Human Health and Ecological Risk Assessment for the Use of Wildlife Damage Management Methods by USDA-APHIS-Wildlife Services

Chapter XXVI

The Use of Chlorophacinone in Wildlife Damage Management

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EXECUTIVE SUMMARY

Chlorophacinone is a first-generation anticoagulant rodenticide used by APHIS Wildlife Services (WS) to control various rodents in terrestrial environments. Chlorophacinone is registered for use to control rodents at rangelands, forestry areas, agricultural sites, in and around animal burrows and buildings (agricultural, public, industrial, commercial, residences, and food processing facilities), transport vehicles such as ships, trains, and aircraft, and in non-crop areas such as fence lines, gullies, ditches, and railroad rights-of-way, lawns, turf, golf courses, airports, and ornamental flower and shrub gardens.

WS applied 4 chlorophacinone products in 6 states (Table 1) from FY11 to FY20 to control mountain beavers to protect standing and seedling trees, ground squirrels on airports that are preyed upon by predators to protect aircraft that become airstrike hazards, black-tailed prairie dogs to protect rangelands and non-crop areas adjacent to pastures, and on airports, and pocket gophers to protect turf, alfalfa, and rangeland.

WS evaluated chlorophacinone's human health and ecological risk under the proposed use patterns. The risk to the public is minimal due to the limited volume applied annually and WS adherence to label requirements. Dermal exposure to workers is a risk, but the proper use of label-mandated personal protective equipment, adherence to label instructions, and limitations on the amount of product a worker may apply in one day reduce the risk of injury.

The exposure risk to terrestrial plants and aquatic environments is negligible based on the use pattern. WS has a single record of nontarget species take through its use of chlorophacinone bait. However, WS recognizes it is not possible to detect all nontarget take because animals may die belowground, they can be difficult to find in certain habitats, or species are wide-ranging and dispersed outside of the treatment area. WS monitors treatment sites and avoids treating burrows where they detect nontarget species. Despite this monitoring, WS recognizes nontarget species will be exposed to chlorophacinone bait. WS expects most target animals baited belowground with chlorophacinone will die in their burrows, which reduces secondary exposure potential to nontarget species; however, some target animals will die aboveground. The Rozol Prairie Dog Bait label requires applicators to return to the site within 4 days after bait application and at 1- to 2-day intervals to collect and dispose of any bait or dead or dying prairie dogs and nontarget animals found aboveground. Despite these mitigations, poisoned animals that die aboveground between searches or are missed during searches remain available to scavengers. Birds are less sensitive to chlorophacinone than mammals, and the risk of mortality to predatory or scavenging birds consuming poisoned animals is low. However, birds may experience sublethal effects. WS finds its use of chlorophacinone will have the greatest risk to mammals that access treated burrows where they may ingest bait or poisoned animals. Mammalian predators and scavengers are potentially at risk from poisoned animals that die aboveground.

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1 INTRODUCTION

Several rodent species are controlled with the rodenticide chlorophacinone, including commensal Old-World rodents (black rats[1], brown rats, and house mice) and several burrowing rodents such as mountain beavers, prairie dogs, pocket gophers, and voles. These species commonly cause a variety of damage to property such as residences (commensal rodents), crops, trees, and shrubs and can cause severe damage in a short time. The United States Department of Agriculture's (USDA), Animal and Plant Health Inspection Service (APHIS), Wildlife Services (WS) may manage rodent populations and their damage per label instructions by placing chlorophacinone baits where these species feed, but in general, does not conduct commensal rodent control in urban areas.

Chlorophacinone was first registered as a vertebrate control agent in the United States in 1971 (USEPA 2015c). The registered uses of chlorophacinone include rodent control at agricultural sites (alfalfa, artichoke, barley, oats, pome, and stone fruit tree orchards, nurseries, and rangelands, Christmas tree, and other tree and forestry plantations), in and around animal burrows and buildings (agricultural, public, industrial/commercial, homes, and food processing facilities), transport vehicles (ships, trains, and aircraft), in non-crop areas (such as fence lines, gullies, ditches, and railroad rights-of-way), lawns, turf, golf courses, and ornamental flower and shrub gardens (USEPA 2015e). WS has used chlorophacinone products to reduce damage from prairie dogs, pocket gophers, ground squirrels, and mountain beavers in rangelands and adjacent non-crop areas, and forestry areas. WS has not used chlorophacinone products in and around buildings or at many other registered-use sites.

As a first-generation anticoagulant rodenticide, chlorophacinone usually requires multiple feedings by the target animal to deliver a lethal dose. Anticoagulants interfere with blood clotting and cause death due to internal bleeding generally within 5 to 7 days. Specifically, anticoagulants inhibit the vitamin K(1)-2,3 epoxide reductase (VKOR) enzyme and, therefore, the synthesis of vitamin K and clotting factors II (prothrombin), VII, IX, and X, critical components in blood clotting (USEPA 2020b).

Chlorophacinone baits are applied in aboveground bait stations or belowground in rodent burrows to ensure that people and pets cannot access the baits. A mechanical broadcast bait spreader and spot applications can be made for voles and spot applications for ground squirrels. It is also available as a tracking powder, which is placed in areas inside buildings or their periphery along rodent runways, especially in burrows, where children, pets, and nontarget wildlife do not have access. The tracking powder is picked up by rodents on their fur and ingested when grooming. WS does not use tracking powder formulations. For most WS applications, baits are placed by hand or through tubes from hoppers with a bait dispenser where a measured amount can be dropped directly into burrows. For pocket gophers, specifically, a probe is often used; applicators find burrow runways by pressing a probe into the ground about a foot from gopher mounds to find the main runway (the probe will easily drop when it hits a burrow). The probes are hollow tubes with a bait dispenser or side funnel that allows up to ½ cup of bait to be inserted into the burrow through the tube. Solid probes can be used, and the hole into the burrow from the probe is widened so up to ½ cup of bait can be deposited into the burrow system. The holes created by probes are then covered with debris and dirt while being careful not to cover the bait with dirt to discourage pocket gophers from plugging the hole themselves.

[1] Scientific names are given in *Chapter 1: Introduction to Risk Assessments for Methods Used in Wildlife Damage Management* and not in this document except for species not in that chapter.

This human health and ecological risk assessment provides an evaluation of potential risks and hazards to human health and the environment, including nontarget animals, as a result of exposure to chlorophacinone from the use of chlorophacinone products by WS. The methods used to assess potential human health effects follow standard regulatory guidance and methodologies (National Research Council 1983, USEPA 2016) and align with the procedures and methodologies of other Federal agencies, e.g., the U.S. Environmental Protection Agency (USEPA 2022). The methods used to assess potential ecological risk to nontarget species generally follow USEPA (2022) methodologies.

This risk assessment starts with problem formulation (identifying hazards) and then evaluates toxicity (dose-response assessment) and exposure (identifying potentially exposed populations and determining potential exposure pathways for these populations). Lastly, the integration of the toxicity and exposure assessments provides a characterization of risks (determining if adverse human health or ecological risks are present and their significance). A discussion of the uncertainties associated with the risk assessment and cumulative effects is also included in this risk assessment.

1.1 Use Pattern of Chlorophacinone

WS applicators primarily apply chlorophacinone baits using hand spot baiting directly into subterranean burrow systems of specific burrowing rodents (to control prairie dogs, pocket gophers, and mountain beavers) or scattered on the ground just outside burrows (to control ground squirrels). Application rates vary with the density of rodent populations and target species being controlled. Under the Rozol Vole Bait (EPA Reg. No. 7173-242) label, WS could potentially use mechanical broadcasters, hand spot baiting, or bait stations to apply the bait if they used this product to target voles in the future. However, WS has not used this product or mechanical broadcast application method to date.

Hand spot baiting involves placing the bait within an active burrow opening (not for ground squirrels) or scattering it on trails, runways, or bare ground adjacent to burrow entrances and covering each placement with grass or shingle to avoid exposing nontarget organisms. For open burrow systems, applicators may directly hand bait or use a tube or hose from a bait dispenser typically mounted on the rear of an all-terrain vehicle to insert bait into burrows. Applicators may also use a bait dispensing probe for pocket gopher burrows. Probes are hollow tubes or metal rods used to locate a burrow and release bait into the burrow. The number of applications per pocket gopher burrow system often depends on the number of burrow mounds because baits are placed a foot to a yard away from each mound in the main underground runways with a probe or into the main burrow after the plug at the base of a mound is removed, and bait is inserted into the main tunnel as far as possible; the burrow is re-covered with dirt but not enough to cover the bait.

Many burrowing rodents taken with chlorophacinone baits will die belowground (Lee and Hyngstrom 2007, Nolte and Wagner 2001, Ramey et al. 2007). Thus, it is not possible to count the exact number of burrowing rodents taken with treatments because WS does not dig up burrows to determine the actual take of target or nontarget species. In the Management Information System (MIS)[2], WS personnel generally record the number of acres or burrows

2 MIS - Computer-based Management Information System used for nationally tracking APHIS-WS WDM methods used and activities. Methods and activities are tracked such as chlorophacinone projects but take is not always estimated.

treated or estimate the number of target species taken with treatments. The quantity of bait applied is always recorded in the MIS.

If WS specialists estimated take in the MIS, that number was used when estimating average annual take numbers. If take was not estimated in the MIS, take numbers were estimated based on average occupancy of burrows by adults and young (number per burrow) or were estimated based on the expected number of target animals taken per pound of bait applied (number per lb.) or expected density (number per acre). In general, these methods likely overestimate actual take numbers because they assume 100% take of the target animals assumed to be present and exposed, which rarely occurs under actual field conditions. The following parameters and assumptions were used to estimate WS take with chlorophacinone baits for each target rodent species:

- **Mountain beavers:** Mountain beavers are territorial. Burrows are usually occupied by a single individual. Females breed once and average 3 young per year, which are weaned at 6 to 8 weeks of age. Young leave the burrow soon after being weaned. To estimate the number taken per burrow, it was assumed that 50% of burrows contained 4 mountain beavers (mother with 3 young) for 3 months, and there is 1 male in all of the other burrows (this assumes a 50:50 ratio of females to males). For the remaining 9 months of the year, 100% of burrows are occupied by just 1 mountain beaver. Therefore, this risk assessment estimated the average number of mountain beavers taken per burrow was approximately 1.5 per burrow treated for every single 12-oz packet of bait applied.

- **Black-tailed prairie dogs:** A typical prairie dog town contains groups of prairie dogs known as coteries. A typical coterie consists of one adult male, three or four adult females, and their young up to one year of age. The residents of each coterie protect their territory from intruders, including prairie dogs from other coteries within the town. Coteries typically use many burrows. Black-tailed prairie dog densities range from approximately 5 to 20 prairie dogs per acre, depending on the season. Prairie dog burrow density per acre ranges from approximately 10 to 50 burrows per acre in some locations. Therefore, this risk assessment estimated take as 1 black-tailed prairie dog per burrow treated or 12 prairie dogs per acre treated based on all their life history parameters.

- **Richardson's ground squirrels:** Take of Richardson's ground squirrel was mostly estimated by WS specialists in the MIS. When take was not estimated, this risk assessment estimated take as 10 Richardson's ground squirrels per acre treated.

- **Plains and Knox Jones' pocket gophers**: These pocket gopher species are very territorial and live solitary lives except for breeding and mothers with young. They generally have about 4 young per litter and 1 litter per year in the north and 2 or more per year in the south part of their range, where they do not hibernate in the winter. WS take occurred in northern Texas but in areas where it was possible that they could have 1 or 2 litters per year. Young are weaned in 3–4 weeks and quickly leave the burrow after that. Assuming they have young in the burrow for 1.5 months per litter, have 2 litters per year, and are otherwise solitary, this risk assessment estimated that on average 2 pocket gophers would be taken per burrow treated. Pocket gophers can occur at densities up to 8 per acre in high-density situations but this risk assessment estimated that 4 pocket gophers were taken per acre on average.

Overall, WS applied 4 chlorophacinone products in 6 states (Table 1) from FY11 to FY20 to control mountain beavers to protect standing and seedling trees, ground squirrels on airports that a preyed upon by predators to protect aircraft that become airstrike hazards, black-tailed prairie

dogs to protect rangelands and non-crop areas adjacent to pastures, and on airports, and pocket gophers to protect turf, alfalfa, and rangeland.

Table 1. Annual average target animal take and chlorophacinone products applied or sold from FY11 to FY15 and FY16 to FY20.

	FY11–FY15		FY16–FY20			
Products Applied						
Species	**Number taken [a]**	**Pounds Used**	**Number taken [a]**	**Pounds Used**	**EPA Reg. Number**	**States**
Mountain Beaver	7	3.6	91	45.3	WA-060019 [c]	WA
Black-tailed Prairie Dog	5,078	886.0	-	-	7173-286	CO KS NM
Richardson's Ground Squirrel [b]	329	66.4	-	-	MT-000007 [c]	MT
Plains Pocket Gopher	185	16.5	7	0.65	7173-184	TX
Knox Jones' Pocket Gopher	1	0.1	2	0.25	7173-184	TX
Average Annual Take (5 spp.)	**5,600**	**972.6**	**100**	**46.2**		
Products Sold						
Product Name	**Pounds Sold**		**Pounds Sold**		**EPA Reg. Number**	**States**
Rozol Prairie Dog Bait	568		1,270		7173-286	NM
Rozol Pocket Gopher Bait	141		136		7173-184	NM TX
Rozol Pocket Gopher Bait Burrow Builder Formula	6		-		7173-244	NM
Average Annual Pounds Sold	**715**		**1,406**			

[a] The number of target animals taken. If the WS applicator did not estimate take, the number of targets taken was estimated.
[b] An annual average of 1 nontarget meadow vole was taken.
[c] SLN = Special Local Need registration

Estimates of the annual average number of target rodents killed with chlorophacinone baits by WS in WDM activities and the annual average amounts of chlorophacinone baits used from FY11 to FY15 and from FY16 to FY20 throughout the United States are provided in Table 1. The only chlorophacinone product applied or sold by WS during FY11–FY20 was Rozol Prairie Dog Bait for black-tailed prairie dogs, Rozol Pocket Gopher Bait for four species of pocket gophers, Rozol Ground Squirrel Bait under a Special Local Need (SLN) label in Montana for Richardson's ground squirrels, and Rozol Pellets under an SLN label in Washington for mountain beavers (Table 1). Between FY11 and FY15, WS used an average of 972.6 pounds of chlorophacinone baits to take an annual average of 7 mountain beavers, 5,078 black-tailed prairie dogs, 329 Richardson's ground squirrels, 185 plains pocket gophers, and 1 Knox Jones' pocket gopher. Between FY16 and FY20, WS use decreased to an annual average of 46.2 pounds of chlorophacinone baits to take an annual average of 91 mountain beavers and 9 pocket gophers of two species (Table 1). All applications were belowground directly into the burrow except for the ground squirrels, which were aboveground adjacent to the burrow. These products were applied in 6 states, including Colorado, Kansas, Montana, New Mexico, Texas, and Washington (Table 1). The only known nontarget take was during FY11–FY15, when WS took an annual average of 1 nontarget meadow vole when controlling ground squirrels at airports (Table 1).

WS also sold Rozol Prairie Dog Bait and Rozol Pocket Gopher Bait Burrow Builder Formula to certified pesticide applicators, given that they are RUPs (87% of total lb. sold from FY11 to FY20), and sold Rozol Pocket Gopher Bait as a general use pesticide (13%) (Table 1). Most chlorophacinone products were sold in New Mexico, with some Rozol Pocket Gopher Bait sold in Texas. Other than the species above, the Rozol Pocket Gopher Bait was also sold for the control of Northern and Botta's pocket gophers.

2 PROBLEM FORMULATION

The following sections discuss the chemical description and product use, physical and chemical properties, environmental fate, and hazard identification for chlorophacinone.

2.1 Chemical Description

Chlorophacinone (2-[2-(4-chlorophenyl)-2-phenylacetyl]indan-1,3-dione; $C_{23}H_{15}ClO_3$; CAS # 3691-35-8) is a pesticide active ingredient and an organic compound with a molecular weight of 374.82 g/mol and molecular structure shown in Figure 1.

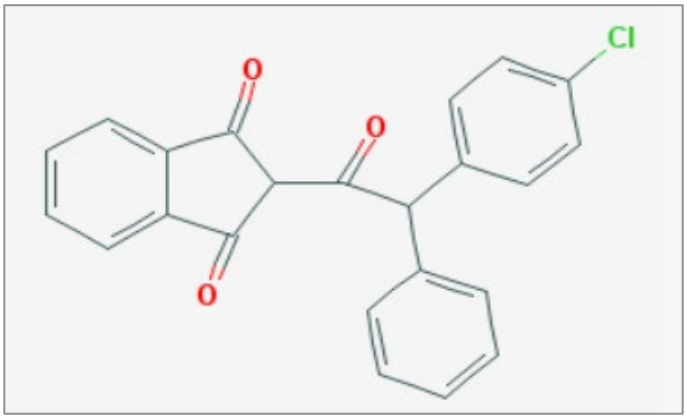

Figure 1. Chemical structure for chlorophacinone.

2.2 Physical and Chemical Properties

Chlorophacinone is a pale yellow microcrystalline powder (NIH 2021). It has a low vapor pressure of 3.58 x 10^{-6} torr and Henry's law constant of 5.12 x 10^{-7} atm-m^3/mol suggesting a low potential to volatilize from water or soil into the atmosphere (USEPA 2015e;2020a). Its water solubility is 3.43 milligrams (mg)/Liter (L) at 25°C (USEPA 2015e). Chlorophacinone has an octanol/water partition coefficient (K_{ow}) of 94.5 and a soil adsorption coefficient (K_{oc}) of 20,299 milliliters (ml)/gram (g) (USEPA 2015d).

2.3 Environmental Fate

Environmental fate describes the processes by which chlorophacinone moves and transforms in the environment. The environmental fate processes include 1) persistence and degradation in the environment, 2) mobility, and 3) migration potential to groundwater and surface water.

Chlorophacinone is slightly to moderately persistent in the environment (USEPA 2015e;2020a). Chlorophacinone has low vapor pressure with a low potential for dissipation through air volatilization (USEPA 1998b). Chlorophacinone degrades mainly through aerobic soil metabolism with half-lives of 17 days (sandy loam) and 47.2 days (sandy clay loam) (USEPA 2011). Degradation by photolysis for soil is not a significant source of degradation for belowground applications (SERA 2015). Chlorophacinone is hardly mobile (practically immobile) in soil (USEPA 2015e). It binds strongly to organic materials such as the formulated baits with little available for leaching to groundwater or runoff to surface water (USEPA 2015d).

In water, chlorophacinone is stable at pH 7 and 9 and degrades slowly at pH 5 with a half-life of 232 days (USEPA 2015e). Degradation in water is not expected to be a major route of degradation due to the negligible exposure to water resources per label restrictions (see Section 4, Exposure Assessment and Risk Characterization). Chlorophacinone does not bioconcentrate in aquatic organisms (USEPA 2020a).

2.4 Hazard Identification

Chlorophacinone is highly toxic to mammals via oral, inhalation, and dermal exposure routes (USEPA 2015b). The following section summarizes available acute and chronic toxicity data for mammals used to evaluate the hazards of chlorophacinone to human health and nontarget mammals.

2.4.1 Mechanism of Action and Metabolism

Chlorophacinone is a first-generation anticoagulant rodenticide (USEPA 2015b). Chlorophacinone is an indandione that disrupts the vitamin K cycle necessary for blood-clotting factors to function (USEPA 2015b). Animals exposed to chlorophacinone have increased blood coagulation times which can result in mortality (USEPA 2015b). Toxic symptoms include dyspnea (labored breathing), lethargy, hemorrhage from the nose, and urethral bleeding (NIH 2021). Death follows excessive external and internal bleeding (USEPA 2015b).

The single oral dose evaluation in rats found chlorophacinone absorption peaked between 4 and 6 hours with a half-life ($t_{½}$) of approximately 10 hours and distributed systemically; the highest concentrations are found within the liver and kidneys. The blood concentration of chlorophacinone in rats after repeated oral doses indicates bioaccumulation. Chlorophacinone excretion over 4 days was predominately through feces (94.7–108.6% administered dose) with a minor excretion (<1% administered dose) through urine and respiration. A biliary excretion assay indicated approximately 26% of an administrated dose of chlorophacinone is excreted within eight hours post-exposure via the bile (USEPA 2015b).

2.4.2 Human Incidents

The USEPA reviewed human incident reports for rodenticides, including chlorophacinone, for incidents reported to the USEPA Office of Pesticide Programs (OPP) Incident Data System (IDS), the National Pesticide Information Center (NPIC), the Centers for Disease Control and Prevention/National Institute for Occupational Safety and Health (CDC/NIOSH), Sentinel Event Notification System for Occupational Risk-Pesticides (SENSOR), and Agricultural Health Study databases between 2004 and 2018 (USEPA 2015d). These reviews suggested that the USEPA's mitigation measures to prevent accidental exposures to rodenticides that were implemented by USEPA in their 2008 Risk Mitigation Decision (RMD) (USEPA 2008) may have contributed to an overall decrease in exposure incidents involving second-generation anticoagulant rodenticides and incident counts for first-generation anticoagulant rodenticides remained low (USEPA 2020a). The 2008 RMD mitigation measures included using mandatory bait stations for all residential and general sales and for second-generation anticoagulant rodenticides used in outdoor aboveground settings. Additionally, sales and distribution limits were put in place for four of the 10 rodenticides that cause the greatest risk to wildlife. Compliance with these mitigation measures required by the RMD (USEPA 2008) resulted in a 65% reduction in reportable exposure incidents in children under 5 years of age (Gummin et al. 2020, Mowry et al. 2013). Non-occupational exposure incidents were expected to continue to decrease because of the completion of the phasing out of non-compliant products in March 2015 (USEPA 2015d).

Between January 1, 2010, and May 27, 2015, the Main IDS reported one incident from exposure to chlorophacinone (an adult female suicide attempt) classified as moderate severity (USEPA 2015d). The Aggregate IDS reported one incident involving chlorophacinone classified as having no or unknown effects. The SENSOR-pesticide database from 1998 to 2011 identified 12 cases involving chlorophacinone. Nine cases were from a single active ingredient exposure, with one case being moderate severity and eight being low severity. The moderate severity case involved an insulation worker who experienced shakiness, fever, and vomiting, as well as respiratory, neurological, gastrointestinal, renal, and cardiovascular symptoms after touching and/or inhaling chlorophacinone dust while performing insulation work in a school attic. Inhalation of the product "dust" was the cause of eight low-severity cases. Eight of the 12 cases reported respiratory and neurological symptoms, and eight were occupational. One involved a homeowner who accidentally inhaled chlorophacinone while opening a can of gopher bait and experienced shortness of breath and coughing (USEPA 2015d). WS did not have any reported incidents.

The Agricultural Health Study evaluates the link between pesticide use and various health outcomes, including cancer, private and commercial pesticide applicators, and their spouses. However, commensal rodenticides are not included in the Agricultural Health Study database.

2.4.3 Acute Toxicity

Technical chlorophacinone has high acute toxicity (Toxicity Category I) via the oral, dermal, and inhalation exposure routes. It is not a dermal irritant, eye irritant (Toxicity Category IV), or dermal sensitizer (Table 2; (USEPA 2015b)).

An acute oral toxicity study to determine the lethal dose for 50% (LD_{50}) [3] of technical chlorophacinone was conducted in Sprague Dawley rats[4] (10 rodents/treatment group/sex). Male rat mortalities were observed at all treatment doses, including 0 (0/10), 2 (4/10), 3.2 (6/10), 5.2 (4/10), 8.2 (8/10), 13.2 (10/10), 21 (9/10) mg/kilogram (kg)-body weight (bw) (deceased/total). No female mortalities occurred at the two lowest doses. The results were an LD_{50} of 3.15 mg/kg-bw for males, 10.95 mg/kg-bw for females, and a combined LD_{50} of 6.26 mg/kg-bw for this study. All deaths occurred four to 13 days after exposure. Chlorophacinone is a Toxicity Category I compound for oral exposure (USEPA 1998b).

Male New Zealand white rabbits[5] were dermally exposed for 24-hrs to 0.25, 0.5, and 0.75 mg/kg-bw technical chlorophacinone. Animals were observed for 21 days post-exposure. Deaths occurred at all doses between days five and 19, resulting in a dermal LD_{50} of 0.329 mg/kg-bw. Chlorophacinone is in the Toxicity Category I for dermal exposure (USEPA 1998b).

Groups of seven to nine Sprague Dawley rats were exposed (nasally) to 4-hour doses of 1.33, 10.3, 11.5, or 14.5 µg/Liter (L) technical chlorophacinone. During the 21-day study monitoring period, both male and female rats died due to non-treatment-related complications. No treatment-related mortalities were observed at the lowest (1.33 µg/L) dose. Mortalities accompanied by signs of anticoagulant activity occurred 3–8 days post-treatment, starting at 10.3 µg/L. The inhalation lethal concentration for 50% (LC_{50}) of male and female rats was 7 µg/L and 12 µg/L, respectively, and the combined LC_{50} was 9.3 µg/L. Chlorophacinone is in the Toxicity Category I for inhalation exposure (USEPA 1998b).

[3] LD_{50}, or lethal dose, is the amount of a chemical given all at once that kills 50% of a population of test animals

[4] Sprague Dawley rats are a domesticated form of the brown rat (*Rattus norvegicus domestica*). They are widely used as a laboratory rat due to their temperament and longevity but have some physiological differences from their wild counterpart.

[5] New Zealand white rabbits (*Oryctolagus cuniculus*) are domesticated European rabbits that are often used for laboratory studies due to their quick growth, docile nature, and longevity.

The end-use formulations containing 0.005% chlorophacinone have low acute oral, dermal, and inhalation toxicity. Both formulations are mild transient eye irritants (Table 2; USEPA 2015c).

Table 2. Acute technical grade and formulation chlorophacinone toxicity data for mammals (USEPA 2008).

Species	Test	Toxicity Value	Toxicity Category
Chlorophacinone Technical Grade			
Laboratory Rat	Oral LD_{50}[2]	3.15 mg/kg-bw[1] ♂; 10.95 mg/kg-bw ♀; combined: 6.26 mg/kg-bw	I
Laboratory Rabbit	Dermal LD_{50}	0.329 mg/kg-bw ♂	I
Laboratory Rat	Inhalation LC_{50}[3]	7 µg/L ♂; 12 µg/L ♀; combined: 9.3 µg/L	I
Laboratory Rabbit	Eye Irritation	No eye irritation	IV
Laboratory Rabbit	Dermal Irritation	No skin irritation	IV
Guinea Pig	Dermal sensitization	Not a skin sensitizer	N/A
Rozol® Prairie Dog Bait (EPA Reg. No: 7173-286) (Liphatech 2017) Rozol Pocket Gopher Bait (EPA Reg. No: 7173-184) (Liphatech 2007)			
Laboratory Rat	Oral LD_{50}	>5,000 mg/kg-bw	IV
Laboratory Rat	Inhalation LC_{50}	186 mg/L (extrapolated)	IV
Laboratory Rabbit	Dermal LD_{50}	>2,000 mg/kg-bw	III
Laboratory Rabbit	Eye Irritation	Mild, transient irritant	III

[1] Milligrams (mg) per kilogram bodyweight (kg-bw).
[2] LD_{50}, or lethal dose, is the amount of a chemical given all at once that kills 50% of a population of test animals.
[3] LC_{50}, or lethal concentration, is the concentration of a chemical in the air or water that will kill 50% of the test animals when they are exposed to the chemical for a set period.

2.4.4 Subchronic and Chronic Toxicities

In a repeat-dose oral toxicity study, groups of 10 Sprague Dawley rats were gavaged with technical chlorophacinone at 0, 0.005, 0.01, 0.02, 0.04, 0.08, and 0.16 mg/kg-bw/day, seven days per week for 113 days. The treatment group dosed at 0.005 mg/kg-bw/day was discontinued after 77 days due to no observed toxicity. Groups treated with 0.08 and 0.16 mg/kg-bw/day were terminated due to 100% mortality between treatment days 3 and 13. At 0.02 mg/kg-bw/day, four of 10 male rats and zero of 10 female rats died between treatment days 105 and 111. At the conclusion of this study, the 0.01 mg/kg-bw/day group males showed a 28% increase in coagulation time, while the female rats showed a 6% increase. A no observable adverse effect level (NOAEL) of 0.005 mg/kg-bw/day and a lowest observable adverse effect level (LOAEL) of 0.01 mg/kg-bw/day was identified from this study (USEPA 1998b).

In a 21-day dermal toxicity study, five rabbits/treatment/sex were dermally exposed to technical chlorophacinone 6 hours per day, five days a week at 0.08, 0.4, and 2 mg/kg-bw/day. At 2 mg/kg-bw/day, 4/5 male and 1/5 female rabbits died between treatment days 14 and 21. Elevated

prothrombin time was observed at 0.4 mg/kg/day. The NOAEL for this study was 0.8 mg/kg-bw/day, with a LOAEL of 0.4 mg/kg-bw/day) (USEPA 1998b).

2.4.5 Developmental and Reproductive Effects

Two studies evaluated the prenatal developmental toxicity of chlorophacinone administered to Sprague Dawley rats and rabbits orally. Pregnant Sprague Dawley rats were orally administered chlorophacinone by gavage at 0, 0.0125, 0.025, 0.05, and 0.1 mg/kg-bw/day for nine days (gestation days 6–15). No maternal toxicity was observed at 0.05 mg/kg-bw/day (NOAEL). The LOAEL for maternal toxicity was 0.1 mg/kg-bw/day based on mortality. For developmental toxicity, treatment-related effects for developmental anomalies such as hydroureter, distended ureter, and total ureter anomalies were observed at all doses, and a NOAEL for developmental toxicity could not be determined (NOAEL <0.0125 mg/kg-bw/day, LOAEL = 0.0125 mg/kg-bw/day) (USEPA 1998b).

In a prenatal developmental toxicity study in rabbits conducted at 0, 0.005, 0.01, 0.025, and 0.075 mg/kg-bw/day, maternal toxicity (i.e., increased coagulation times) occurred at 0.01 mg/kg-bw/day (LOAEL). In this study, the NOAEL for maternal toxicity was 0.005 mg/kg-bw/day, 10x lower than the LOAEL for mortality in rats. In addition, the NOAEL and LOAEL for developmental toxicity were lower than in the rat study, with a NOAEL of 0.01 mg/kg-bw/day and LOAEL of 0.025 mg/kg-bw/day, but were based on the lack of sufficient fetuses/litters available for evaluation (USEPA 1998a;2015b). The surviving litters at treatment doses below 0.025 mg/kg-bw/day were not evaluated for developmental anomalies. Physical anomalies may have occurred at lower doses (USEPA 1998b).

2.4.6 Neurotoxicity and Immunotoxicity Effects

The Hazard and Science Policy Council (HASPOC) waived neurotoxicity studies and immunotoxicity studies for chlorophacinone because available studies adequately characterize toxicity for any quantitative risk assessments (USEPA 2015d). Chlorophacinone disrupts blood clotting at low doses and is unlikely to have different toxicity in repeat oral dose studies (USEPA 2015b).

2.4.7 Carcinogenicity and Mutagenicity

A cancer risk assessment has not been conducted for chlorophacinone because long-term studies are not available, and chronic exposure is not likely to occur (USEPA 2015b). The mutagenicity studies did not indicate evidence of mutagenicity concerns for chlorophacinone (USEPA 2015b).

2.4.8 Endocrine System Effects

USEPA developed the Endocrine Disruptor Screening Program (EDSP) to characterize endocrine activity in commercial products, pesticides, and environmental contaminants (USEPA 2023). The EDSP utilizes a two-tier risk characterization approach consisting of screening candidate compounds for estrogen, androgenic, and thyroid receptor activity followed by the quantification of impact on environmental and human health (USEPA 2023). Prior to 2012, Tier 1 screening involved five *in vitro* and six *in vivo* assays (Browne et al. 2015). To address the growing need for a more rapid but equally comprehensive review of thousands of candidate compounds, EDSP revised Tier 1 screening to include computational endocrine activity models and high-throughput assays. Tier 2 testing data characterizes the endocrine-related health effects, dose response, and health risks of candidate compounds and substances.

EDSP reported chlorophacinone to have an ER agonist activity of 0 and an ER antagonist activity of 0.0307 with the standard of 17β estradiol agonist ER activity of 1 (USEPA 2015a). Based on the ToxCast™ Phase II endocrine disruption activity results, chlorophacinone was also reported to be active in 9 out of 21 estrogen receptor response assays and 10 out of 16 androgen receptor response assays. Therefore, the EDSP summarized chlorophacinone as having "significant estrogen and androgenic activity" (Williams et al. 2017).

2.4.9 Toxicity of Other Ingredients

Approximately 99.995% of the ingredients in the chlorophacinone products used by WS are "other" ingredients (Liphatech 2017;2020b). The other ingredients are considered confidential business information and are not included on the safety data sheets of either formulation. Thus, it is believed that these ingredients are likely, not toxic.

2.5 Chlorophacinone Formulations

Chlorophacinone is commercially available in multiple pesticide products registered by USEPA under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), including pelleted or whole grain (e.g., hulled oat groats) baits containing 0.005% chlorophacinone (Liphatech 2016;2017;2018;2020a;b, USEPA 2015c;2020b). Liphatech, Inc. (Milwaukee, Wisconsin) is the only registrant of chlorophacinone products in the United States.

Each chlorophacinone formulation has specific label instructions that applicators must follow when applying the baits. Many chlorophacinone products are restricted to underground use only to control burrowing rodents in rangelands, croplands, forests, cropland borders, dormant vineyards, non-agricultural areas, and on infested bare ground areas in pastures, alfalfa, wheat, barley, or oat fields as specified on their labels. Some products are registered for use aboveground in bait stations or by mechanical broadcast equipment. Some products may be used in urban areas inside structures and immediately outside these buildings. Application rates on the labels vary with the density of rodent populations and species being controlled. Most chlorophacinone products are classified as restricted use pesticides (RUP), which may only be applied by certified pesticide applicators. WS personnel must follow the label instructions when applying the baits.

The chlorophacinone products used or sold by WS from FY11[6] to FY20 and their labeled target species are listed in Table 3, along with the USEPA registration number, application rates, and target species. Other registrations are available but were not used by WS, and WS does not plan to use them in wildlife damage management (WDM) at this time. The maximum concentration of active ingredient (a.i.) of any product that WS used was 0.005% chlorophacinone. WS used chlorophacinone products to control mountain beavers, prairie dogs, pocket gophers, and ground squirrels.

[6] FY11 denotes the federal Fiscal Year 2011, which is October 1, 2010–September 30, 2011 (the year is denoted by FY12, FY13, and so on).

Table 3. Registered chlorophacinone products WS applied or sold for wildlife damage management with their USEPA or Special Local Needs (SLN) registration number, application rates, and target species allowed for each product.

Product Name (classification)	**EPA Reg. Number** (current label version date)	**Formulation**	**Application Rate** (pounds or ounces of product applied per acre)	**Target Animal**
Rozol Pellets (Restricted Use Pesticide (RUP))	SLN No. WA-060019 (label version expired 12/31/2021) Parent label 7173-151 (12/14/2020)	Chlorophacinone: 0.005% Other ingredients: 99.995%	12 oz/burrow hole and maximum of 24 oz per burrow system per year; Generally, ~3 lb/acre for a density of 4 mountain beavers/acre	Mountain beavers (*Aplodontia rufa*)
Rozol Prairie Dog Bait (RUP)	7173-286 (04/20/2017)		1.6–8 lb/acre	Black-tailed prairie dogs (*Cynomys ludovicianus*)
Rozol Pocket Gopher Bait (general use pesticide)	7173-184 (06/18/2007)		Up to 0.96 lb/ burrow system (max applied is ~58 lb/acre)	Pocket gophers (*Thomomys* and *Geomys* spp.)
Rozol Pocket Gopher Bait Burrow Builder Formula (RUP)	7173-244 (09/09/2009)		Make burrows the same depth as natural burrows, about 20–30 ft apart with 6–8 lb/acre. Can also be used for hand application.	Pocket gophers (*Thomomys* and *Geomys* spp.)
Rozol Ground Squirrel Oat Bait (RUP)	SLN No. MT-000007 (label version expires 12/31/2025) [b]		1 tbsp. bait around active burrows on bare ground or apply in bait stations 20–200 ft apart filled with 1–4 lb bait	Columbian ground squirrels (*Urocitellus columbianus*), Richardson's ground squirrels (*U. richardsonii*)
Rozol Vole Bait [c] (RUP)	7173-242 (11/03/2021)		1.5 oz/burrow	Voles (*Microtus* spp.)

[a] SLN Reg. No. WA-060019 was cancelled by Liphatech in 2022. WS is working with Liphatech on submitting a replacement SLN application to the Washington State Department of Agriculture in 2023 under the Rozol Vole Bait parent label.
[b] SLN product does not have a "parent" FIFRA Section 3 registration.
[c] This product was not used or sold by WS between FY11–FY20. However, this product will become the parent label for the new WA SLN for mountain beaver in 2023.

3 DOSE-RESPONSE ASSESSMENT

3.1 Human Health Dose-Response Assessment

In the repeat-dose oral toxicity study (Section 2.4.4), 28% of male rats exhibited dose-related increases in coagulation times starting at 0.01 mg/kg/day compared to 6% of female rats. In the

0.020 mg/kg-bw/day exposure group, 100% of male rats had increased coagulation times compared to 11% of female rats. These results, along with lower estimated acute oral and inhalation LD_{50} values for male rats compared to female rats, suggests that male mammals are more sensitive than female mammals to chlorophacinone.

The repeat-dose dermal toxicity studies conducted in rabbits have yielded highly variable results, and there is no repeat-dose inhalation toxicity data for chlorophacinone. Although chlorophacinone has a high dermal permeability coefficient, adverse effects from these exposure routes are the same as for oral exposure once chlorophacinone crosses the dermal barrier. As a result, USEPA (2015a) selected the developmental toxicity study in rats as the key reference study due to the applicable exposure route, dose regimen, treatment schedule, and relevance of the critical effect, which was elevated increased coagulation or prothrombin times for hazard characterization for the 0.005% chlorophacinone baits during registration review. USEPA selected the NOAEL of 0.05 mg/kg-bw/day (maternal toxicity NOAEL) as the Point of Departure (POD)[7] for their human occupational exposure risk assessment based on elevated prothrombin and activated partial thromboplastin times seen at 0.01 mg/kg-bw/day. The use of this POD did not result in Margins of Exposure (MOE) above the Level of Concern (LOC), including a 10x database uncertainty factor when an oral exposure POD was used to predict toxicity from an inhalation route of exposure (USEPA 2016b). Furthermore, chlorophacinone has only non-food uses. Thus, no food tolerances are established by the USEPA (USEPA 2015b;d).

An uncertainty factor is a human health risk assessment conceptual tool based on the assumption that a biological response increases or decreases in relation to increasing or decreasing exposure to a biologically active compound. If a sufficient reduction in exposure from the first known threshold for adverse effects can be accomplished, then an exposure limit that is protective of populations, including the vulnerable, can be determined (Dankovic et al. 2015). Uncertainty factors are used to address the differences between experimental data and actual human health effects. These include uncertainties for interspecies and intraspecies differences, differences in duration of exposure, and incomplete or insufficient toxicity data.

Table 4. Relevant reference studies from oral exposure.

Test Species	Test Duration	Critical Effect	N(L)OAEL/Uncertainty factors/RfD (mg/kg-bw/day)	Reference
Rat[1]	9 days	Prolonged prothrombin times	0.05(0.1)/90/0.00055	(USEPA 2015b)
Rat[1]	9 days	Prenatal developmental abnormalities	≤0.0125/300/0.000042	(USEPA 2015b)
Human	Single exposure	Lower prothrombin levels	0.29/100/0.00029	(Watt et al. 2005, WHO 1995)

NOAEL = No Observable Adverse Effect Level; LOAEL = Lowest Observable Adverse Effect Level; RfD – Reference Dose; [1]Sprague Dawley Laboratory Rats

For this risk assessment, uncertainty factors of 10 and the square root of 10 (√10) were applied to the NOAEL to account for genetic variability between humans and the variability between animals and humans. To accommodate for the absence of male rodents in the reference study (developmental toxicity study), an additional factor of √10 was applied to the uncertainty extrapolation for a total uncertainty factor of 100. The application of uncertainty factors to the POD would result in a reference dose (RfD) of 0.00055 mg/kg-bw/day (Table 4).

[7] Point of Departure (POD): A data point or an estimated point that is derived from observed dose-response data and use to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures.

Other studies are available to assess adverse effects associated with chlorophacinone use in study animals (Table 4). Prolonged prothrombin time (time to clotting), which is expected with anticoagulant exposure, has been observed in single exposure studies with humans (USEPA 2015b, Watt et al. 2005, WHO 1995). Prenatal developmental abnormalities have also been observed (USEPA 2015b).

3.2 Ecological Effects Analysis

This section summarizes available chlorophacinone toxicity data for terrestrial and aquatic species.

3.2.1 Aquatic Effects Analysis

3.2.1.1 Aquatic Vertebrates and Invertebrates

Chlorophacinone is highly toxic to freshwater fish such as rainbow trout (LC_{50}[8] is 0.452 mg/L) and freshwater aquatic invertebrates such as water fleas (EC_{50} is 0.640 mg/L) (Table 5) (USEPA 2020a). *Daphnia magna* has a No Observable Adverse Effect Concentration (NOAEC) of 0.28 mg/L (USEPA 2021a).

Table 5. Chlorophacinone toxicity in aquatic species.

Test Species	Scientific Name	Test	LC_{50}/EC_{50} (mg/L)	Reference
Bluegill Sunfish	*Lepomis macrochirus*	96-hour LC_{50}	0.71	As cited in (SERA 2015)
Rainbow Trout	*Oncorhynchus mykiss*	96-hour LC_{50}	0.452	(USEPA 2020a)
Water Flea	*Daphnia magna*	48-hour EC_{50}	0.64	(USEPA 2020a)

3.2.1.2 Aquatic Plants

Data for chlorophacinone toxicity to aquatic plants is not available.

3.2.2 Terrestrial Effects Analysis

3.2.2.1 Mammals and Birds

Chlorophacinone has very high acute oral and dietary toxicity in mammals (Table 6) (USEPA 2020a). In rats, the acute oral toxicity LD_{50}[9] is 0.8 mg ai/kg-bw, and the acute dietary LC_{50} is 1.14 mg ai/kg-diet (USEPA 2020a). The developmental NOAEL for mammals is 0.010 mg/kg-bw/day, based on a 2-generation reproduction study in rabbits, using the lack of sufficient fetuses at the end of the study as the endpoint (USEPA 2020a).

[8] LC_{50}, or lethal concentration, is the concentration of a chemical in the air or water that will kill 50% of the test animals when they are exposed to the chemical for a set period.
[9] LD_{50}, or lethal dose, is the amount of a chemical given all at once that kills 50% of a population of test animals

Table 6. Chlorophacinone toxicity in mammals.

Test species	Test	Reference
Black-tailed Prairie Dog	LD_{50} = 1.94 mg/kg-bw, oral gavage, single dose	(USEPA 2011)
Brown Rat (lab)	LC_{50} = 1.14 mg/kg-diet, 5-day dietary exposure	(USEPA 2011)
	Acute oral LD_{50} = 0.8 mg/kg-bw, doses of 0.16 mg/kg-bw for five days to equal LD_{50} dose	(USEPA 2020a)
Domestic Rabbit	Developmental NOAEL = 10 µg/kg-bw/day, oral gavage, daily from days 7 to 19 of gestation	(USEPA 2011)
	Acute oral LD_{50} = 50 mg/kg-bw	(WHO 1995)

Target and nontarget mammals that ingest chlorophacinone baits may take several days to die from toxicity (e.g., mountain beavers fed 5 g of 0.005% chlorophacinone bait daily died within 15 days (Arjo et al., 2004)). Due to this delay in symptoms, animals may continue to eat available bait, ingesting more than a sufficient dose to cause toxicity. After a single oral dose of 0.336 mg, chlorophacinone had a blood half-life of 11.7 days and a liver half-life of 35.4 days in the mouse (USEPA 2020a). Chlorophacinone has a blood half-life of 0.4 days in rats that received a single dose of 4–5 mg/kg-bw (USEPA 2020a) and a liver half-life of 5.9 days in black-tailed prairie dogs that received a single dose of 23 mg (USEPA 2020a, Witmer et al. 2016).

USEPA (2011) summarized laboratory studies on the secondary hazard of chlorophacinone to mongoose, coyote, red fox, weasel, and European ferret that were fed one or more poisoned prey for one to 90 days. Prey were poisoned with 0.0025%–0.01% chlorophacinone bait. Across these studies, 27 (49%) of 55 test mammals died after feeding on poisoned rodents (USEPA 2015e).

In birds, chlorophacinone is moderately toxic based on an acute oral basis (acute oral LD_{50} of 258 mg/kg-bw in northern bobwhite and is highly toxic based on a subacute dietary basis (subacute dietary LC_{50} of 56 mg/kg-diet in northern bobwhite) (Table 7) (USEPA 2020a). The red-winged blackbird has an acute oral LD_{50} of 430 mg/kg-bw, and the mallard has an acute dietary LC_{50} of 172 mg/kg-diet (USEPA 2004). In chronic exposure studies, chlorophacinone has a NOAEC of 0.046 mg/kg-diet and a Lowest Observable Adverse Effect Concentration (LOAEC) of 0.096 mg/kg-diet, based on a reduction in mean body weight of survivors in a 14-day reproductive toxicity study in mallard ducks (USEPA 2020a). The standardized acute toxicity studies conducted for first-generation anticoagulant rodenticides such as chlorophacinone may make these rodenticides appear less toxic than they are (Vyas and Rattner 2012). The time course of action for first-generation anticoagulant rodenticides requires large dosages in acute toxicity studies resulting in high LD_{50} values. However, several studies on birds and mammals have found these animals are more sensitive to first-generation anticoagulant rodenticides given at low dosages over several days than in the standardized acute oral toxicity test (Vyas and Rattner 2012).

Table 7. Chlorophacinone toxicity in birds.

Test species	Test	Reference
Northern Bobwhite (*Colinus virginianus*)	Acute oral LD_{50} = 258 mg/kg-bw	(USEPA 2020a)
	Acute dietary LC_{50} = 56 mg/kg-diet	(USEPA 2020a)
Red-winged Blackbird	Acute oral LD_{50} = 430 mg/kg-bw	(USEPA 2004)
Mallard (*Anas platyrhynchos*)	Acute dietary LC_{50} = 172 mg/kg-diet	(USEPA 2004)
	NOAEC[1] = 0.046 mg/kg-diet	(USEPA 2020a)
	LOAEC[2] = 0.096 mg/kg-diet	(USEPA 2020a)

[1] NOAEC = No Observable Adverse Effect Concentration
[2] LOAEC = Lowest Observable Adverse Effect Concentration

USEPA (2011) summarized laboratory studies on the secondary hazard of chlorophacinone to carnivorous birds that were fed one or more poisoned prey for 3 to 61 days. Prey were poisoned

with 0.005%–0.01% chlorophacinone bait. No deaths were recorded in the secondary bird exposure studies that included 106 carnivorous birds from nine species (barn owl, great horned owl, tawny owl (*Strix aluco*), red-tailed hawk, American kestrel, Eurasian buzzard (*Buteo buteo*), carrion crow (*Corvus corone*), black-billed magpie, and white stork (*Ciconia ciconia*). Some birds exhibited symptoms of chlorophacinone toxicity, such as external bleeding (n = 20), internal hematoma (n = 20), and increased blood coagulation time (n = 28) by the end of the study duration (USEPA 2015e).

Between 1990 and 2008, 54 wildlife incident reports of chlorophacinone exposure were reported in the Incident Data System maintained by the USEPA. Of these incidents, 8 were detectable chlorophacinone residues in live animals. Of the remaining incidents involving carcasses, 21 were classified as "highly probable," 14 as "probable," and 11 as "possible" chlorophacinone exposure (USEPA 2020a). Incidents involving avian species exposed to chlorophacinone included geese, quail, wild turkeys, barn owls, turkey vultures, bald eagles, and red-tailed hawks. Mammals included squirrels, raccoons, wild boars, badgers, black bears, coyotes, and bobcats (USEPA 2020a). Federally listed and protected species included the bald eagle, golden eagle, and San Joaquin kit fox (*Vulpes macrotis mutica*). Some of these exposures occurred after broadcast application aboveground, where baits and target animals are more accessible to nontarget species. Belowground applications reduce some exposure to nontarget species. These incidents did not involve WS applications.

Between 2014 and 2018, the California Department of Pesticide Regulation tested animals for anticoagulant residues (CDPR 2018, USEPA 2020a). Chlorophacinone was detected in 12 out of 152 animals tested. The species tested were not provided, nor was the application method (e.g., aboveground broadcast application versus belowground application).

USEPA (2004) queried the American Society for Prevention of Cruelty to Animals (ASPCA) Poison Control Center from November 1, 2001, to June 16, 2003, for pet exposures, primarily dogs, to chlorophacinone. There were 42 cases involving chlorophacinone exposure out of 2,334 cases involving rodenticides. These exposures did not involve WS applications.

WS has found relatively few nontarget species in areas where chlorophacinone bait had been applied. From FY11 to FY20, five dead nontarget meadow voles were found at one application. It is probable that other nontarget species were taken because WS does not dig up burrows, but the species likely taken are not listed as threatened or endangered species because WS does not treat in areas where those could be impacted.

3.2.2.2 Reptiles and Terrestrial Phase Amphibians

Acute, subacute, and chronic toxicity information is lacking for reptiles and amphibians. Birds are surrogate species for terrestrial amphibians and reptiles, indicating chlorophacinone has moderate acute oral toxicity and is highly toxic based on a subacute dietary basis in these species.

3.2.2.3 Terrestrial Invertebrates and Microorganisms

In redworms (*Eisenia fetida*), the subchronic LC_{50} is >1000 mg/kg-soil, and the NOAEC for mortality is 309 mg/kg-soil (USEPA 2011). Decreased body weights (sublethal effect) were observed at 95 mg/kg-soil.

In a study on the reproductive effects of chlorophacinone on the burying beetle (*Nicrophorus orbicollis*), larvae were fed for 5–10 days on rat carcasses poisoned with 0.005% chlorophacinone bait (the residue amount in the carcasses was not provided) and adults were fed 3 mg/kg-diet

chlorophacinone contaminated ground beef for 28 days with no effects on reproduction but there was observed decrease in larval emergence (USEPA 2011).

Information on the effects of chlorophacinone on microorganisms is limited. USFS (2015) summarized two studies on the exposure of bacteria to chlorophacinone, where no adverse effects were observed.

3.2.2.4 Terrestrial Plants

There is a lack of information on chlorophacinone toxicity in terrestrial plants. USEPA (USEPA 2004;2020a) finds the exposure and risks to terrestrial plants are likely to be minimal.

4 EXPOSURE ASSESSMENT AND RISK CHARACTERIZATION

The exposure assessment for chlorophacinone begins with an assessment of human health and ecological exposure pathways for chlorophacinone. For human health exposure, a complete exposure pathway includes (1) a release from a source (an application of chlorophacinone bait), (2) an exposure point where human contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal contact where contact can occur (USEPA 2019).

For ecological exposures, WS applies chlorophacinone baits directly into burrows or tunnels mechanically or by hand and aboveground adjacent to the burrow for the ground squirrels. Between fiscal years 2016 and 2020, all WS applications were by hand directly to burrows. The exposure assessment focuses on both belowground and aboveground applications for ecological receptors.

Exposures for relevant human and ecological populations are then quantitatively evaluated for each pathway, accounting for factors such as the frequency and duration of exposure, the toxicity of the chemical, and the sensitivity of the exposed population.

Risk is the likelihood of harm from a specific hazard and exposure to that hazard. This section also provides quantitative and qualitative assessments of human health and ecological risks associated with WS's uses of chlorophacinone products. The evaluation of documented chlorophacinone health exposure data and relevant animal exposure studies can quantify the risk of impact on human health and non-target fish and wildlife if accidentally exposed. Deterministic methods are used, where appropriate, to determine if expected environmental residues exceed toxicity data suggesting possible risk. In other cases, a more qualitative discussion regarding risk may be used, relying on literature and additional information to further elaborate on the potential for injury or harm.

The results of the exposure assessment and risk characterization can be used to inform risk management decisions and to develop strategies to minimize exposures and potential harm to human and ecological health.

4.1 Human Health Exposure and Risk Characterization

This section discusses the potential exposure pathways for chlorophacinone on human health. It examines the populations that are most at risk for exposure, the various methods of application, and the personal protective equipment used to minimize exposure. It also evaluates the potential for accidental exposure and assesses the associated risks. Finally, it provides a risk

characterization for WS's use of chlorophacinone products based on the available data on human health.

4.1.1 Potentially Exposed Human Populations and Complete Exposure Pathways

Based on the expected WS use pattern for chlorophacinone applications, workers who apply rodenticide baits are the subpopulation with the highest risk of exposure. Exposure during transportation is not anticipated because the material is in sealed containers. The baits are ready to use off the shelf with no mixing required. The application methods for WS use of chlorophacinone pelleted baits include bait stations, burrow baiting, and aboveground treatments or in or beside the infested burrow (no less than six inches into active brown or black rat burrows) (Liphatech 2020b). Mechanical broadcast bait spreading and aboveground spot applications can also be made for voles. Rozol Prairie Dog Bait (treated grain bait) can be applied by hand scoop or a mechanical bait application machine. It may only be used in underground applications between October 1st and March 15th (Liphatech 2017). The mechanical bait application machine is designed, constructed, and operated to ensure that bait is placed at least six inches into active prairie dog burrows. For bait stations specifically, units must be secured or otherwise immobilized if bait can be shaken from stations when lifted.

Following label directions, including the use of proper personal protective equipment (PPE), will minimize worker exposure to chlorophacinone baits via inhalation and dermal contact routes when manually or mechanically applying chlorophacinone bait. Waterproof gloves are required for any person who applies chlorophacinone baits as well as any WS personnel who retrieves carcasses or unused bait following application. Additional required PPE includes a long-sleeved shirt, long pants, shoes, and socks. Rozol Prairie Dog Bait and Rozol Vole Bait are restricted use pesticides that can only be used by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicator's certification.

Although the potential for exposure from the proposed WS use pattern is low, accidental exposure may occur during application. Accidental occupational exposure for workers was further quantified for the dermal contact route associated with the bait formulations. Ingestion routes are not considered in this exposure assessment because the formulations used by WS are either treated grain, pellets, or packets of pellets, and the risk of incidental ingestion is extremely low. The risk of exposure inhalation is deemed to be minimal due to outdoor (open air) only use of label-mandated application restrictions and PPE.

As per label requirements, chlorophacinone products used aboveground, such as Rozol Pellets (Liphatech 2020b), are only allowed for use in locations out of reach to children, pets, domestic animals, and nontarget wildlife or in tamper-resistant bait stations. Tamper-resistant bait stations prevent access to bait compartments and must be used if treatment areas are accessible to children and pets. Tamper-resistant packaging also prevents unauthorized post-application exposure for adults or the public. Any bait spilled during treatment must be collected to reduce the risk of nontarget animal exposure. Stronger bait stations are needed in areas open to hoofed livestock, raccoons, bears, or other potentially destructive animals and places prone to vandalism. As a result of these use restrictions, the public is not considered a vulnerable population for direct exposure to chlorophacinone utilized by WS.

The potential exposure to chlorophacinone associated with belowground applications, such as Rozol Prairie Dog Bait or Rozol Pocket Gopher Bait, is minimal for the public. Although oral exposure to all formulations of chlorophacinone is hazardous, label restrictions and the use of prepackaged bait suggest that dietary exposure is most always an incomplete exposure pathway.

Chlorophacinone has a low potential for volatilization due to its low vapor pressure. It will adsorb readily to organic material in the soil, minimizing inhalation risks and leaching into nearby water bodies or aquifers. In addition, label restrictions state that no applications are allowed directly to water, areas where surface water is present, or intertidal areas below the mean high-water mark (Liphatech 2019). As a result, surface and groundwater exposure pathways are also incomplete.

4.1.2 Exposure Evaluation

This section quantitatively evaluates worker exposures from an accidental, direct dermal contact pathway while applying baits. Under the accidental exposure scenario, it is assumed that the applicator's chemical-resistant gloves are broken. This exposure evaluation scenario considers potential exposures to pelleted formulations. Bait block formulations have not been evaluated due to the negligible risk of accidental dermal exposure.

The estimates of exposure to certified applicators are based on surrogate study data available in the Pesticide Handlers Exposure Database (PHED) (USEPA 2021b). The "trap/bait station refillable" or "applicator granules by hand" exposure scenario in the PHED table is the closest scenario representing potential exposure for the application method on the label for Rozol Pellets and sachets containing 0.005% chlorophacinone baits. Under this exposure scenario, the exposure unit for dermal contact under the single-layer (gloves, long-sleeve shirt, long pants, shoes plus socks) and double-layer PPE is 71.38 and 40.68 mg/lb. of active ingredient (lb. ai) applied, respectively. The exposure unit for a scenario where a WS applicator lacks single-layer PPE or wears inadequate hand protection, such as broken gloves, is 104 mg/lb. ai applied.

Lower and upper application use rates were estimated from pocket gopher and prairie dog ecological studies (Colorado State University Extension 2011, Miller 1950, Oklahoma Cooperative Extension Service 2017) and label-mandated treatments (Liphatech 2017). For example, pocket gopher density per acre can range from 16 to 60 individual burrows in some areas (Andelt and Case 2016, Baldwin 2019, Oklahoma Cooperative Extension Service 2017). The Rozol Pocket Gopher Bait label has a maximum application rate of 4.8×10^{-5} lb. ai per burrow (Liphatech 2007). Thus, the maximum amount of chlorophacinone per acre in pocket gopher applications would be 0.000768–0.00288 lb. (350– 1270 mg). Prairie dog density per acre ranges from approximately 10 to 50 burrows per acre in some locations (Colorado State University Extension 2011, National Park Service 2021). The Rozol Prairie Dog Bait label has a maximum application rate of 8×10^{-6} lb. ai lb. ai per burrow (Liphatech 2017). Thus, the maximum amount of chlorophacinone per acre would be 0.00008–0.0004 lb. (36–181 mg)) in prairie dog applications.

The other relevant, conservative assumptions used in this exposure evaluation included an assumption that an applicator weighs 70 kg, spends 30 minutes per pesticide treatment application, and there is accidental dermal contact with 1% of the bait applied when PPE integrity is compromised without replacement for 8 hours (USEPA 2016). The following equations are used to estimate the exposure dose of direct contact for workers:

Exposure Dose = Daily Dose Rate/Body Weight
Daily Dose Rate = Unit Exposure (mg/lb ai) x Application Rate (lb ai/acre) x Area Treated (acre/day) x Dermal Absorption Rate (%)

Exposure doses were estimated for the application rates specified on the labels and summarized in Table 8.

Table 8. Risk estimation for accidental occupational dermal exposure.

Parameter	Units	Values		Values		Values		Source
		‡No gloves/damaged PPE[1]		‡Single layer gloves		‡Double layer PPE[1]		
PDR[1]=UE[1]*AR[1]*A[1]*ABS[1]								
UE[1] applicator granules by hand	mg/lb ai	104		71		40.3		(USEPA 2021b)
		AR[1] lb ai/acre	**A/D[1]**	**AR[1] lb ai/acre**	**A/D[1]**	**AR[1] lb ai/acre**	**A/D[1]**	
Mountain Beaver SLN Labels								
Prepackaged sachets	12 oz. sachet	0.00113	33	0.00113	48	0.00113	85	Calculated on WS use
Rozol Prairie Dog Bait Label								
†High AR[1]	8 lb/acre	0.0004	>100	0.0004	>100	0.0004	>100	Calculated based on label
Low AR[1]	1.6 lb/acre	0.00008	>100	0.00008	>100	0.00008	>100	
Rozol Pocket Gopher Bait Label								
High AR[1]	58 lb/acre	0.00288	12	0.00288	17	0.00288	30	Calculated based on label
Low AR[1]	15 lb/acre	0.00077	43.8	0.00077	64	0.00077	>100	
ABS[1]	%	0.01		0.01		0.01		(USEPA 2007)
PDR[1]	mg/day	0.035		0.035		0.035		Calculated
Dose = PDR/BW								
BW[1]	kg	70		70		70		(USEPA 2007)
Dose	mg/kg-bw/day	0.00055		0.00055		0.00055		Calculated
***Hazard Quotient = Dose/RfD**								
RfD[1]	mg/kg-bw/day	0.00055		0.00055		0.00055		^NOAEL[1] of 0.05 mg/kg-bw/day
Hazard Quotient		1		1		1		

[1] PPE = Personal Protective Equipment; UE = Unit Exposure; AR = Application Rate; A/D = Acres/Day; ABS = % Material Absorbed Dermally; PDR = Potential Daily Rate; BW = Body Weight; RfD = Reference Dose; NOAEL = No Observable Adverse Effect Level

* The ratio of the potential exposure to the substance and the level at which no adverse effects are expected. If the Hazard Quotient is calculated to be less than 1, then no adverse health effects are expected as a result of exposure. If the Hazard Quotient is greater than 1, then adverse health effects are possible. The Hazard Quotient cannot be translated to a probability that adverse health effects will occur and is unlikely to be proportional to risk. It is especially important to note that a Hazard Quotient exceeding 1 does not necessarily mean that adverse effects will occur.

† Application density and treatment levels are based on label restrictions.

‡ Based on hand application estimates of exposure by Pesticide handler exposure database.

^ Based on a NOAEL of 0.05 mg/kg-bw/day from the developmental toxicity study in rats as the Point of Departure (see Section 3.1).

4.1.3 Human Health Risk Characterization

This section discusses the quantitative characterization of risks for adverse human health effects associated with potential accidental occupational exposure to chlorophacinone baits for WS use of more potentially hazardous "loose" bait products, Rozol Prairie Dog Bait and Rozol Pocket Gopher Bait. The volume of chlorophacinone baits applied annually is limited, and personnel follow label requirements, resulting in minimal risks to the public.

To quantify the human health risks to applicators associated with accidental occupational dermal exposure to chlorophacinone, a hazard quotient (HQ) was calculated using the USEPA risk estimation equation for non-carcinogens. The maximum number of acres a certified applicator could apply 0.005% chlorophacinone baits under the proposed WS uses without an increased risk was calculated using a hazard quotient of one. The calculated acres a WS employee could safely work per day are summarized in Table 9.

Table 9. Estimated number of acres treated per day using USEPA hazard quotient benchmark for human health.

Personal Protection Equipment[1]	**Maximum Number of Acres to be Treated Per Day**[3]			
	Rozol Prairie Dog Bait (7173-286)		Rozol Pocket Gopher Bait (7173-184)	
	***Low AR**[2,3] (10 placements/acre)	**High AR**[2,3] (50 placements/acre)	**Low AR**[2,4] (16 placements/acre)	**High AR**[2,4] (60 placements/acre)
No or Broken Gloves	>100	>100	44	12
Single-layer PPE	>100	>100	67	17
Double-layer PPE	>100	>100	>100	30

[1] Pesticide Handlers Exposure Database; single layer = gloves, long sleeve shirt, long pants, shoes, and socks; double layer = single layer PPE + coveralls
[2] Hazard quotient of 1
[3] Calculated from Rozol Prairie Dog Bait label, and (Colorado State University Extension 2011),
[4] Calculated from Rozol Pocket Gopher Bait label, and (Miller 1950, Oklahoma Cooperative Extension Service 2017).

HQs above a value of 1 suggest an increased risk to applicators based on exposure assumptions. A single applicator should apply chlorophacinone baits to no more than 27 and 83 acres per day for high-density and low-density applications, respectively. The risks of injury to chlorophacinone rodenticides are low when label instructions are followed, and there is minimal risk of chlorophacinone-induced injury for applicators. To maintain minimal to no risks of injury for applicators, individual applicators should not exceed the recommended maximum acres treated per day.

In summary, the limited volume of chlorophacinone baits applied annually, and personnel adherence to label requirements result in minimal risks to the public. The calculated acres a WS employee could safely work per day are summarized in Table 9, and individual applicators should not exceed the recommended maximum acres treated per day to maintain minimal to no risks of injury.

4.2 Ecological Exposure and Risk Characterization

Risk characterization combines information from the dose-response assessment with the exposure assessment to determine the potential adverse effects on aquatic and terrestrial species. USEPA refers to this ratio as the risk quotient and compares this to pre-established acute and chronic Levels of Concern (LOC). USEPA (USEPA 2011;2020b) characterized risks from

direct chlorophacinone bait consumption and consumption of chlorophacinone-contaminated carcasses for aquatic and terrestrial vertebrates and invertebrates. In their risk characterization, USEPA used broadcast applications in the exposure scenario. In this risk assessment, WS uses USEPA's risk evaluations (USEPA 2011;2020b), peer-reviewed scientific literature, product labels, and WS use patterns and take data (Table 1) to characterize the ecological risks associated with WS applications of chlorophacinone bait.

4.2.1 Aquatic Exposure Assessment and Risk Characterization

The potential for aquatic exposure to chlorophacinone bait products used by WS was evaluated. Table 3 shows the types of chlorophacinone bait products that WS could use. Applicators are not allowed to apply these products to water or areas where surface water is present or to intertidal areas below the mean high-water mark. Rozol Pocket Gopher Bait and Rozol Prairie Dog Bait are applied belowground, and although the Rozol Pellets label allows some aboveground use, the label restricts aboveground outdoor use to bait stations. WS did not use chlorophacinone baits aboveground from FY11 to FY20, but it could use Rozol Pellets for aboveground applications in orchards to control voles in the future. However, the prior 10-year use pattern suggests that almost all future applications will be belowground.

An accidental spill of chlorophacinone bait next to or into a water body could result in exposure to aquatic species. WS does not expect accidental water exposure to occur based on its use patterns. In the unlikely event that there is an accidental spill, it is unlikely that a hazardous amount of chlorophacinone would end up in the water. USEPA queried its Incident Data System (IDS) for reports of chlorophacinone exposure to nontarget species between 1990 and 2008 and found no reports for aquatic species.

USEPA (2015e) modeled aquatic exposure for chlorophacinone and found the estimated environmental concentrations for the peak concentration, 21-day average concentration, and 60-day average concentration were orders of magnitude lower than the aquatic toxicity endpoints. USEPA (2015e) found the likelihood of aquatic impacts from potential exposure is insignificant. WS does not anticipate aquatic exposure through its use of chlorophacinone. WS treatments are primarily belowground. Chlorophacinone is not mobile in soils and binds strongly to the other ingredients in the bait formulations. These characteristics indicate chlorophacinone will not leach from the baits or burrows into groundwater or run off into surface waters (USEPA 2015d).

The exposure assessment found aquatic exposure to be negligible based on WS use pattern and label restrictions, as well as findings from USEPA's ecological risk assessment (USEPA 2020a). The USDA Forest Service (USFS) conducted a risk assessment on the belowground application of chlorophacinone bait to control black-tailed prairie dogs and found aquatic exposure to be negligible (SERA 2015).

USEPA estimated aquatic exposure potential (summarized in section 4.2.1) and found aquatic taxa are not at risk from chlorophacinone (USEPA 2020a). USEPA used the highest modeled exposure in their estimate, which was broadcast application of chlorophacinone in an orchard; USEPA's analysis included chronic exposure to freshwater fish and freshwater invertebrates (*Daphnia*), acute exposure to green algae, and acute and chronic exposure to saltwater fish and Mysid shrimp (USEPA 2020a). Based on USEPA risk estimates from aquatic exposure, label restrictions, and WS typical use pattern, which involves direct application to burrows by hand, APHIS considers the risk to aquatic species negligible. Even for broadcast applications in orchards, the risk is considered minimal.

4.2.2 Terrestrial Exposure Assessment

Exposure of nontarget terrestrial animals to chlorophacinone may be directly through eating bait (primary exposure) or by preying on or scavenging animals poisoned with chlorophacinone (secondary exposure). Exposure to aquatic sources is not expected; thus, drinking contaminated water is not an exposure pathway considered in this assessment.

The labels for the chlorophacinone products that WS may use provide instructions to reduce nontarget exposure to chlorophacinone. The Rozol Vole Bait label instructs applicators using hand-baiting to place bait in the hole, trail, or runway and to cover the bait with grass or shingle to avoid exposing nontarget organisms or to place the bait in a tamper-resistant bait station and not to apply where raptors are actively feeding on voles (Liphatech 2020a). These measures would reduce some exposure to nontarget predators and scavenger species. The Rozol Prairie Dog Bait label, Rozol Pocket Gopher Bait label, and the Rozol Pellets SLN label to control mountain beavers allow for belowground use only (Liphatech 2007;2016;2017;2018). The Rozol Prairie Dog Bait label limits applications to October through March, when the target animal is most likely to consume the bait. Similarly, the Rozol Pellets SLN label limits applications to October through February. The restricted time reduces exposure to some animals, particularly those that are not in the area or active during that time. The Rozol Prairie Dog Bait label also instructs applicators to remove bait that spills aboveground or is placed less than six inches down the burrow entrance and requires the applicator to return to the site within four days after bait application, and at one to two day intervals to collect and dispose of any bait or dead or dying prairie dogs found on the surface. This search must continue for at least two weeks, but longer if carcasses are still found at that time. The removal of aboveground carcasses of poisoned animals reduces secondary exposure to predators and scavengers.

4.2.2.1 Primary Exposure

Between FY11 and FY20, all WS applications were belowground (Table 1). Direct exposure of nontarget species to treated bait from these applications is mostly limited to those animals that can access the burrow. However, WS expects a percentage of bait to be moved aboveground as animals enter and exit the burrow (USEPA 2009).

Small granivorous mammals that share a treated burrow with the target animal are likely to ingest a toxic amount of chlorophacinone bait. USEPA (2004) summarized a study where 0.01% and 0.005% chlorophacinone baits were used to treat California ground squirrels in rangelands. Bait was applied by spot baiting or in bait stations. For the nontarget mice (deer mice, San Joaquin pocket mice (*Perognathus inornatus*), and woodrats) found dead, at least 86% of the mortality was likely due to primary exposure to baits.

Birds that are herbivorous or insectivorous are not expected to be attracted to chlorophacinone baits, which are grain-based. Exposure of birds to underground applications of bait is expected to be minimal but not likely zero (USEPA 1998b). Two wild adult turkey deaths were attributed to chlorophacinone poisoning, likely from primary exposure to bait applied within a prairie dog colony but not applied by WS (Ruder et al. 2011). Grain baits were found in the crop and ventriculus of both turkeys, and chlorophacinone was detected in the livers. Applications to prairie dog burrows are supposed to be directly into the burrow and not applied at the surface. Access by the turkeys indicates that either the chlorophacinone bait was close to the surface due to the angle of the burrow entrance, that bait was spilled aboveground (Ruder et al. 2011), or bait was moved to the surface through animal movement in and out of the burrow (USEPA 2009). Any of these alternatives could have resulted in enough bait reaching the surface for the turkeys to ingest a

toxic dose. A dead western meadowlark, which is a ground-foraging songbird, was also found in a prairie dog colony that was treated with chlorophacinone bait. The bird had signs of hemorrhaging in the brain and pectoral muscle tissue and chlorophacinone residues of 0.59 and 0.49 µg/g in the liver and intestinal contents, respectively, indicating chlorophacinone exposure (Vyas et al. 2013). WS was not involved in this incident either.

Exposure of terrestrial and soil-dwelling invertebrates could occur should they come into direct contact with chlorophacinone bait in burrows. Insects may be attracted to and feed on baits placed in burrows and tunnels and subsequently be consumed by insectivorous wildlife. Chlorophacinone is immobile in soil and is not expected to leach into the soil, indicating a localized effect. WS' use pattern should not result in widespread exposure to invertebrates. Chlorophacinone is minimally toxic to redworms (*Eisenia fetida*) with a 14-day LC_{50} greater than 300 mg a.i./kg soil (USEPA 2020a). In a laboratory experiment in France, residue levels detected in gray garden slugs (*Deroceras reticulatum*) exposed to 5 g of 0.005% chlorophacinone pat bait (not available in the U.S.) between one and five days was 0.6 to 3.3 mg/kg tissue (Alomar et al. 2018). The authors estimated the elimination half-life in slugs as four days. The slugs did not display adverse effects in the study. This study suggests that terrestrial mollusks that ingest chlorophacinone bait could be a source of secondary exposure to species that feed on mollusks.

Exposure to terrestrial plants is negligible based on WS use patterns.

4.2.2.2 Secondary Exposure

Secondary exposure could occur for predators and scavengers that can access burrows with poisoned animals or if they kill or scavenge poisoned animals aboveground. Mammalian carnivores and scavengers are particularly at mortality risk from chlorophacinone, although sublethal effects in birds may result in decreased survival or reproduction (see section 3.2.2 for a review of secondary exposure studies). It can take four to 10 or more days for a target animal to die after ingesting a toxic dose of chlorophacinone bait (USEPA 2020a, Vyas et al. 2012). In one laboratory study, the average time to death for prairie dogs that consumed, on average, 47 g of 0.005% chlorophacinone bait was 15 days (Witmer et al. 2016). During this time, the animal continued to feed and move about. Researchers have observed predators and scavengers hunting treated areas more than nearby untreated areas (Vyas et al. 2012, Vyas et al. 2017), likely because poisoned target animals become lethargic prior to death and are easier to capture (USEPA 2020a).

In a field study, Vyas et al. (2017) compared the number of visits by ferruginous hawks to black-tailed prairie dog colonies treated with Rozol Prairie Dog Bait (0.005% chlorophacinone) to control (untreated) colonies. They found the hawks hunted in the treated colonies only, likely because the poisoned prairie dogs were lethargic and not as aware of their surroundings, making them easier to capture. In a field study across 10 treated prairie dog towns, 10 animal carcasses, 9 of which were prairie dogs, were found aboveground (Lee and Hyngstrom 2007, USEPA 2009). Eight of the carcasses were intact, but two had been scavenged. The rate of prairie dog carcasses was one per 14 acres searched. The researchers also noted that they saw five impaired prairie dogs 10 days or more after bait applications.

In another field study evaluating secondary poisoning from chlorophacinone bait applications to control Richardson's ground squirrels, the chlorophacinone bait was placed in the burrow openings, which were then left open. A second application was made 48 hours later. An American badger and 3 long-tailed weasels died nine days after these chlorophacinone bait applications and had signs of bleeding and hemorrhages (Proulx 2010). In a study conducted in Kansas (Lee

and Hyngstrom 2007), nine prairie dogs and one cottontail rabbit were found dead aboveground out of 11,479 treated burrows illustrating the minimal potential for belowground treatments to potentially have an impact on non-fossorial animals.

A target animal typically must feed multiple times on bait to receive a lethal dose of chlorophacinone. The accumulation of chlorophacinone residues in an animal depends on the amount of bait the animal eats, how close together the feedings are, how long since the prior consumption of chlorophacinone, and its metabolism rate of chlorophacinone.

One study found the greatest risk of secondary exposure to chlorophacinone residues in prairie dogs that fed on an average of 47 g over two days of 0.005% Rozol Prairie Dog Bait was within 14 days of application (Witmer et al. 2016). Residues were highest three to six days after exposure. The half-life of chlorophacinone residues in the prairie dogs was 5.9 days for liver tissue and 6.3 days for whole bodies (minus the liver). At the average of 15 days to death, chlorophacinone residues in prairie dogs declined, reducing the risk of secondary poisoning (Witmer et al. 2016). In the Witmer et al. (2016) study, the two-day exposure to chlorophacinone baits likely underestimates the intake and residue levels from field applications, where bait is available to animals for more than two days.

Vyas et al. (2012) also found a decline of hepatic (liver) chlorophacinone residues over time in black-tailed prairie dogs and thirteen-lined ground squirrels. Vyas et al. (2012) identified several factors that may have caused this decline, including the short hepatic half-life of chlorophacinone, poisoned animals that may stop feeding on bait as they develop symptoms, and reduced availability of bait over time. In a study on the efficacy of 0.01% chlorophacinone bait for Belding's ground squirrels, 38 whole squirrel carcasses were located aboveground (mostly near burrow entrances), and 86% had detectable levels of chlorophacinone (Ramey et al. 2007). The mean level of chlorophacinone in the whole body of ground squirrel carcasses was 0.16 mg/kg tissue, and in the liver, 0.13 mg/kg tissue. Carcasses were predominately found between 24 and 48 hours after one bait application and between 48 and 96 hours after a second application that occurred two days later. The authors summarized that a few (2.4%) of the poisoned ground squirrels died aboveground, and only some of these carcasses posed a secondary hazard to scavengers depending on the tissues consumed. USEPA (2004) summarized several additional studies measuring whole-carcass chlorophacinone residue levels in ground squirrels, mice, rats, voles, and pocket gophers fed 0.005–0.01% chlorophacinone baits. In ground squirrels given either 0.005% or 0.01% bait in the field (number of exposure days was unknown), the whole-carcass residue levels were 0.57 and 1.27 mg/kg tissue, respectively. In the laboratory, rats given 0.005% bait for 5 days has a whole-carcass residue level of 0.47 mg/kg tissue. Voles fed 0.005% bait in the laboratory for less than 9 days had an average whole-carcass residue level of 3.2 mg/kg tissue. House mice had whole-carcass residue levels of 6.0 mg/kg tissue after being fed 0.0075% bait for three days.

The Rozol Prairie Dog Bait label requires applicators to return to the treatment site at 1- to 2-day intervals after baiting to collect and dispose of any bait or dead or dying prairie dogs found on the surface (Liphatech 2017). The search for dead or dying prairie dogs and other nontarget animals must continue for at least 2 weeks or longer if carcasses are still being found. The removal of dying or dead animals would reduce some secondary exposure. Follow-up visits take time and resources to conduct, and possible non-compliance with label requirements intended to reduce secondary exposure would negate the benefits (Vyas 2013). However, WS applicators are trained to comply with label requirements, and WS does not expect non-compliance with the label's secondary exposure mitigation measures.

A review of select secondary exposure laboratory studies is in section 3.2.2. Mammals are sensitive to secondary exposure to chlorophacinone. Across the laboratory studies on secondary exposure USEPA (2015e) evaluated, 27 (49%) of the 55 test mammals died after feeding on poisoned rodents. In the studies summarized in section 3.2.2, exposure of carnivorous birds to poisoned prey did not result in bird deaths (USEPA 2015e); however, sublethal effects in birds may result in decreased survival and reproduction (Rattner et al. 2015). A study in kestrels examined secondary exposure mortality and sublethal effects in kestrels that were fed for 21-days on mice that consumed an average of 1.14 mg ai chlorophacinone. No kestrels died; however, sublethal effects in the form of hemorrhaging were reported (Radvanyi et al. 1988). Localized bleeding outside of blood vessels (hematoma) was observed on the lungs, liver, heart, and pectoral muscles of exposed birds. In another study, kestrels were fed tissue from rats fed Rozol bait and similarly had evidence of hemorrhage most frequently observed in the pectoral muscle and heart (Rattner et al. 2015), along with other sublethal effects. Based on the sublethal responses in kestrels, the authors found environmentally realistic concentrations of chlorophacinone (e.g., reported chlorophacinone concentrations found in small mammals following field baiting trials) could affect the survival of free-ranging raptors (Rattner et al. 2015).

4.2.3 Terrestrial Primary and Secondary Risk Characterization

It can take several days of consecutive feedings to deliver a lethal dose of chlorophacinone to the target animal, as well as nontarget species (USEPA 2020a). Similarly, secondary exposure to nontarget species would usually require that carnivores and scavengers consume multiple prey items poisoned with chlorophacinone to receive a lethal dose. The lethal exposure of nontarget terrestrial species is reduced but not eliminated by belowground applications. Most target animals die belowground (Lee and Hyngstrom 2007, Primus et al. 2001, USEPA 2009), reducing secondary exposure potential.

APHIS expects minimal risk to terrestrial plants based on lack of exposure through WS use pattern and chlorophacinone's mode of action. Birds are less sensitive than mammals to chlorophacinone, but some adverse effects, including sublethal effects, are possible through direct and secondary exposure. Small granivorous mammals that can access belowground treatment sites could consume enough bait to receive a toxic dose. Terrestrial invertebrates can experience sublethal effects from chlorophacinone bait exposure, as demonstrated by larval survival effects for burying beetles (*Nicrophorus orbicollis*), weight change in redworms (USEPA 2011;2020a), and chlorophacinone residues detected in a terrestrial mollusk (Alomar et al. 2018).

USEPA (2020a) calculated the single-day and 6-day primary bait exposure risk quotients for Passeriformes birds (songbirds) and rodents at 3 weight classes. USEPA calculated risk quotients by dividing an estimated environmental concentration from broadcast applications by a toxicity endpoint. Only rodents in the 15- and 35-kg weight classes had risk quotients that exceeded the LOC after a 1-day exposure, and all 3 mammal weight classes had risk quotients that exceeded LOCs after a 6-day exposure. The LOCs for acute and chronic risks to vertebrates are 0.5 and 1.0 and are meant to be protective of community-level effects. USEPA found direct consumption of bait by bird species is unlikely to lead to toxic exposure, but rodents and other mammals that consume enough bait are at risk of exposure. USEPA (2020a) risk estimation using broadcast applications exceeds that for WS use patterns, which are predominantly belowground applications. In an evaluation of exposure risks, USEPA (1998b) found minimal exposure to birds is anticipated from underground applications. APHIS emphasizes that although the exposure risk to birds is minimal and it is unlikely that granivorous birds would consume a toxic dose of chlorophacinone bait administered belowground, the risk of toxicity from the consumption of bait is not negligible ((Ruder et al. 2011, Vyas et al. 2013), see Section 4.2.2). Birds that are mainly

herbivorous or insectivorous are not expected to be at risk from primary exposure to chlorophacinone bait. However, secondary risks could also occur for nontarget species that rely on terrestrial invertebrates during some portion of their lifecycle.

In a field study on secondary exposure to predators and scavengers, chlorophacinone residues were measured in the liver and carcasses of Belding's ground squirrels, and voles (*Microtus* sp.) collected aboveground and Botta's pocket gophers collected underground (Primus et al. 2001). Field applications were made by spot baiting or bait stations. The maximum residue levels (0.82 µg/g Belding squirrel and 4.1 µg/g voles) were then used to assess secondary toxicity to birds and mammals in 3 weight classes using USEPA's standard evaluation procedures to calculate a risk quotient, as described above. Similar to the findings in the USEPA evaluation (USEPA 2020a), there is little risk of secondary toxicity for avian species, but the acute risk is predicted for all three weight classes of mammals.

USEPA (2004) conducted a comparative risk evaluation of several rodenticides and concluded primary risks of broadcast-applied chlorophacinone to birds were low to moderate and secondary risks were low. Using birds as surrogate species, consuming chlorophacinone bait by terrestrial reptiles and amphibians would have the same primary and secondary risks as birds. In mammals, primary and secondary risks were evaluated as high (USEPA 2004). WS finds the risks associated with WS' use of chlorophacinone bait will be lower than the USEPA estimates (USEPA 2004;2020a) due to primarily conducting applications belowground.

A predator or scavenger feeding on a single animal poisoned with chlorophacinone may not result in death; the predator or scavenger would likely need to feed on several poisoned animals to cause sublethal effects and mortality. USEPA (2004) summarized several laboratory studies on the secondary hazards of chlorophacinone to predatory and scavenging birds. The lack of mortality in these laboratory studies in birds may have been due to the carcasses they were fed having low residue levels due to the relatively rapid metabolism and excretion of chlorophacinone. For example, in rats given 1.4 mg chlorophacinone, about 90% of chlorophacinone was metabolized or excreted within 2 days (unpublished study cited in (Primus et al. 2001)).

The reduction in available prey in an area due to chlorophacinone treatment could impact food availability for predators. WS anticipates predators would extend their hunting range into new areas to accommodate for the loss of prey in any given area.

WS maintains records of nontarget species take in WDM, including the use of chlorophacinone baits. WS has no records of nontarget take through its use of chlorophacinone bait for FY16–FY20 but took an annual average of one meadow vole during FY11–FY15. WS recognizes it is not possible to detect all nontarget take because animals mostly die belowground, may be difficult to detect in certain habitats, or are wide-ranging and dispersed outside the treatment area after exposure. WS monitors proposed treatment sites and avoids treating burrows where they detect nontarget species. Despite this monitoring, WS recognizes nontarget species that can access treated burrows may be exposed to chlorophacinone bait. In a study using a different anticoagulant (brodifacoum), 90% of plains pocket gophers died belowground (as cited in (Primus et al. 2001)). In a study using chlorophacinone, the baiting of 10 prairie dog towns produced only 10 carcasses, 9 that were prairie dogs, which were found aboveground (about 1 carcass per 14 acres) (Lee and Hyngstrom 2007, USEPA 2009). WS expects most of the target animals it baits belowground with chlorophacinone will die underground, reducing exposure to scavenging nontarget species; however, some die aboveground, but typically very few. The Rozol Prairie Dog Bait label instructs applicators to return to the site within 4 days after bait application and at 1- to 2-day intervals to collect and dispose of any bait or dead or dying prairie dogs found on the

surface. Despite these mitigations, poisoned animals may die aboveground between searches or are missed during searches and remain available to predators and scavengers. Birds are not as sensitive to chlorophacinone as mammals, and the risk of mortality to predatory and scavenging birds that consume poisoned animals is lower compared to nontarget mammals. However, birds feeding on poisoned animals may experience sublethal effects. WS finds the use of chlorophacinone will have the greatest risk to mammals that access treated burrows where they may ingest bait or poisoned animals. Some risk to mammalian predators and scavengers occurs from eating poisoned animals that die aboveground, with the most risk for those that can feed on animals that died in their burrows.

5 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from a lack of toxicity information for all chlorophacinone formulations. USEPA reviews and Safety Data Sheets for chlorophacinone products provide some toxicity values that can be used to make general comparisons between the formulations. However, variations in toxicity study design, formulations, and active ingredient concentration limit this. Uncertainties related to chronic and sublethal effects data for some fish and wildlife, as well as surrogacy of test organisms, are typical for most pesticides; however, field data related to nontarget chlorophacinone poisoning of wildlife is more abundant.

Conservative assumptions of exposure, behavior, and human variability are used to develop estimates of impacts on the environment and human health. Using these conservative assumptions, when label-mandated application instructions and PPE procedures are followed, impacts on human health and the environment should be minor. Individuals with impaired liver function may be at greater risk than other members of the population because chlorophacinone is metabolized by liver mixed-function oxidases (i.e., the cytochrome P450 enzyme system) (NIH 2021).

In a study investigating *in-utero* (unborn offspring) exposure in rats, researchers found malformations in unborn rat offspring. A NOAEL of chlorophacinone exposure to unborn Sprague-Dawley rats could not be established. Based on this study, APHIS suggests that WS-certified applicators who are pregnant do not work with chlorophacinone and avoid areas treated with chlorophacinone.

Another area of potential uncertainty in this risk assessment is the potential for cumulative impacts on human health and the environment from the use of chlorophacinone in the WS program. Areas where cumulative impacts could occur are 1) repeated worker and environmental exposures to chlorophacinone from program application, 2) co-exposure to other chemicals with a similar mode of action, and 3) exposures to other chemicals affecting the toxicity of chlorophacinone. The Rozol Prairie Dog Bait label does not allow the use of other rodenticides containing anticoagulants in prairie dog towns during the treatment period allowed on the label (Liphatech 2017). Repeated exposures that could lead to increased risks of injury from accidental chlorophacinone exposure by WS applications are expected to be minimal due to strict WS applicator adherence to label-required PPE.

Due to WS' use of anticoagulant rodenticides in addition to chlorophacinone in its program to control rodents, WS personnel could potentially be exposed to multiple compounds of similar mechanisms of action. Since the Rozol Prairie Dog Bait label does not allow other rodenticides containing anticoagulants such as diphacinone to be used during the treatment period, co-

exposure to a single applicator during the application of chlorophacinone baits is likely reduced, although WS personnel could possibly treat one area with chlorophacinone and another with another anticoagulant. However, when the products are applied according to label requirements, workers' exposure and aggregate risks should be minimal.

Human health effects and environmental impacts of chlorophacinone in combination with other pesticide chemicals are not well understood. As a result, product label use requirements should be strictly followed, including the proper use of PPE when loading, applying, or handling chlorophacinone-containing products. The risk of public exposure to chlorophacinone should be minimal.

Chlorophacinone baits that are not consumed are retrieved from the field by WS applicators for certain application methods. Any unrecoverable baits left in the environment from WS use will begin to biodegrade, with a half-life of 47 days in soil (USEPA 2015e), which minimizes human risks and nontarget take.

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7 PREPARERS: WRITERS, EDITORS, AND REVIEWERS

7.1 APHIS WS Methods Risk Assessment Committee

Writers for "Use of Chlorophacinone in Wildlife Damage Management Risk Assessment":

Primary Writer: Andrea Lemay
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Experience: Ten years of experience conducting human toxicological research at Florida Agriculture and Mechanical University, University of Nebraska Medical Center, and Tulane University. Four years of experience conducting human health and environmental toxicological risk assessments and assisting environmental compliance programs at the Florida Department of Health, Commonwealth of Pennsylvania, and USDA.

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Writer: Thomas C. Hall
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Experience: Special expertise in wildlife biology, identification, ecology, and damage management. Thirty-seven years of service in APHIS Wildlife Services including operations and research in CO for research and OR, GU, CA, OK, and NV for operations conducting a wide variety of programs including bird damage research and management, livestock protection, invasive species management, wildlife hazard management at airports, property and natural resource protection including waterfowl, brown tree snake, feral swine, rodent, and beaver damage management. Applied and supervised chlorophacinone use.

Writer-editor: Luciana Paz

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Editors/Contributors for "Use of Chlorophacinone in Wildlife Damage Management Risk Assessment":

Editor: Shelagh DeLiberto
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Experience: Nine years of experience with APHIS WS NWRC preparing and reviewing vertebrate pesticide registration data submissions and other registration materials and providing pesticide regulatory guidance to WS, WS NWRC, and collaborators. Prior experience before joining APHIS includes seven years of conducting field and laboratory wildlife research at CSU, and environmental policy research for the U.S. Geological Survey.

Editor: Ryan Wimberly
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7.2 Internal Reviewers

USDA APHIS Wildlife Services

Reviewer: Katherine Horak
Position: USDA-APHIS-WS
Education: B.S. Mathematics, Biology, Northern Arizona University; Ph.D. Pharmacology and Toxicology, The University of Arizona
Experience: Fifteen years of experience with APHIS WS determining the risks of anticoagulant rodenticides to nontarget species. Expert in nontarget and ecological risk assessments

Reviewer: Jon Grant
Position: USDA-APHIS-WS, State Director, Albuquerque, NM
Education: BS Wildlife - Univ. Wisconsin, Stevens Point
Experience: Expertise in wildlife biology and wildlife damage management operations and research. Thirty years of service in APHIS Wildlife Services operational programs in WI and NM. Experience in a wide variety of damage management to include feral swine, livestock protection, bird damage, wildlife hazard management at airports. Have extensive experience applying and supervising the use of zinc phosphide.

Reviewer: Tom Halstead
Position: USDA-APHIS-WS, State Director Kansas
Education: BS Wildlife Management – University of Nebraska - Lincoln
Experience: Thirty three years experience with APHIS Wildlife Services in operations in Nebraska, Arizona, Washington and Kansas. Experienced in wildlife damage management techniques used for predation management, feral swine, bird damage, prairie dog management, and wildlife hazard management at airports. Have used and supervised the use of Rozol and zinc phosphide.

7.3 Peer Review

The Office of Management and Budget requires agencies to have peer review guidelines for scientific documents. The APHIS guidelines were followed to have "Use of Carcass Disposal in Wildlife Damage Management" peer reviewed. WS worked with the Association of Fish and Wildlife Agencies to have experts review the documents.

7.3.1 Peer Reviewers Selected by the Association of Fish and Wildlife Agencies

South Dakota Game, Fish, and Parks

Louisiana Department of Wildlife and Fisheries

Michigan Department of Natural Resources

7.3.2 Comments

1. While it is useful and appreciated that the risk assessment provided exposure information in non-target species from the ASPCA Animal Poison Control Center database and the USEPA Ecological Incident Data System, it would be beneficial to include information from state wildlife agencies that perform necropsies and ancillary diagnostic testing such as testing animals for anticoagulant residues. State veterinary diagnostic laboratories with a toxicology service will also have useful results that could be included in future risk assessments. Collectively, this will capture more information about exposure and toxicosis in free-ranging wildlife species.

Response: We appreciate this comment and agree that results from state veterinary diagnostic laboratories may be informative in terms of exposure of chlorophacinone to free-ranging wildlife species. However, state veterinary diagnostic laboratory testing results are not readily available without contacting individual laboratories for such

data. In addition, the Risk Assessment covers WS use and risk associated with the use of chlorophacinone, not the use of the product by the general public or other pesticide applicators. We provide the ASPCA Animal Poison Center and USEPA Ecological Incident Data System exposure information as a comparison to the exposure due to use by WS.

2. The WDM methods and activities are tracked in MIS, but take from Chlorophacinone is not always estimated. The risk assessment states that there are inherent challenges associated with counting the number of dead target and nontarget animals underground, but an estimate based on the number of acres or burrows should be recorded everytime. The risk assessment indicates that the quantity of bait applied is *always* recorded but the number of acres or burrows treated is *generally recorded.* This is an area that could be improved.

Response: WS records the amount of chlorophacinone and other pesticides used during each field application by entering the quantity of pesticide applied in the Management Information System (MIS), as described in Section 1.1. As also stated in Section 1.1, applications of Chlorophacinone are generally documented in the MIS system with a corresponding unit of measure (e.g., "acres treated") to help express how the quantity of pesticide was applied. Estimated take numbers for this risk assessment were based on the average occupancy of burrows by adults and young (number per burrow) or were estimated based on the expected number of target animals taken per pound of bait applied (number per lb.) or expected density (number per acre). These methods likely overestimate actual take numbers because they assume 100% take of the target animals assumed to be present and exposed. The take estimates have been provided for the Risk Assessment to inform the analysis of the exposure and risk based on WS use of Chlorophacinone. Estimates of take are not required under EPA registrations for pesticides.

Comments received not requiring a response.

1. The chlorophacinone review was very thorough and detailed. The author(s) methodically describe bait placement techniques and their reasoning. It was obvious that WS personnel go to great lengths to reduce exposure and subsequent impacts to non-target wildlife.

2. Non-target take, and accidental exposures were expounded upon at length. It was made clear in most of the cases that WS personnel were not involved in inappropriate bait placement actions, which resulted in non-target mortalities.

3. Methods of research pertinent to lethal dosages in various species and exposure methods were well explained, and the dosages were presented in an easily digestible and understandable fashion.

4. Clearly, the methodologies used for WDM via chlorophacinone are effective and about as safe as any landscape-level poison can be. Stressing methodologies to reduce non-target and human exposure is very important, and the author(s) touch on it multiple times throughout the document.

5. Upon reading this document, I had no ambiguities. All assumptions and uncertainties were clearly stated. Additionally, the large number of references, many directly related to

WDM via poisoning and the use of chlorophacinone, seemed quite adequate for the document.

6. This document provides a thorough review of the use of Chlorophacinone in wildlife damage management. We appreciate the opportunity to review this document and participate in the risk assessment reviews. The use pattern is clearly defined and includes direct hand baiting or using a tube or hose from a bait dispenser or a bait dispensing probe. Wildlife Services' use of Chlorophacinone is primarily through belowground application. The standard operating procedures and mitigations to prevent adverse impacts are defined and include PPE, above ground products limited to locations out of reach of children, pets, domestic animals, and non-target wildlife or in tamper-resistant bait stations, cleaning up spilled bait, not allowing applications near water or areas where surface water is present, not applying poison in areas where raptors are actively feeding on voles, and requiring the applicator to return to the site within 1-2 day intervals (over at least a two week period) to collect and dispose of bait and dead or dying rodents.

7. The review of secondary exposure of nontarget predators and scavengers is fairly comprehensive – likely because there is substantial field data relating to nontarget Chlorophacinone poisoning of wildlife. Chlorophacinone exposure in terrestrial mammals often results in high levels of mortality in most studies. Exposure in birds results in more moderate toxicity and sublethal effects such as decreased survival and reproduction. The report refers to numerous studies documenting that predators and scavengers may be attracted to areas with poisoned rodents because lethargic prey are easier to capture. The risk assessment included information from the USEPA Ecological Incident Data System documenting take of threatened and endangered species due to Chlorophacinone exposure, including bald and golden eagles and the San Joaquin kit fox. Fortunately, Wildlife Services states that they do not treat in areas where threatened and endangered species are likely to be impacted.

8. Assumptions and uncertainties are stated in the risk assessment, for example, acknowledging the exposure of nontarget animals that can access the burrow (predators and animals that share a burrow with the target species) but recognizing that this take is difficult to quantify. The risk assessment also identifies that there are uncertainties regarding toxicity information for all Chlorophacinone formulations, chronic and sublethal effects on nontarget wildlife species, effects of co-occurring toxic exposures, and cumulative or repeated impacts to people and animals. The selection of references in the risk assessment seemed appropriate.