identified during the ECOTOX open literature search that the Agency conducted are not included in the summary table provided in **Appendix E**. The registrant-submitted studies provided the most sensitive endpoints for cholecalciferol. Citations of open literature papers that provide toxicological data for target rodent species are listed in **Appendix D** with the code "TARGET" given after the citation. While toxicological findings were not included in the summary of acute and chronic toxicity endpoints in this document, some of these papers which were deemed useful and were obtained to provide supplemental information for characterizing the toxicity of

cholecalciferol, such as information on the sublethal effects and the mode of action of cholecalciferol.

Data that pass the ECOTOX screen are evaluated along with the registrant-submitted data, and may be incorporated qualitatively or quantitatively into this endangered species assessment. In general, effects data in the open literature that are more conservative than the registrant-submitted data are considered. The degree to which open literature data are quantitatively or qualitatively characterized for the effects determination is dependent on whether the information is relevant to the assessment endpoints (*i.e.*, survival, reproduction, and growth) identified in **Section 2.8**. For example, endpoints such as behavior modifications are likely to be qualitatively evaluated, because quantitative relationships between modifications and reduction in species survival, reproduction, and/or growth are not available. Although the effects determination relies on endpoints that are relevant to the assessment endpoints of survival, growth, or reproduction, it is important to note that the full suite of sublethal endpoints potentially available in the effects literature (regardless of their significance to the assessment endpoints) are considered, as they are relevant to the understanding of the area with potential effects, as defined for the action area.

Citations of all open literature not considered as part of this assessment because they were either rejected by the ECOTOX screen or accepted by ECOTOX but not used (*e.g.*, the endpoint is less sensitive) are included in **Appendix D**. **Appendix D** also includes a rationale for rejection of those studies that did not pass the ECOTOX screen and those that were not evaluated as part of this endangered species risk assessment. A detailed spreadsheet of the available ECOTOX open literature data, including the full suite of lethal and sublethal endpoints is presented in **Appendix E**.

In addition to registrant-submitted and open literature toxicity information, other sources of information, including use of the acute probit dose-response relationship (*i.e.*, slope) to establish the probability of an individual effect and reviews of ecological incident data, are considered to further refine the characterization of potential ecological effects associated with exposure to cholecalciferol. There are no incident data reported for cholecalciferol.

A detailed summary of all available ecological toxicity information for cholecalciferol technical grade and end use product formulations can be found **Appendix B**. No toxicity data are available for cholecalciferol's degradates.

4.2. Toxicity of Cholecalciferol to Terrestrial Organisms

Table 4-1 summarizes the most sensitive toxicity endpoints for primary cholecalciferol exposure, based on an evaluation of both registrant-submitted studies and the open literature. Additional information is provided in **Appendix B**.

Table 4-1. Terrestrial Toxicity Profile for Cholecalciferol

Taxa	Study Type	Species Tested	Toxicity Value Used in Risk Assessment	Citation MRID/ ECOTOX Reference No.	Classification and Comment
Mammals	Acute oral (24-hr feeding)	Wistar Rat	LD ₅₀ = 11.8 mg a.i./kg Slope= 4.5 (95% CI: 9.1-15 mg a.i./kg)	MRID 42725701	Acceptable. Test substance was formulated bait pellets.

N/A: not applicable; bw = body weight

Acute toxicity to terrestrial animals is categorized using the classification system shown in **Table 4-2** (U.S. EPA, 2004a). Toxicity categories for terrestrial plants have not been defined.

Table 4-2. Categories of Acute Toxicity for Avian and Mammalian Studies

Toxicity Category	Oral LD ₅₀	Dietary LC ₅₀
Very highly toxic	< 10 mg/kg	< 50 mg/kg-diet
Highly toxic	10 - 50 mg/kg	50 - 500 mg/kg-diet
Moderately toxic	51 - 500 mg/kg	501 - 1000 mg/kg-diet
Slightly toxic	501 - 2000 mg/kg	1001 - 5000 mg/kg-diet
Practically non-toxic	> 2000 mg/kg	> 5000 mg/kg-diet

4.2.1. Toxicity to Mammals

Few studies are available on the acute toxicity of cholecalciferol, but it is well established that a small amount can cause irreversible, severe acute toxicity after a single dose. A summary of acute mammalian data, including data published in the open literature, is provided below in **Sections 3.2.2.a** through **3.2.2.b**.

4.2.1.a. Primary Toxicity to Mammals: Acute Exposure (Mortality) Studies

Cholecalciferol is classified highly toxic to mammals on an acute oral exposure basis. Dogs are more sensitive than rodents. Mice are less susceptible than rats.¹⁰

The most sensitive acute toxicity study indicated that the LD₅₀ for rats is 11.8 mg a.i./kg bw. Five male and five female rats were dosed per level (7.99, 9.35, 11.8 or 24.9 mg a.i./kg bw). In the study, rats were fed formulated bait (containing 0.075% cholecalciferol). It is not clear whether the test substance fed to rats was similar to that of the registered products containing cholecalciferol. The test substance (bait form) was administered over 24 hours through feeding. Animals were monitored for 14 days following dose administration. Clinical observations

¹⁰ U.S. EPA, 1993a.

among treated animals included thinness, lethargy, rough coat and occasional nasal bleeding. This study was classified as acceptable (MRID 42725701).

In another acute toxicity study in rats, cholecalciferol resulted in an LD₅₀ of 42 mg a.i./kg bw. Sublethal effects were not reported. The dose of 168,000 IU/kg was translated into terms of mg/kg bw (1 mg of cholecalciferol is equivalent to 40,000 IU). The LD₅₀ value was determined to be 42 mg/kg-bw (95% CI: 33.25-53.00 mg a.i./kg bw; Accession No. 250304). This study was classified as acceptable.

A published acute toxicity study is available in the open literature using small wild rodent mammals (approximately the same size as the SMHM-10 g). In the study, published in the journal of *Crop Protection* (Moran, 1996) the social vole *Microtus tristrami* was found to have an LD₅₀ of 16.52 mg a.i./kg bw.

An acute dietary toxicity study with rats (in which an LC₅₀ was calculated) was not available for use in this assessment.

Overall, cholecalciferol is highly toxic to mammals on an acute basis and a very small oral dose can result in irreversible effects through mineralization of the vital organs within 5-7 days.¹¹

4.2.1.b. Primary Toxicity to Mammals: Chronic Exposure (Growth, Reproduction) Studies

Chronic toxicity data are not available for cholecalciferol. In the absence of these data, toxicity on a chronic basis is presumed based on the high acute toxicity of cholecalciferol.

4.3. Incident Database Review

A review of the Ecological Incident Information System (EIIS, version 2.1.1), which is maintained by the Agency's Office of Pesticide Programs (OPP), the Avian Monitoring Information System (AIMS), which is maintained by the American Bird Conservancy, and the Aggregate Summary Module (ASM) (v.1.0) of OPP's incident database, which is maintained by the Information Technology and Resource Management Division, for ecological incidents involving cholecalciferol was completed on 12 October 2011. There were no records of reported incidents for cholecalciferol. However, as mentioned above, the Agency reviewed reports of adverse effects in dogs following accidental ingestion (U.S. EPA, 1993a).

5. Risk Characterization

Risk characterization is the integration of the exposure and effects characterizations. Risk characterization is used to determine the potential for direct and/or indirect effects to the SMHM from the use of cholecalciferol in CA. The risk characterization provides an estimation (**Section 5.1**) and a description (**Section 5.2**) of the likelihood of adverse effects; articulates risk assessment assumptions, limitations, and uncertainties; and synthesizes an overall conclusion

¹¹ U.S. EPA, 1993a.

regarding the likelihood of adverse effects to the assessed species or their designated critical habitat (*i.e.*, “no effect,” “likely to adversely affect,” or “may affect, but not likely to adversely affect”). In the risk estimation section, risk quotients are calculated using standard EFED procedures and models. In the risk description section, additional analyses may be conducted to help characterize the potential for risk.

5.1. Risk Estimation

Risk is estimated by calculating the ratio of exposure to toxicity. This ratio is the risk quotient (RQ) which is then compared to pre-established acute and chronic levels of concern (LOCs) for each category evaluated (**Appendix A**). For acute exposures to birds (surrogates for reptiles and terrestrial-phase amphibians) and mammals, the Endangered Species LOC is 0.1. The LOC for chronic exposures to animals is 1.0.

Acute risks to terrestrial mammals are estimated based on primary exposures resulting from application of cholecalciferol (**Section 3.3**) and the appropriate toxicity endpoints from **Table 4-1**.

5.1.1. Exposures in the Aquatic Habitat

The only aquatic taxon relevant to this assessment is aquatic plants for indirect effects to the SMHM, and no aquatic plant toxicity data were available. Given that cholecalciferol is used in very small quantities in baits that are only available within bait stations, the probability that it will come into contact with water is minimal. Therefore, no significant aquatic exposure is expected; no aquatic exposure assessment was performed; and indirect effects to the SMHM from exposure of aquatic plants to cholecalciferol are not expected to occur.

5.1.2. Exposures in the Terrestrial Habitat: Birds

Potential direct effects to birds were not evaluated because all outdoor uses for cholecalciferol require that bait be placed within bait stations which are expected to preclude exposure of birds that are likely to provide rearing sites for the SMHM.

5.1.3. Exposures in the Terrestrial Habitat: Mammals

Potential direct effects to the SMHM were evaluated by considering dose- and dietary-based exposures (**Sections 5.1.3.a**) through consumption of bait. Direct effects to mammals, particularly rodents, may result in indirect effects to the SMHM because the SMHM may nest in abandoned rodent burrows. Therefore, potential direct effects to mammals were evaluated by considering dose- and dietary-based primary exposure (**Sections 5.1.3.a** and **5.1.3.b**).

5.1.3.a. Mammals: Dose-based Acute Risks from Primary Exposure

For primary exposure, it was assumed that cholecalciferol bait is ingested by the SMHM and non-target rodents. Dose-based exposure estimates for the SMHM and other rodents were calculated as mg a.i./kg-bw/day (**Table 3-2**).

Acute toxicity of cholecalciferol to rodents was estimated using the LD₅₀ (measured as mg a.i./kg-bw) obtained from the 24-hr feeding study with rats (MRID 42725701). The LD₅₀ value was adjusted for the weight of the assessed rodent mammals (10, 15, 35, 435 g) according to the formula in **Table 5-1**.

Dose-based acute RQs for primary exposure of the SMHM and rodent mammals were calculated as the ratio of cholecalciferol intake (exposure) to adjusted LD₅₀ (toxicity) and are provided in **Table 5-2**; the Acute Endangered Species, Acute Restricted Use and Acute Risk LOCs were exceeded for primary exposure of the SMHM and all small rodent mammals.

Table 5-1. Formulas for Calculation of Weight-Adjusted Mammalian Cholecalciferol LD₅₀'s

$\frac{\text{Adjusted Mammalian LD}_{50}}{\text{Adj. LD}_{50} = \text{LD}_{50}}$	
<i>Where:</i> Adj. LD₅₀ = adjusted LD₅₀ (mg a.i./kg-bw) LD₅₀ = endpoint reported from mammal study (11.8 mg a.i./kg-bw) TW = body weight of tested animal (232 g rat, Wistar albino) AW = body weight of assessed animal (g)	
From: Wildlife Exposure Factors Handbook (U.S. EPA, 1993b)	

Table 5-2. Dose-based Acute RQs for Primary Exposure of the SMHM and Small (Rodent) Mammals

Species or Taxa	Cholecalciferol Concentration in Bait (mg a.i./kg-bait)	Weight (g)	Cholecalciferol Intake (mg a.i./kg-bw/day) ¹	Adjusted LD ₅₀ (mg a.i./kg-bw) ²	Dose-based Acute RQ ³
SMHM	750	10	3469	5.38	645
Rodent mammals	750	15	2907	5.95	489
		35	2009	7.35	273
		485	670	14.2	47

¹ See Table 3-1 for derivation.

² See Table 5-1 for derivation.

³ RQ=Cholecalciferol Intake/Adjusted LD₅₀. **Bolded RQs** exceed the Acute Endangered Species, Acute Restricted Use and Acute Risk LOCs.

5.1.3.b. Mammals: Dietary-based Acute Risks from Primary Exposure

An acute dietary toxicity study (in which an LC₅₀ was calculated) was not available for use in this assessment. However, the amount of bait that a SMHM would have to consume to reach the LD₅₀ of 11.8 mg a.i./kg can be calculated. This value, in comparison to the daily food intake, allows one to compare the small amount of bait (*e.g.*, 0.07 g) a non-target animal could consume to reach a lethal dose.

Table 5-3. Formula for Calculation of Amount of Bait Consumed to Reach LD₅₀ Dose

Amount of Bait to be Consumed to Reach LD₅₀ Dose (mg bait/animal) =Adj. LD₅₀ x AW / Concentration in Bait <i>Where:</i> Adj. LD₅₀ = adjusted LD₅₀ (mg a.i./kg-bw)¹ LD₅₀ = endpoint reported from mammal study (11.8 mg a.i./kg-bw) AW = body weight of assessed animal (kg) Concentration a.i. in bait (mg a.i./g bait)	
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1. See Table 5.2 for adjusted LD₅₀ values.

Table 5-4. Amount of Bait to be Consumed to Reach LD₅₀ Dose for SMHM and Small Mammals.

Species or Taxa	Cholecalciferol Concentration in Bait (mg a.i./g-bait)	Weight (kg)	Adjusted LD ₅₀ (mg a.i./kg-bw) ¹	Amount of Bait to be Consumed to Reach Adjusted LD ₅₀ (g bait) ²	Daily food Intake (g) ³
SMHM	0.750	0.01	5.38	0.072	46
Rodent mammals	0.750	0.015	5.95	0.12	58
		0.035	7.35	0.34	94
		0.485	14.2	9.18	413

¹ See Table 5.2 for adjusted LD₅₀ values.

² See Table 5-3 for derivation.

³ See Table 3-1 for derivation.

5.1.4. Exposures in the Terrestrial Habitat: Terrestrial Invertebrates

Exposure to terrestrial invertebrates can occur through ingestion and contact with bait. Exposed individuals could be adversely affected or be available for consumption by the SMHM as well as other animals. However, indirect effects to the SMHM mediated through exposure of terrestrial invertebrates are expected to be negligible given that invertebrates represent only an occasional food item among a mainly plant-based diet for the SMHM. Therefore, no terrestrial invertebrate exposure assessment was conducted. It should be noted that EFED does not currently have a methodology for estimation of terrestrial invertebrate exposure through contact with bait. In addition, EFED does not currently have any cholecalciferol data for estimation of invertebrate body burden.

5.1.4.a. Exposures in the Terrestrial Habitat: Terrestrial Plants

Since cholecalciferol is not applied directly onto plants, and because so little is expected to leach from the bait and be available for plant uptake, exposure is expected to be minimal. Therefore, the Agency presumes that direct risks to terrestrial plants are not expected. Further, indirect

effects to the SMHM from exposure of terrestrial plants to cholecalciferol are expected to be negligible.

5.2. Risk Description

The risk description synthesizes overall conclusions regarding the likelihood of adverse impacts leading to a preliminary effects determination (*i.e.*, “no effect,” “may affect, but not likely to adversely affect,” or “likely to adversely affect”) for the assessed species and the potential for modification of their designated critical habitat based on analysis of risk quotients and a comparison to the Level of Concern. The spatial extent of potential effects is discussed for each of the listed species including any potential overlap between areas where potential usage may result in LAA effects and areas where species are expected to occur (including any designated critical habitat). The final No Effect/May Affect determination is made after the spatial analysis is completed at the end of the risk description for each species. If there is no overlap of the species habitat and occurrence sections with the Potential Area of LAA Effects a No Effect determination is made.

If the RQs presented in the Risk Estimation (**Section 5.1**) show no direct or indirect effects for the assessed species and no modification to PCEs of the designated critical habitat, a preliminary “no effect” determination is made, based on cholecalciferol’s use within the action area. However, if LOCs for direct or indirect effect are exceeded or effects may modify the PCEs of the critical habitat, the Agency concludes a preliminary “may affect” determination for the FIFRA regulatory action regarding cholecalciferol. A preliminary effects determination of “may effect” was made for the assessed species (SMHM). A summary of the risk estimation results are provided in **Table 5-5** for the assessed taxa that may directly or indirectly affect the listed species.

Table 5-5. Risk Estimation Summary for Cholecalciferol – Direct and Indirect Effects

Taxa	LOC Exceedances (Yes/No)	Description of Results of Risk Estimation	Assessed Species Potentially Affected
Mammals	Non-listed Species (Yes)	Risks of acute and chronic (presumed) effects via consumption of bait (<i>i.e.</i> , primary exposure) and consumption of prey that ingested bait (<i>i.e.</i> , secondary exposure).	<u>Indirect Effects</u> : SMHM
	Listed Species (Yes)	Risks of acute and chronic (presumed) effects via consumption of bait (<i>i.e.</i> , primary exposure) or consumption of prey that ingested bait (<i>i.e.</i> , secondary exposure).	<u>Direct Effects</u> : SMHM

Following a preliminary “may affect” determination, additional information is considered to refine the potential for exposure at the predicted levels based on the life history characteristics

(*i.e.*, habitat range, feeding preferences, *etc.*) of the assessed species. Based on the best available information, the Agency uses the refined evaluation to distinguish those actions that “may affect, but are not likely to adversely affect” from those actions that are “likely to adversely affect” the assessed species and its designated critical habitat.

The criteria used to make determinations that the effects of an action are “not likely to adversely affect” the assessed species or modify its designated critical habitat include the following:

- Significance of Effect: Insignificant effects are those that cannot be meaningfully measured, detected, or evaluated in the context of a level of effect where “take” occurs for even a single individual. “Take” in this context means to harass or harm, defined as the following:
 - Harm includes significant habitat modification or degradation that results in death or injury to listed species by significantly impairing behavioral patterns such as breeding, feeding, or sheltering.
 - Harass is defined as actions that create the likelihood of injury to listed species to such an extent as to significantly disrupt normal behavior patterns which include, but are not limited to, breeding, feeding, or sheltering.
- Likelihood of the Effect Occurring: Discountable effects are those that are extremely unlikely to occur.
- Adverse Nature of Effect: Effects that are wholly beneficial without any adverse effects are not considered adverse.

A description of the risk and effects determination for each of the established assessment endpoints for the assessed species and their designated critical habitat is provided in **Section 5.2.1**. The effects determination section for the SMHM will start with a discussion of the potential for direct effects, followed by a discussion of the potential for indirect effects. These discussions do not consider the spatial analysis. Finally, a discussion of any potential overlap between areas of concern and the species is presented. If there is no overlap of the species habitat and occurrence sections with the Potential Area of LAA Effects a No Effect determination is made.

5.2.1. Salt Marsh Harvest Mouse

5.2.1.a. Direct Effects

The SMHM is at risk from the registered use of cholecalciferol. The SMHM may directly consume cholecalciferol bait as the bait is formulated specifically as grain for attracting rodents, and SMHM’s diet has a grain-based component (*e.g.*, seeds). Dose-based acute RQs for primary exposure of the SMHM exceeded the Acute Endangered Species, Acute Restricted Use, and Acute Risk LOCs (**Tables 5-2 and 5-3**). The dietary analysis indicates that the SMHM need only consume a tiny amount of bait (0.07 g) to reach a lethal dose. Therefore, there is potential for mortality to the SMHM through consumption of bait for a single day. Also, while chronic toxicity data are not available, direct chronic risk to the SMHM is presumed based on the high acute risk of cholecalciferol.

For individual chance of effect calculations, dose-based acute RQs for primary exposure of the SMHM were used. The probability of an individual effect to the SMHM using the dose-based RQ was calculated using a default slope estimate of 4.5 because a probit slope for the dose-response could not be calculated for the associated acute oral study (**Table 4-1**; MRID 42725701). The estimated chance of an individual acute mortality of the SMHM at a dose-based acute RQ of 645 is 1 in 1 (the probability at the both the 95% upper and lower confidence intervals is also 1 in 1). These results indicate that the probability of an individual mortality occurrence is high and that cholecalciferol has the potential to directly affect the SMHM via primary exposure.

5.2.1.b. Indirect Effects

Direct effects of cholecalciferol use to mammals may result in indirect effects to the SMHM due to a reduction in rearing/nesting sites. However, as stated in Section 1.3.1, indirect risk to the SMHM mediated through exposure to birds, plants and invertebrates was not assessed. Birds were not evaluated because all outdoor uses for cholecalciferol require that bait be placed in bait stations which are expected to preclude exposure to those birds that may build nests in plants (that could be used by the SMHM for nesting sites). Since cholecalciferol is not applied directly onto plants, and because so little is expected to leach from the bait and be available for plant uptake, exposure to plants is expected to be minimal. Effects to the SMHM mediated through exposure of terrestrial invertebrates are expected to be negligible given that the SMHM is primarily an herbivore and that invertebrates would represent only one type of food item among many for the SMHM.

Potential direct effects of cholecalciferol to small mammals that provide rearing sites for the SMHM were evaluated. For small mammals that consume bait directly, dose-based acute RQs exceeded Acute Endangered Species, Acute Restricted Use, Acute, and Chronic Risk LOCs (**Tables 5-2 and 5-3**). The dietary analysis indicates that the SMHM need only consume a tiny amount of bait (0.07 g) to reach a lethal dose. In addition, the probability of an individual mortality occurrence is very high for small mammals ingesting cholecalciferol bait directly. Overall, there is a high likelihood that the availability of rearing sites for SMHM use may decrease due to reductions in populations of small mammals. Also, while chronic toxicity data are not available, direct chronic risk to the SMHM is presumed based on the high acute risk of cholecalciferol.

5.2.1.c. Spatial Extent of Potential Risks

Generally, the Agency conducts analysis of the spatial extent of potential LAA effects whenever LOCs are exceeded. This analysis typically is needed to determine where adverse effects may occur in relation to the treated site. This spatial analysis typically determines if the potential area of usage, and the subsequent Potential Area of LAA Effects, overlaps with areas of occurrence and/or critical habitat of the species. However, because cholecalciferol is a vertebrate pest control agent that may be used in a wide variety of urban and non-urban areas, the spatial extent of cholecalciferol cannot be limited to defined areas. The Agency assumes that cholecalciferol may be potentially used in any area of the state of California and that use may occur in any of the land use categories that are identified in the NLCD. Therefore, a spatial analysis was not

conducted to identify this overlap. All areas where the SMHM occurs are assumed to lie within the potential use area of cholecalciferol.

An alternative type of spatial analysis was conducted to characterize the potential use of cholecalciferol bait products within the region where the SMHM may occur. Since outdoor use of cholecalciferol bait is restricted to within 50 feet of buildings, the extent of cholecalciferol use is expected to be highly correlated with human development. Therefore, a spatial analysis was conducted in which the occurrence locations of the SMHM were overlaid with a representation of human development. The “developed” land cover classes of the NLCD were used to represent the intensity of human development. These land cover classes were displayed with gray shading, with darker grays representing areas of more intense development. This layer was overlaid on segments and points that represent the location of the SMHM. The results of this spatial analysis are shown in **Figure 5-1** for the SMHM.

Areas with higher human development are expected to represent areas where cholecalciferol bait would be more intensively used and where the SMHM would be most vulnerable to exposure to cholecalciferol. On the scale displayed, the map has limited usefulness for identifying specific areas of vulnerability. However, the map does show that the SMHM occurs in a region of California where development is widespread, and a significant portion of the range of the species occurs in areas with moderate to high development. Since the SMHM occurs in areas where cholecalciferol bait may be intensively used, the SMHM would be susceptible to exposure to cholecalciferol.

5.2.1.a. Effects Determination

The results of this risk assessment indicate that the registered uses of cholecalciferol pose direct acute and presumed chronic risks to the SMHM based on primary exposure. This species has the potential to come into contact with cholecalciferol bait placed for rodent control. Furthermore, indirect effects to the SMHM, in the form of a reduction in rearing sites, may occur from effects of cholecalciferol use to small mammals. Finally, the SMHM occurs in areas where cholecalciferol bait may be intensively used. Therefore, the Agency makes a “**May Affect**” and “**Likely to Adversely Affect**” determination for the SMHM based on direct and indirect effects to the SMHM.

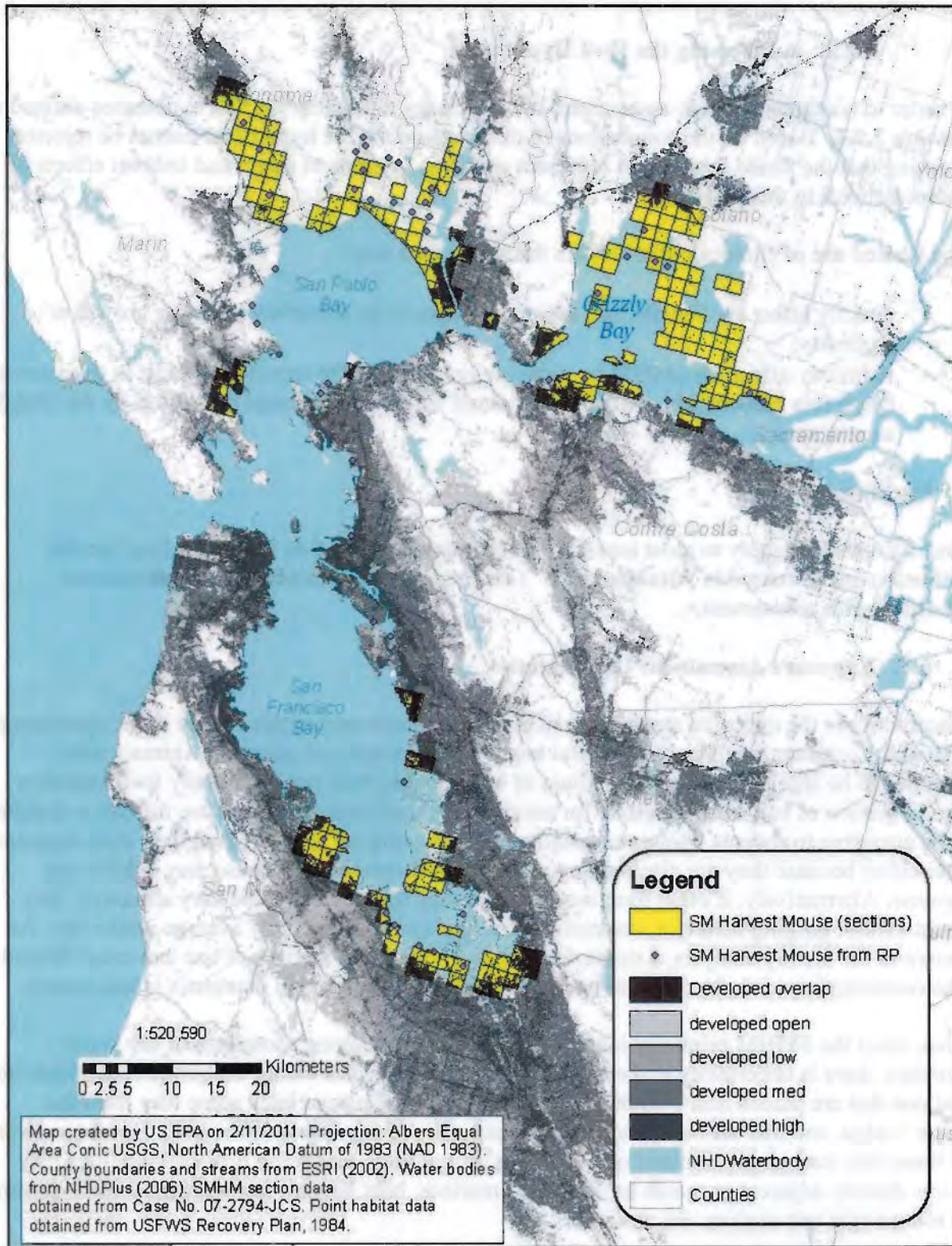


Figure 5-1. Map showing occurrences of the Salt Marsh Harvest Mouse in relation to the intensity of human development

5.2.2. Addressing the Risk Hypotheses

In order to conclude this risk assessment, it is necessary to address the risk hypotheses defined in **Section 2.9.1**. Based on the conclusions of this assessment, the hypotheses cannot be rejected, meaning that the stated hypotheses represent concerns in terms of direct and indirect effects of cholecalciferol to the SMHM.

The labeled use of cholecalciferol within the action area may:

- directly affect the SMHM by causing mortality or by adversely affecting growth or fecundity;
- indirectly affect the SMHM by reducing or changing the terrestrial habitat in their current range (via reduction in availability of small burrowing mammal nests used by the SMHM as nest sites).

6. Uncertainties

Uncertainties that apply to most assessments completed for the San Francisco Bay Species Litigation are discussed in **Attachment I**. This section describes additional uncertainties specific to this assessment.

6.1. Exposure Assessment Uncertainties

Uncertainty in the exposure assessment stems mainly from assumptions made in the assessment related to consumption of cholecalciferol bait by various types of animals. Animals were assumed to be able to consume an amount of bait equal to their predicted daily food ingestion rate. Ingestion of bait is most certain for omnivorous small mammals because the bait is designed to be attractive to rodents. However, small mammals could eat less bait than their daily ingestion rate, either because they are also feeding on other food sources or because they exhibit bait shyness. Alternatively, if other food is scarce and they find the bait to be very attractive, they could exhibit gorging behavior, consuming bait in excess of their daily average intake rate. As shown in the dietary analysis, a single feeding on a very small amount of bait can cause lethality. The consumption of cholecalciferol bait by animals other than small mammals is less certain.

Also, since the SMHM primarily inhabits vegetated habitat along shorelines of salt water marshes, there is uncertainty in the assumption that this species would encounter rodenticide bait stations that are placed near buildings. Most buildings are placed back some way from the water's edge, and this set-back may limit the exposure of the mouse to the bait. However, as use of these bait stations are allowed near all types of buildings, and some types of buildings may occur directly adjacent to marsh habitats (e.g. marinas, boat houses, restaurants), some exposure to rodenticide bait stations are possible.

6.2. Use of Surrogate Species Effects Data

Guideline toxicity tests and open literature data on cholecalciferol were not available for evaluating chronic risk to mammals. However, in the absence of chronic mammal data, risk was presumed due to the high toxicity from cholecalciferol on an acute basis.

6.3. Data Gaps and Uncertainties

The environmental fate and ecological effects data requirements for cholecalciferol have changed since the issuance of the first risk assessment (U.S. EPA, 1999). The data requirements are now consistent with the 40 CFR Part 158 guideline requirements for terrestrial, aquatic, and outdoor residential use patterns (Federal Register: October 26, 2007 (Volume 72, Number 207).

Data from the following guideline studies are considered to have low potential to add value to the ecological risk assessment because exposure of the associated taxa to cholecalciferol is expected to be insignificant (Series 850 Ecological Effects Test Guidelines) or the environmental fate of cholecalciferol is limited by placement of bait in bait stations for outdoor uses (Series 835 Fate, Transport and Transformation Test Guidelines):

- Avian Acute Oral Toxicity (850.2100).
- Avian Reproduction (850.2300).
- Algal Toxicity, Tier I (850.5400)
- Aquatic Plant Toxicity Test using *Lemna* spp., Tier I (850.4400)
- Seedling Emergence, Tier I (850.4100)
- Vegetative Vigor, Tier I (850.4150)
- Honey Bee Acute Contact Toxicity (850.3020)
- Freshwater Invertebrate Acute Toxicity (850.1010)
- Freshwater Fish Acute Toxicity, warm water species (850.1075)
- Freshwater Invertebrates Life Cycle (850.1300)
- Early Life Stage Toxicity of Freshwater fish (850.1400)
- Estuarine/Marine Acute Toxicity (850.1025, 850.1035, 850.1045, 850.1055, 850.1075)
- Adsorption/Desorption and Leaching (835.1230)
- Hydrolysis (835.2120)
- Photolysis in Water (835.2240)
- Photolysis in Soil (835.2410)
- Aerobic Soil Metabolism (835.4100)
- Anaerobic Soil Metabolism (835.4200)
- Aerobic Aquatic Metabolism (835.4300)
- Anaerobic Aquatic Metabolism (835.4400)
- Terrestrial Field Dissipation (835.6100)
- Bioconcentration in Fish (850.1730)

Although not an ecological effects data requirement under CFR40 Part 158, a chronic rodent study (e.g., 870.4100) was not available to assess chronic risk to mammals.

6.4. Sublethal Effects

When assessing acute risk, the screening risk assessment relies on the acute mortality endpoint as well as a suite of sublethal responses to the pesticide, as determined by the testing of species response to chronic exposure conditions and subsequent chronic risk assessment. Consideration of additional sublethal data in the effects determination is exercised on a case-by-case basis and only after careful consideration of the nature of the sublethal effect measured and the extent and quality of available data to support establishing a plausible relationship between the measure of effect (sublethal endpoint) and the assessment endpoints. However, the full suite of sublethal effects from valid open literature studies is considered for the characterization purposes.

7. Risk Conclusions

In fulfilling its obligations under Section 7(a)(2) of the Endangered Species Act, the information presented in this endangered species risk assessment represents the best data currently available to assess the potential risks of cholecalciferol to the SMHM.

Based on the best available information, the Agency makes a *Likely to Adversely Affect* determination for the SMHM. Given the LAA determination, a description of the baseline status and cumulative effects for this species is provided in **Attachment III**.

A summary of the risk conclusions and effects determinations for the SMHM, considering the uncertainties discussed in Section 6 and Attachment I, is presented in **Table 7-1**. Use specific effects determinations are provided in Table 7-2.

Table 7-1. Effects Determination Summary for Effects of Cholecalciferol on the SMHM.

Species	Effects Determination	Basis for Determination
Salt Marsh Harvest Mouse (SMHM) (<i>Reithrodontomys raviventris</i>)	<i>May Affect</i> , and <i>Likely to Adversely Affect</i> (LAA)	Potential for Direct Effects
		Risk assessment indicates that the use of cholecalciferol may result in direct effects to the SMHM from acute and chronic toxicity. Dose-based exposure estimates and data on acute toxicity to small mammals result in acute RQs that exceed the LOC for primary exposure. This species is predicted to be susceptible to primary exposure through direct contact with cholecalciferol bait products. This contact may result in ingestion of the bait which would likely result in acute and chronic toxic effects.
		Potential for Indirect Effects <i>Habitat modifications</i> Risk assessment indicates the use of cholecalciferol may adversely modify the habitat of this species by reducing the availability of nest sites. This conclusion is based on acute RQs for mammals that exceed the LOC. Adverse effects to mammals may result in a reduction of abandoned mammal nests, which are used as nest sites by the SMHM.

Table 7-2. Use Specific Summary of the Potential for Adverse Effects to the SMHM.

Uses	Potential for Effects to Identified Taxa:					
	SMHM and Small Mammals ¹		Birds	Invertebrates	Terrestrial Plants	Aquatic Plants
	Acute	Chronic ²				
Bait for rat and mouse control in and around buildings, in alleys and transport vehicles	Yes	Yes	No	No	No	No

¹ A yes in this column indicates a potential for direct effects to the SMHM and indirect effects to the SMHM.

² While chronic toxicity data are not available, chronic risk is assumed based on the high acute toxicity of cholecalciferol.

Based on the conclusions of this assessment, a formal consultation with the U. S. Fish and Wildlife Service under Section 7 of the Endangered Species Act should be initiated.

When evaluating the significance of this risk assessment's direct and indirect effects determinations, it is important to note that pesticide exposures and predicted risks to the listed species and its resources (*i.e.*, food and habitat) are not expected to be uniform across the action area. Exposure to cholecalciferol and associated risks to the species and its resources are expected to decrease rapidly with increasing distance away from the sites of bait placement. Evaluation of the implication of this non-uniform distribution of risk to the species would require information and assessment techniques that are not currently available. Examples of such information and methodology required for this type of analysis would include the following:

- Enhanced information on the density and distribution of SMHM life stages within the action area and/or applicable designated critical habitat. This information would allow for quantitative extrapolation of the present risk assessment's predictions of individual effects to the proportion of the population extant within geographical areas where those effects are predicted. Furthermore, such population information would allow for a more comprehensive evaluation of the significance of potential resource impairment to individuals of the assessed species.

8. References

A bibliography of ECOTOX references, identified by the letter E followed by a number, is located in **Appendix D**.

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Submitted Studies for Cholecalciferol

202901 Cholecalciferol Vitamin D3 Bibliography

71-2 Avian Dietary Toxicity

MRID		Citation Reference
120350	2072932	Fletcher, D. (1982) Report to Bell Laboratories, Inc.: 8-day Dietary LC50 Study with Cholecalciferol Oil Concentrate in Mallard Ducklings: BLAL No. 82 DC 22 . (Unpublished study received Dec 15, 1982 under 12455-60; prepared by Bio-Life Assoc., Ltd., submitted by Bell Laboratories, Madison, WI; CDL:249057-A)
120353 ACC 249059	DER not located	Fletcher, D. (1982) Report to Bell Laboratories, Inc.: 8-day Dietary LC50 Study with Cholecalciferol Oil Concentrate in Bobwhite Quail: BLAL No. 82 QC 22 . (Unpublished study received Dec 15, 1982 under 12455-60; prepared by Bio-Life Assoc., Ltd., submitted by Bell Laboratories, Madison, WI; CDL:249059-A)
120355 Acc 249063	Same as 120350?	Fletcher, D. (1982) Report to Bell Laboratories, Inc.: Acute Oral Toxicity Study with Cholecalciferol Oil Concentrate in Mallard Ducks: BLAL No. 82 DD 12 . (Unpublished study received Dec 15, 1982 under 12455-60; prepared by Bio-Life Assoc., Ltd., submitted by Bell Laboratories, Madison, WI; CDL:249063-A)

71-5 Simulated or Actual Field Testing

MRID		Citation Reference
42067003	See 2072934	Marsh, R. (1990) Potential Secondary Hazards of Cholecalciferol. Unpublished study prepared by Univ. of Cal., Davis; Dept. of Wildlife and Fisheries Biology. 22 p. Part 2 poisoning of a predacious snake
42067003	2072933	Marsh, R. (1991) Potential Secondary Hazards of Cholecalciferol. Unpublished study prepared by Univ. of Cal., Davis; Dept. of Wildlife and Fisheries Biology. Part 1 Poisoning of predacious birds and mammal

Mammalian Predator Toxicity

42774801	2072935	
No MRID	2072936	Letters regarding Toxicity from American Veterinary Medical Association
No MRID	2072937	Memo regarding Under-estimation of toxicity to dogs by the registrant and Published article on this topic

Non Guideline Selections (also many small rodent efficacy tests available)

40366001		Beard, M.; Maupin, G.; Barnes, A.; et al. (1986) Laboratory Trials of Cholecalciferol used as a Rodenticide against Rock Squirrels: Laboratory ID: Tests No. 1a, 2, 3, 4, 5. Unpublished study prepared by Center for Disease Control. 13 p.
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