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

Chapter XXXII

USE OF BROMETHALIN IN WILDLIFE DAMAGE MANAGEMENT

Draft

September 2024

Final

April 2025

Table of Contents

EXECUTIVE SUMMARY

Bromethalin is a neurotoxicant registered to control rodents under a variety of agricultural and nonagricultural uses. The United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Wildlife Services (WS) use bromethalin for invasive rodent control and eradication in island conservation projects. WS has also used bromethalin in bait stations at airports to reduce rodent prey availability for raptors, protect machinery and equipment from damage, and at a state and national historic landmark for rodent control to protect a seabird colony.

USDA APHIS evaluated the potential human health and ecological risks from the proposed use of four bromethalin products in its WS damage management program. APHIS is the registrant for two products labeled for island conservation, Bromethalin-100 Conservation Blocks and Bromethalin-100 Conservation Place Packs. These are restricted use pesticides for sale only to employees of federal agencies working on wildlife management projects for conservation purposes. They are to be used only by certified applicators or persons under their direct supervision. Bromethalin is acutely toxic through oral and inhalation exposure routes and moderately toxic through dermal exposure routes. It causes slight eye irritation and is not a dermal irritant or dermal sensitizer. Exposure is greatest for workers who handle and apply the bait; however, required personal protective equipment results in low potential for exposure and risk when factoring in available health effects. The potential exposure and risk to the public is low due to the use pattern and label restrictions that do not allow applications to food or feed crops.

Ecological risks to aquatic nontarget organisms from WS bromethalin use are negligible based on the use pattern, available toxicity data, and labeled mitigation measures designed to reduce exposure to aquatic habitats. Risks to terrestrial invertebrates and plants are also negligible based on available effects data and the method of application. Risk is greatest for terrestrial nontarget vertebrates, but these risks are reduced by the use pattern, and label requirements that reduce exposure and risk.

1 INTRODUCTION

Bromethalin is a rodenticide used by the U.S. Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS), Wildlife Services (WS) that can be used to control and eradicate invasive rodents for conservation purposes, as well as to control rodents in and around manmade structures. This human health risk assessment (HHRA) and ecological risk assessment (ERA) provide a qualitative evaluation of potential risks and hazards to human health and the environment, including nontarget fish and wildlife. The methods used for the human health risk assessment to evaluate potential human health effects follow standard regulatory guidance and methodologies and generally conform to other Federal agencies such as the U.S. Environmental Protection Agency (USEPA) (National Research Council 1983, USEPA 2016a). The methods used for the ecological risk assessment to assess potential ecological risk to nontarget fish and wildlife generally follow USEPA methodologies (USEPA 2016a).

This risk assessment uses a standard approach of first identifying the hazard during problem formulation. Next, the toxicity of the hazard is evaluated in the dose-response assessment, followed by the determination of potential exposure populations and pathways. Lastly, the toxicity and exposure assessment information are integrated into the risk characterization (determining if there is adverse human health and ecological risk). This risk assessment also includes a discussion of the uncertainties associated with the risk assessment and cumulative impacts.

1.1 Use Pattern of Bromethalin

Bromethalin is currently registered with the USEPA for the control of rats, mice, and other rodent species. WS uses four products in its wildlife damage management program. APHIS is the registrant for two of the products: Bromethalin-100 Conservation Blocks (USEPA Registration No. 56228-65) and Bromethalin-100 Conservation Place Packs (USEPA Registration No. 56228-66), which are currently labeled for the control and eradication of invasive rodents on islands for conservation purposes. Additionally, these products could potentially be used under supplemental labels for individual island projects in the future. The other two products (same formulations as the APHIS Bromethalin-100 Conservation products) that WS uses are Fastrac® All-Weather Blox® (Alternate brand name: F-trac All-Weather Blox®; USEPA Registration No.12455-95, Bell Laboratories, Inc.) and Fastrac® Place Pacs (Alternate brand name: F-trac Place Pacs; USEPA Registration No. 12455-97, Bell Laboratories, Inc.), which are labeled to control rats, mice, and meadow voles (Table 1).

Between fiscal years (FY) 2016 and 2020 (FY16–FY20), WS used Fastrac® All-Weather Blox® in an annual average of 3.6 work tasks in Oklahoma and Fastrac® Place Pacs in 0.2 work tasks in Virginia; tamper resistant bait stations were used for these applications (Table 2). The work tasks in Oklahoma were at an airport to reduce the risk of bird strikes with aircraft by removing rodent prey and to prevent damage to equipment and machinery. The work task in Virginia was at Fort Wool, a state and national historic landmark, to help with rodent control to protect a seabird colony from predation from rodents (VA DWR 2020).

WS applications are not for urban, suburban, or residential rodent control purposes. Currently, there is also no WS use in agricultural fields with applications directly to food or feed crops. WS currently use bromethalin for natural resource protection, and human health and safety (airports) purposes.

To date, WS has no records of known nontarget take because of bromethalin applications.

Table 1. Bromethalin formulations WS uses in its animal damage management program.

Product **Bromethalin 0.01% w/w** **Inert ingredients 99.99% w/w**	**Application Rate**	**Use Pattern**
Bromethalin-100 Conservation Blocks USEPA Registration No. 56228-65 EPA acceptance date: 7/15/2024 Label version: 56228-65-July-17-2025	Tamper-resistant bait stations and unsafe vessel and abandoned structure placement: • For rats: 2–12 blocks at an interval of approximately 16–328 ft (5–100 m) • For mice: 1–5 blocks at an interval of 10–65 ft (3–20 m) For rats and mice during canopy baiting: 2–12 blocks placed at intervals of less than or equal to (≤) 160 ft (≤49 m) For rats and mice during subterranean (belowground infrastructure) baiting: Place 2–12 blocks at intervals of 16–82 ft (5–25 m)	Eradicate Norway rats (*R. norvegicus*), roof rats (*R. rattus*), Polynesian rats (*R. exulans*), Asian house rats (*R. tanezumi*), house mice (*M. musculus*), or other types of non-native or invasive rodents on islands for conservation purposes, or on grounded vessels or vessels in peril of grounding.
Bromethalin-100 Conservation Place Packs USEPA Registration No. 56228-66 EPA acceptance date: 7/9/2024 Label version: 56228-66-July-17-2024	Tamper-resistant bait stations and unsafe vessel and abandoned structure placement: • For rats: 2–12 of the 0.53-ounce (oz) (15-gram (g)) place packs or 1–2 of the 3 oz (85 g) at an interval of approximately 16–328 feet (ft) (5–100 meters (m)) • For mice: 1–5 of the 0.53 oz (15 g) place packs or 1–2 of the 3 oz (85 g) place packs at an interval of 10–65 ft (3–20 m) for bait stations and 16–82 ft (5–25 m) for structure baiting For rats and mice during canopy baiting: 2–12 of the 0.53 oz (15 g) place packs or 1–2 of the 3 oz (85 g) place packs at intervals of less than or equal to (≤) 160 ft (≤49 m) For rats and mice during burrow baiting: Place 1 place pack per active burrow entrance	Eradicate Norway rats (*Rattus norvegicus*), roof rats (*R. rattus*), Polynesian rats (*R. exulans*), Asian house rats (*R. tanezumi*), house mice (*Mus musculus*), or other types of non-native or invasive rodents on islands for conservation purposes, or on grounded vessels or vessels in peril of grounding.
Fastrac® All-Weather Blox® USEPA Registration No. 12455-95 Bell Laboratories, Inc. Label acceptance date: 4/3/2017	For rats: 2–12 blocks per placement at intervals 15- to 30-ft (4.5-9 m) apart Bait station required for outdoor, above ground use. Tamper-resistant bait station required wherever children, pets, and nontarget mammals or birds may have access to bait placement location.	Control the following rodent pests in and around man-made structures: House mouse (*M. musculus*), Norway rat (*R. norvegicus*), roof rat (*R. rattus*), cotton rat (*Sigmodon hispidus*), Eastern harvest mouse (*Reithrodontomys humuli*), golden mouse (*Ochrotomys nuttalli*), Polynesian rat (*R.*

Product Bromethalin 0.01% w/w Inert ingredients 99.99% w/w	**Application Rate**	**Use Pattern**
Label version: 121218/04-17	For mice and voles: One bait block per placement (two blocks for extremely high rodent activity) at intervals 8- to 12-ft (2.4-3.7 m) apart	*exulans*), meadow vole (*Microtus pennsylvanicus*), white-throated woodrat (*Neotoma albigula*), Southern plains woodrat (*N. micropus*), and Mexican woodrat (*N. mexicana*) (see footnote 1)
Fastrac® Place Pacs USEPA Registration No. 12455-97 Bell Laboratories, Inc. Label acceptance date: 12/13/2019 Label version: 010320/12-19	Bait station required for outdoor, above ground use. Tamper-resistant bait station required wherever children, pets, and nontarget mammals or birds may have access to bait placement location. For rats: 2–12 0.53 oz (15 g) pacs or 1–2 3.0 oz (85 g) pacs at intervals 15- to 30-ft (4.5-9 m) apart For mice and meadow voles: One 0.53 oz (15 g) or 3.0 oz (85 g) pac at intervals of 8- to 12-ft (2.4-3.7 m) apart (two pacs in extremely high rodent activity at both application rates)	Control the following rodent pests in and around man-made structures: House mouse (*M. musculus*), Norway rat (*R. norvegicus*), roof rat (*R. rattus*), cotton rat (*S. hispidus*), Eastern harvest mouse (*R. humuli*), golden mouse (*O. nuttalli*), Polynesian rat (*R. exulans*), meadow vole (*M. pennsylvanicus*), white-throated woodrat (*N. albigula*), Southern plains woodrat (*N. micropus*), and Mexican woodrat (*N. mexicana*)[1]. This product must be used in and within 100 feet (30 m) of man-made structures.

[1]The label does not permit use against the following species in California: cotton rat, Eastern harvest mouse, golden mouse, Polynesian rat, meadow vole, white-throated woodrat, Southern plains woodrat, and Mexican woodrat.
References: (USEPA 2017;2019;2023e;a)

Table 2. The annual average number of target rodents killed with bromethalin by WS in WDM activities for FY16 to FY20 throughout the United States and the pounds of bromethalin used. No known nontarget take occurred during this time.

Formulation	Species	States Used	Take	Pounds Bait*
Fastrac® All-Weather Blox®	Brown rat	OK	41	1.2
Fastrac® All-Weather Blox®	House mouse	OK	25	0.8
Fastrac® All-Weather Blox®	White-footed deer mouse	OK	20	0.4
Fastrac® Place Pacs	Brown rat	VA	35	0.6
Annual Average Take and Use	**3 species**	**2 states**	**121**	**3.0**

*3 pounds (lb.) of bait equals 0.0003 lb. active ingredient.

2 PROBLEM FORMULATION

The following sections discuss physical and chemical properties, environmental fate, and hazard identification for bromethalin.

2.1 Physical and Chemical Properties

Bromethalin (synonym: N-Methyl-2,4-dinitro-N-(2,4,6-tribromophenyl)-6-(trifluoromethyl)benzenamine, molecular formula: $C_{14}H_7Br_3F_3N_3O_4$, CAS No. 63333-35-7) is an organic compound with a molecular weight of 577.93 grams per mol (g/mol) and a molecular structure shown in Figure 1 (NCBI 2024).

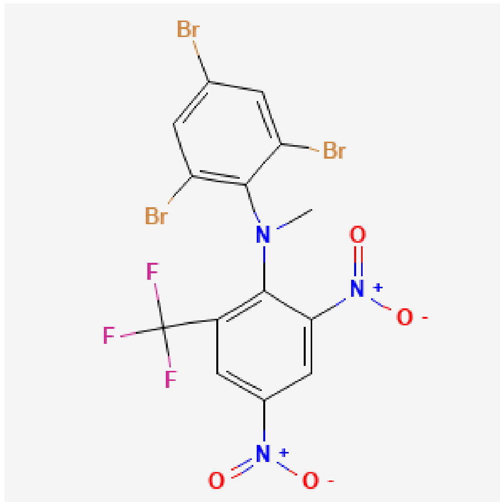

Figure 1. Chemical structure for bromethalin (NCBI 2024).

Bromethalin is a pale white, odorless crystalline solid at 25 degrees Celsius (˚C) with a melting point of 150–151˚C (USEPA 2016b, NCBI 2024). It is insoluble in water (less than 0.01 milligrams/Liter (mg/L) at 20˚C) (USEPA 2016b, NCBI 2024). It has a bulk density of 2.065 g/cubic centimeter (cm^3) (USEPA 2016c) and a relative density (specific gravity) of 1.36 g/milliliter (ml) (USEPA 2016b). It has a vapor pressure of 9.7 x 10^{-8} millimeter of mercury (mm Hg) (0.013 megapascal (mPa)) at 25˚C (NCBI 2024). The calculated Henry's Law constant at 25˚C is 3.7 x 10^{-5} to 7.4 x 10^{-4} atm m^3/mol (USEPA 2016b). Its acid dissociation constant (pKa) is 9.0 (NCBI 2024) and its octanol water partition coefficient at pH of 7 and 20˚C is 4.79 x 10^7 (log P_{ow} = 7.68) (USEPA 2016b) (the log P_{ow} of 7.62 is also reported (USEPA 2016c)). The organic carbon (OC) adsorption constant (K_{oc}) is 55,000 ml/g_{oc} (USEPA 2016b).

2.2 Environmental Fate

Environmental fate describes the processes by which chemicals move and degrade in the environment. The environmental fate processes include 1) persistence, degradation, and mobility in soil; 2) movement to air; 3) migration potential to groundwater and surface water; 4) degradation in water; and 5) plant uptake.

Bromethalin is considered insoluble and hardly mobile in soil (USEPA 2016b). It has a low migration potential to surface water and groundwater. It is stable to hydrolysis (USEPA 2016b). Bromethalin is persistent, with a half-life of 132 to 235 days in an aerobic soil metabolism study; desmethylbromethalin was a major degradate of bromethalin (USEPA 2016b). Desmethylbromethalin appears to be persistent; however, its mobility is not known (USEPA 2016b).

Bromethalin has a low vapor pressure and low Henry's Law Constant, suggesting low potential for volatilization into the atmosphere from soil and water. There was a 50% decrease in bromethalin concentration following a 2–3-hour exposure to a 75-watt incandescent lamp, indicating photodegradation may be an important dissipation route (Dorman et al. 1990).

However, the concentration of desmethylbromethalin was minimally decreased with less than a 10% loss during 8 hours of light exposure (Dorman et al. 1990).

The non-island conservation product labels for bromethalin require outdoor, above-ground applications to be in weather-resistant bait stations (USEPA 2017;2019;2023e;a). This use pattern and the minimal leaching potential of bromethalin indicate that both the parent compound and its degradate are unlikely to leach in soil and water (USEPA 2016b).

The potential uptake of bromethalin by plants is low since bromethalin is applied as a bait and not available to plants. Any bromethalin that may be left in the soil due to degradation of the baits is not expected to be available for plant uptake since bromethalin binds to soil organic matter and is not available for uptake. In addition, most of the bait is expected to be removed by the target species, reducing the amount of bromethalin available for any potential plant uptake.

Bromethalin has the potential to bioaccumulate/bioconcentrate in aquatic environments based on its high K_{ow} (7.62). The bioconcentration factor is 120,000 in whole fish (USEPA 2020b).

2.3 Hazard Identification

Bromethalin is a non-anticoagulant rodenticide. It is a neurotoxicant that affects the central nervous system. Common toxicity symptoms include nausea, vomiting, lethargy, abdominal pain, diarrhea, headache, ocular irritation/pain, dermal irritation/pain, dizziness, agitation, tachycardia, and other symptoms (Feldman et al. 2019).

The bromethalin formulations that WS uses contain 0.01% weight-by-weight (w/w) bromethalin. Pesticide label statements regarding the human health effects based on toxicity studies for these bait formulations include the signal word "CAUTION" and the standard label hazard statements "*Harmful if swallowed."* and *"Keep away from children, domestic animals, and pets."* (USEPA 2017;2019;2023e;a).

USEPA (2008) published the Risk Mitigation Decision (RMD) for Ten Rodenticides to minimize exposure to children and ecological systems, including wildlife. In this decision document, the four second-generation anticoagulants were prohibited for use in residential consumer products. USEPA expected an increase in the consumer (residential) use of bromethalin after second-generation anticoagulants became unavailable.

Huntington et al. (2016) evaluated bromethalin exposures reported to the California Poison Control System (CPCS) between 1997 and 2014. Their search criteria included single substance human exposure, resulting in 126 cases matched their criteria. Most exposures (89 incidents; 70.6%) occurred in children younger than 5 years of age, mostly because of exploratory oral exposure. Most patients had no effects post exposure (113 patients; 89.7%), while 10 patients (7.9%) had minor symptoms, mostly gastrointestinal upset that was self-limiting. None of the cases resulted in moderate, major, or fatal effects. For most of the cases, the ingested dose was unavailable. However, the approximate ingested dose was available in six cases, ranging from 0.067 mg/kilogram (kg) to 0.3 mg/kg. A no dose-symptom threshold could be established from the data.

Feldman et al. (2019) analyzed bromethalin exposures reported to the American Association of Poison Control Centers (AAPCC) National Poisoning Data System (NPDS) between 2008 and 2017. There were 7,140 single or multi-substance exposures. The number of exposure incidents increased 114%, from 561 incidents in 2008 to 1,203 in 2017. Only 2,674 incidents met their inclusion criteria of single substance followed by a known medical outcome. Of these, 2,227 (83%)

incidents involving pediatric-aged patients (16 days to 12 years). The outcomes for pediatric patients were 95% had no effect, 3% had minor effects, and 0.45% had moderate effects. No major effects or deaths occurred within this group. In the 56 patients of unknown age, about 2% had major effects and the remaining 98% had moderate, minor, or no effects. No major effects or deaths occurred in unknown-age group. Exposures in patients ages 13–94 (391 adults and adolescents) resulted in no effect in 66%, minor effects in 26%, moderate effects in 6%, and major effects in 2%. Two (0.51%) patients in this age group died. Of the adult and adolescent patients, 186 (about 48%) were intentional exposures. Within the intentional exposures, one death occurred, 4 patients had major effects, and the remaining had minor, moderate, or no effects. The only other death was coded as unknown reason for exposure. The more common symptoms included nausea, vomiting, lethargy, and abdominal pain. Most of the effects lasted for less than 24 hours, but some symptoms lasted up to 3 days. Two of the major effects ranged 3 days to 1-month in duration; however, two incidents involved coagulopathy or prothrombin time prolongations suggesting a possible miscode for the active ingredient involved. The authors conclude that the overall single substance exposure incidents reported in the NPDS suggest a low incidence of major adverse effects or death from incidental ingestion of bromethalin. In addition, the rate of serious effects was also low among intentional ingestions.

The USEPA Health Effects Division (HED) completed an updated analysis of exposure incidents for eleven anticoagulant and non-anticoagulant rodenticides and summarized exposure incidents since the RMD was published (USEPA 2022). USEPA reviewed the Incident Data System (IDS), the AAPCC, The Center for Disease Control's National Institute for Occupational Safety and Health (NIOSH) Sentinel Event Notification System for Occupational Risk (SENSOR)-Pesticides database, and the California Pesticide Illness Surveillance Program (PISP) for rodenticide human exposure incidents, including exposure to bromethalin (USEPA 2022).

In the Main IDS, from January 1, 2015, to July 12, 2019, 37 incidents were reported that involved bromethalin, 35 of which involved bromethalin as the single active ingredient. Two incidents resulted in death (suicide). Two were classified as major severity and 31 incidents were classified as moderate severity. The Aggregate IDS during the same time period contained 195 incidents reported, all classified as minor severity (USEPA 2022)[1].

In the state-level SENSOR-Pesticides incident data from 2011–2015, Texas reported one incident classified as moderate severity involving an occupational exposure to bromethalin. The worker was handling several pesticides, including bromethalin, for 2–3 days prior to his symptoms; he indicated he had inhaled fumes. His symptoms included a burning feeling in his lungs, chest pain, burning sensation and pressure in his back and a cough (USEPA 2022).

Pasquale-Styles et al. (2006) published a case study involving the intentional ingestion of a bromethalin-based rodenticide by a 21-year-old male. The patient self-reported ingesting approximately 17 mg bromethalin (equivalent to 0.33 mg bromethalin/kg). The patient died 7 days after self-reporting. His clinical signs prior to death included altered mental status, lethargy, increased cerebrospinal fluid pressure, and swelling of the brain.

[1] USEPA does not guarantee the completeness or adequacy of the contents of the IDS (USEPA 2022). Pesticide Registration Incident Data System US Environmental Protection Agency https://www.epa.gov/pesticide-incidents/about-incident-data-system-ids

WS has had no "Adverse Incident Reports" under FIFRA (6(a)2) since APHIS became a registrant of bromethalin products in August 2023.

2.3.1 Mechanism of Action and Metabolism

Bromethalin is a nerve toxicant that damages the central nervous system resulting in paralysis, convulsions, respiratory distress, and death (USEPA 2020a). Bromethalin and its metabolite desmethylbromethalin work by uncoupling the metabolic process of oxidative phosphorylation which causes a decrease in adenosine triphosphate (ATP) production leading to the disruption of sodium-potassium gradient regulation within cells (Van Lier and Cherry 1988). This osmotic imbalance and the accumulation of fluid within the central nervous system causes damage to the central nervous system resulting in neurologic signs and death at lethal doses (Van Lier and Cherry 1988).

In a pharmacokinetic study in rats, bromethalin had a plasma half-life of 134 hours (5.6 days) (USEPA 2020a). In this study, blood samples were taken from the orbital sinus at several hour increments for the first 24 hours and at 2, 3, 4, 6, 8, 11, 14, 17, and 21 days after dosing. The major metabolite of bromethalin was desmethylbromethalin (Van Lier and Cherry 1988, USEPA 2016c), and was detected in the blood and liver samples (USEPA 2020a). Studies indicate the metabolite desmethylbromethalin is the activated form responsible for most of the neurotoxicity of bromethalin to mammals (Van Lier and Cherry 1988). This study did not provide any additional information on the absorption, distribution, metabolism, or excretion of bromethalin (USEPA 2016c;2020a).

2.3.2 Toxicity

The acute oral and inhalation median lethality values (LD_{50} and LC_{50}) in the rat indicate that technical bromethalin is highly toxic (USEPA toxicity category I) (USEPA 2020a). Technical bromethalin has moderate acute dermal toxicity in the rabbit (toxicity category III). It causes slight eye irritation (toxicity category III/IV) and is not a dermal irritant (toxicity category IV). It is also not a dermal sensitizer (Table 3).

Table 3. Acute and subacute toxicity data of technical bromethalin and 0.01% w/w bromethalin bait formulations to select mammals.

Test Species	Test	Technical Bromethalin	USEPA Toxicity Category	Bromethalin Bait (0.01% w/w)	USEPA Toxicity Category
Laboratory Brown Rat	Acute Oral LD_{50}	10.7 mg/kg-body weight (bw) (male) 9.1 mg/kg-bw (female)	I	>5,000 mg/kg-bw	Not assigned
Laboratory Brown Rat	Oral LD_{50}	2.11 mg/kg-body weight (bw) (male) 3.17 mg/kg-bw (female) 2.57 mg/kg-bw (both sexes)	I	-	-
Domestic Rabbit	Acute Dermal LD_{50}	2,000 mg/kg-bw	III	>5,001 mg/kg-bw	Not assigned
Laboratory Brown Rat	Acute Inhalation LD_{50}	0.024 mg/L	I	No effect at maximum obtainable concentration	Not assigned
Domestic Rabbit	Acute Eye Irritation	Slight irritation	III/IV	Not an irritant	Not assigned

Test Species	Test	Technical Bromethalin	USEPA Toxicity Category	Bromethalin Bait (0.01% w/w)	USEPA Toxicity Category
Domestic Rabbit	Acute Dermal Irritation	Not an irritant	IV	Not an irritant	Not assigned
Guinea Pig	Dermal Sensitization	Not a sensitizer	Not applicable	Not a sensitizer	Not assigned

Reference: (Jackson et al. 1982, USEPA 2016c, Bell Laboratories 2020)

2.3.3 Sub-chronic/Chronic Toxicity

In 90-day oral toxicity studies in rats and dogs, bromethalin at doses of 0, 5, 25, or 125 mg/kg-bw/day (the dog study also evaluated the dose of 200 mg/kg-bw/day) resulted in a no observed adverse effect level (NOAEL) of 25 mg/kg-bw/day and a lowest observed adverse effect level (LOAEL) of 125 mg/kg-bw/day based on spongy degeneration in several regions of the brain and thoracic spinal cord in male and female rats and dogs, and degeneration in the optic nerve of male rats and dogs (USEPA 2016c).

USEPA (2020a) waived sub-chronic dermal and inhalation toxicity studies for bromethalin, based on the weight of evidence approach, considering the mode of action and the toxicity profile is well understood.

2.3.4 Developmental and Reproductive Effects

USEPA (2020a) waived the reproduction and fertility study based on the weight of evidence approach and consideration of the available hazards and exposure information.

A prenatal development toxicity study in which rats were administered bromethalin at 0, 0.1, 0.3, or 0.5 mg/kg-bw/day (route of exposure unknown), the maternal NOAEL and LOAEL were 0.3 and 0.5 mg/kg-bw/day, respectively, based on hindlimb weakness, decreased muscle tone, and other clinical signs. From this study, the developmental NOAEL was 0.5 mg/kg-bw/day, and the developmental LOAEL was greater than 0.5 mg/kg-bw/day (not established) (USEPA 2016c).

The prenatal developmental toxicity study in rabbits administered bromethalin at 0, 0.1, 0.25, or 0.5 mg/kg-bw/day (route of exposure unknown) resulted in a maternal NOAEL of 0.1 mg/kg-bw/day and a maternal LOAEL of 0.25 mg/kg-bw/day based on clinical signs including nasal discharge, loss of muscle tone, weakness, decreased respiration, abortion, death, and other clinical signs (USEPA 2016c). The developmental NOAEL in the rabbit was 0.5 mg/kg-bw/day, and the developmental LOAEL was greater than 0.5 mg/kg-bw/day (not established) (USEPA 2016c).

In both the rat and rabbit developmental toxicity studies, abortions and maternal deaths were observed at the highest dose tested; no developmental effects were observed in either species apart from abortion at the high-dose level.

2.3.5 Neurotoxicity and Immunotoxicity Effects

USEPA (2016c) waived the acute and sub-chronic neurotoxicity studies and the immunotoxicity study for bromethalin, considering the available toxicity and exposure information.

In an acute neurotoxicity study in rats administered bromethalin at 0, 1.5, and 3.0 mg/kg-bw that USEPA (2016b) deem unacceptable, but upgradeable with rationale for vehicle choice and volume used, test material stability in mineral oil, and body temperature measurements, the NOAEL was 3.0 mg/kg-bw and the LOAEL was greater than 3.0 mg/kg-bw (not determined).

2.3.6 Carcinogenicity and Mutagenicity

In a bacterial reverse mutation test, bromethalin induced a dose-related increase in mutation frequency in four strains of *Salmonella typhimurium* with or without metabolic activation (USEPA 2016c). In an *in vitro* mammalian cell gene mutation test (mouse lymphoma cells) and an unscheduled DNA synthesis in mammalian cells in culture test (rat hepatocytes), bromethalin did not induce mutations, but showed concentration dependent cytotoxicity (USEPA 2016c). In the *in vivo* sister chromatid exchange test in Chinese hamsters at 0, 1.25, 2.5, 5, or 10 mg/kg-bw, bromethalin did not induce sister chromatid exchange, but did cause cytotoxicity and fatalities at the highest dose levels tested (USEPA 2016c).

USEPA (2020a) waived the *in vivo* chromosomal aberration study, based on the weight of evidence approach. A carcinogenicity study was also not required during EPA's registration review. The labels for the formulations WS use are for non-crop uses and do not allow applications to water resources, indicating a lack of exposure through food and drinking water.

2.3.7 Endocrine System Effects

An Endocrine Disruptor Screening Program (EDSP) was developed to characterize endocrine activity in commercial products, pesticides, and environmental contaminants (USEPA 2023c). EDSP uses a two-tier risk characterization approach consisting of screening candidate compounds for estrogen, androgenic, and thyroid receptor activity and quantifying their impact on environmental and human health (USEPA 2023c). Before 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, the 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. Although bromethalin is listed in the EDSP Universe of Chemicals (USEPA 2012;2023b), it was not screened for estrogen receptor bioactivity.

A literature search did not identify any mammalian studies indicating the potential of bromethalin to affect the endocrine system. Bromethalin is not among the group of pesticide active ingredients on the initial and secondary lists to be screened under the USEPA EDSP (USEPA 2024a). However, both lists were generated based on exposure potential and not whether the pesticide is a known or likely chemical to disrupt the endocrine system (USEPA 2024a). Bromethalin is not on the European Union (EU) list of chemicals with the potential to impact the endocrine system (ECHA 2023, The Danish Environmental Protection Agency 2024). The EU list includes three categories: Category 1 – endocrinal effect recorded at least on one type of animal; Category 2 – a record of biological activity *in vitro* leading to disruption; and Category 3 – not enough evidence or no evidence data to confirm or disconfirm endocrinal effect of tested chemicals (Hrouzková and Matisova 2012).

2.3.8 Toxicity of Other Ingredients

The other 99.99 percent of the bromethalin product formulations are other (inert) ingredients (USEPA 2017;2019;2023e;a). The identity and safety profile of the inert ingredient contents of bromethalin bait formulations are not presented on labels or safety data sheets (SDS). The SDSs for Fastrac® All-Weather Blox® and Fastrac® Place Pacs indicate the inert ingredients do not meet the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) hazard criteria for inclusion on the SDSs (Bell Laboratories 2020;2024). The inert ingredients in pesticide products are considered confidential business information and not generally available to the public. However, they still must be approved inert ingredients for non-food use pesticides by USEPA (2023d).

3 DOSE-RESPONSE ASSESSMENT

3.1 Human Health Dose-Response Assessment

A dose-response assessment evaluates the dose levels (toxicity criteria) for potential human health effects, including acute and chronic toxicity. USEPA did not establish an oral reference dose for bromethalin because it does not believe that there is a potential for significant exposure to occupational workers (USEPA 2016c).

For the dermal short-term (1–30 days), dermal intermediate-term (1–6 months), inhalation short-term, and inhalation intermediate-term, the non-occupational and occupational level of concern (LOC) for margin of exposure (MOE) of 100 (an acceptable MOE value) is based on an uncertainty factor (UF) of 10x for extrapolation from animal to human (interspecies) and UF of 10x for potential variation in sensitivity among members of the human population (intraspecies) (USEPA 2016c). USEPA (2016c) used a NOAEL of 0.1 mg/kg/day from the developmental toxicity study in rabbits described above for its dermal short-term and inhalation short-term exposure scenarios. For the dermal intermediate-term and inhalation-intermediate-term exposure scenarios, USEPA (2016c) used a NOAEL of 0.025 mg/kg/day from the oral sub-chronic study in dogs described above. USEPA did not establish a tolerance for bromethalin because there is no registered food or feed uses. The maximum contaminant level for drinking water has not been established. USEPA uses a conservative dermal short- and intermediate-term dermal absorption factor of 10% for bromethalin (USEPA 2016c).

3.2 Ecological Effects Analysis

This section summarizes available bromethalin toxicity data for aquatic and terrestrial species. Data searches included the primary literature, unpublished reports, and databases to find representative effects data for aquatic and terrestrial species.

3.2.1 Aquatic Effects Analysis

Bromethalin is highly toxic to freshwater fish based on acute exposure (USEPA 2016b) (Table 4). Acute LC_{50} values range from >38 µg/L for rainbow trout (*Oncorhynchus mykiss*) and 561 µg/L for bluegill *(Lepomis macrochirus*). However, USEPA (2016b) notes the toxicity endpoints are above the water solubility of bromethalin. Toxicity data for amphibians and marine fish species is unavailable; however, available data for freshwater fish show that bromethalin would be toxic to both groups. Chronic toxicity of bromethalin to aquatic organisms is unavailable (USEPA 2016b).

Bromethalin is considered very highly toxic to aquatic invertebrates based on the available toxicity data for the freshwater cladoceran, *Daphnia magna*. The reported median effective concentration (EC_{50}) is 5.53 µg/L (Table 4) (USEPA 2016b). Marine invertebrate toxicity is unavailable; however, bromethalin is considered toxic to marine invertebrates based on its toxicity to *D. magna*.

No toxicity data is available for aquatic plants. The mode of action for bromethalin suggests low toxicity to aquatic plants. Additionally, its low solubility in water suggests it would not be bioavailable to aquatic plants in quantities that could result in adverse effects.

Table 4. Bromethalin toxicity in aquatic species.

Test Species	Scientific Name	LC_{50}/EC_{50} (µg/L)	Reference
Freshwater Cladoceran	*Daphnia magna*	5.53 (very highly toxic)[1]	(USEPA 2016b)
Freshwater Cladoceran	*D. magna*	27[2]	(Jackson et al. 1982, Van Lier and Cherry 1988)
Rainbow trout	*Oncorhynchus mykiss*	>38 (very highly toxic)[1]	(USEPA 2016b)

Test Species	Scientific Name	LC_{50}/EC_{50} (µg/L)	Reference
Rainbow trout	*O. mykiss*	>33 and <80[2]	(Jackson et al. 1982, Van Lier and Cherry 1988)
Bluegill	*Lepomis macrochirus*	561 (highly toxic)[1,2]	(USEPA 2016b)
Bluegill	*L. macrochirus*	120[2]	(Jackson et al. 1982, Van Lier and Cherry 1988)

[1] USEPA classifies these as supplemental studies due to study deficiencies.
[2] All aquatic LC_{50} values were obtained by introducing bromethalin into the test media with acetone, which allowed the true water solubility of bromethalin (less than 10 ppb) to be exceeded (Jackson et al. 1982). The no-effect levels were also equal to or greater than the water solubility of bromethalin. Jackson et al. (1982) concluded that a significant aquatic environmental hazard does not exist with the use of bromethalin.

3.2.2 Terrestrial Effects Analysis

This section of the ecological effects analysis summarizes available bromethalin terrestrial toxicity data for mammals, birds, reptiles, and amphibians. This section also summarizes available effects data for terrestrial invertebrates and plants.

3.2.2.1 Mammals

Bromethalin is considered very highly acutely toxic to mammals in oral exposures (Table 5). Acute dermal and inhalation toxicity is also high for mammals (Table 3). Sub-chronic exposure (0.125 mg/kg-bw/day) in rats caused spongy degeneration of white matter in the central nervous system (USEPA 2016b). Sublethal signs of toxicity in the rat include hind-limb weakness, paralysis, lethargy, and at higher doses, convulsions (Van Lier and Cherry 1988). Following a single oral dose of 6.25 mg/kg-bw, dogs displayed tremors, seizures, depression, and hyperexcitability (Dorman et al. 1990).

Short- and long-term exposure to bromethalin also results in various sublethal effects that are summarized in Sections 2.3.3 through 2.3.8 of this risk assessment.

Table 5. Bromethalin toxicity to mammals.

Test species	Scientific Name	Test	Value	Reference
Domestic Cat	*Felis catus*	Acute oral	LD_{50} = 1.8 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Domestic Dog	*Canis familiaris*	Acute oral	LD_{50} = 4.7 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Guinea pig	*Cavia porcellus*	Acute oral	LD_{50} >1,000 mg/kg-bw[1]	(Van Lier and Cherry 1988)
Domestic Rabbit	*Oryctolagus cuniculus*	Acute oral	LD_{50} = 13.0 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Domestic Rabbit (Dutch belted)	*O. cuniculus*	Chronic	NOAEC[2] = 3.3 mg/kg-diet LOAEC[3] = 8.25 mg/kg-diet	(USEPA 2016b)
Laboratory Brown Rat	*Rattus norvegicus*	Acute oral	LD_{50} = 2.11 mg/kg-bw (males) and 3.17 mg/kg-bw (females) (very highly toxic)	(USEPA 2020b)

Test species	Scientific Name	Test	Value	Reference
Laboratory Brown Rat	*R. norvegicus*	Acute oral	LD_{50} = 2.0 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Laboratory Brown Rat	*R. norvegicus*	Acute oral	LD_{50} = 2.46 mg/kg-bw (males) and 2.01 mg/kg-bw (females)	(Jackson et al. 1982)
Wild-caught Brown Rat	*R. norvegicus*	Acute oral	LD_{50} = 6.6 mg/kg-bw	(Jackson et al. 1982)
Laboratory Brown Rat	*R. norvegicus*	Subacute dietary	LC_{50} = 5.5 mg/kg-diet (very highly toxic)	(USEPA 2020b)
Laboratory Brown Rat	*R. norvegicus*	Sub-chronic oral	NOAEL[4] = 0.025 mg/kg/day LOAEL[5] = 0.125 mg/kg/day (endpoint: spongy degeneration of central nervous system)	(USEPA 2016b)
Rhesus monkey	*Macaca mulatta*	Acute oral	LD_{50} = 5.0 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Laboratory House Mouse	*Mus musculus*	Acute oral	LD_{50} = 5.3 mg/kg-bw	(Van Lier and Cherry 1988)
Laboratory House Mouse	*M. musculus*	Acute oral	LD_{50} = 5.25 mg/kg-bw (males) and (8.13 mg/kg-bw (females)	(Jackson et al. 1982)

[1]The guinea pig LD_{50} testing the metabolite, desmethlybromethalin, was reported as 7.5 mg/kg. [2]No observable adverse effect concentration. [3]Lowest observable adverse effect concentration. [4]No observable adverse effect level. [5]Lowest observable adverse effect level.

Van Lier and Ottosen (1981) evaluated the effects of secondary exposure to bromethalin in domestic dogs. In a one-day exposure study, domestic dogs were fed 600 grams of meat obtained from rats that fed on bromethalin bait at a concentration of 0.005% w/w. No signs of toxicity and no deaths were reported (Van Lier and Ottosen 1981). WS currently uses products that contain 0.01% w/w bromethalin and there are other registered products that contain 0.025% w/w, so the lack of effects noted in the dog study does not consider exposures at higher residue levels and over longer exposures.

3.2.2.2 Birds

Bromethalin is very highly toxic and highly toxic to birds in acute oral exposure and subacute dietary exposure, respectively. Bobwhite (*Colinus virginianus*) has an acute oral toxicity (LD_{50}) of 4.56 mg/kg-bw and acute dietary (LC_{50}) of 210 mg/kg-diet (Table 6) (USEPA 2020b). Bromethalin toxicosis in birds can include paraparesis that progresses to tetraparesis, ataxia, and dysphagia (Seguel et al. 2022). No chronic toxicity studies are available (USEPA 2020b).

Table 6. Bromethalin toxicity to birds.

Test species	Scientific Name	Test	Reference
Mallard	*Anas platyrhynchos*	LC_{50} = 620 mg/kg-diet	(Jackson et al. 1982, Van Lier and Cherry 1988, USEPA 2016b)
Northern Bobwhite	*Colinus virginianus*	LD_{50} = 4.6 mg/kg-bw	(Jackson et al. 1982, Van Lier and Cherry 1988)
Northern Bobwhite	*C. virginianus*	LC_{50} = 210 mg/kg-diet	(Jackson et al. 1982, Van Lier and Cherry 1988)

Test species	Scientific Name	Test	Reference
Northern Bobwhite	*C. virginianus*	LD_{50} = 4.56 mg/kg-bw (very highly toxic)	(USEPA 2016c;2020b)
Northern Bobwhite	*C. virginianus*	LC_{50} = 210 mg/kg-diet (highly toxic)	(USEPA 2016c;2020b)

3.2.2.3 Reptiles and Amphibians (terrestrial phase)
No toxicity data appears to be available for terrestrial phase amphibians and reptiles after a literature review. USEPA uses bird toxicity data as a surrogate for sensitivity to reptiles. Using birds as a surrogate, bromethalin is assumed to be highly toxic to reptiles and amphibians.

3.2.2.4 Terrestrial Invertebrates and Microorganisms
Data is limited on the toxicity of bromethalin to terrestrial invertebrates and microorganisms (USEPA 2016b). No effect was observed in earthworms exposed to 100 mg/kg-soil (Jackson et al. 1982, Van Lier and Cherry 1988).

3.2.2.5 Terrestrial Plants
No toxicity data appears to be available testing the effects of bromethalin on terrestrial plants (USEPA 2016b). Acute and chronic adverse effects on terrestrial plants are not anticipated based on the mode of action of bromethalin and a lack of a similar pathway in plants.

4 EXPOSURE ASSESSMENT

4.1 Human Health Exposure Assessment
WS uses four bromethalin formulations in its wildlife damage management program. Two formulations, Bromethalin-100 Conservation Blocks and Bromethalin-100 Conservation Place Packs (together referred to as Bromethalin-100 Conservation labels or products in this risk assessment), are labeled for use on islands for the control and eradication of invasive rodents for conservation purposes. The Bromethalin-100 Conservation products are restricted use pesticides. The Bromethalin-100 Conservation labels instruct that the products are available for retail sale only to employees of federal agencies working on wildlife management projects for conservation purposes to be used only by certified applicators or persons under their direct supervision and only for those uses covered by the certified applicator’s certification. The Fastrac® All-Weather Blox® and Fastrac® Place Pacs (together referred to as Fastrac® labels or products in this risk assessment) are general use “consumer” products.

Exposure assessments estimate the potential exposure of humans to bromethalin because of WS applications. An identified exposure pathway for bromethalin includes (1) a release from a source, (2) an exposure point where contact can occur, and (3) an exposure route such as ingestion, inhalation, or dermal contact by which contact can occur (USEPA 1989). Exposures for the identified human populations are qualitatively evaluated for each identified exposure pathway.

The application methods and use sites listed on the two Bromethalin-100 Conservation product labels are similar. Both products are currently labeled to control or eradicate invasive rodents on islands for conservation purposes. Tamper-resistant bait stations are used within and around man-made structures, non-crop areas, including canopies of trees and shrubs, and on uninhabited grounded vessels or vessels in peril of grounding. Floating tamper-resistant bait stations must be tethered and used in intertidal zones or subterranean spaces where the water is calm. Floating bait stations are not allowed to contain bait during stormy weather. EPA defines tamper-resistant bait station criteria. The criteria include: 1) resistance to destruction or weakening by elements of typical non-catastrophic weather, 2) strong enough to prohibit entry or destruction by dogs and children or stronger if in areas frequented by hoofed livestock, raccoons, bears, or other potentially destructive animals, 3) capable of being sealed or locked, 4) capable of being anchored to resist efforts to move the station or displace its contents, 5) equipped with internal structures for containing baits and minimizing spillage, 6) equipped with rodent entrances that allow target animals to access baits but deny access to nontarget species and discourage entry by birds, 7) capable of displaying precautionary statements in a prominent location, and 8) made of a design and color that is not especially attractive to children (USEPA 2024b). For structures and vessels that are unsafe to access, the Bromethalin-100 Conservation labels allow the place packs or blocks to be thrown, dropped, or launched using launching devices or applied using unmanned aerial vehicles (UAV). Canopy baiting is allowed in uninhabited non-crop areas and may be placed by hand or using long poles. The Bromethalin-100 Conservation Place Packs label permits burrow baiting, and the Bromethalin-100 Conservation Blocks label allows subterranean baiting in infrastructure such as sewers, utility tunnels, and other underground spaces. The labels require treated areas with public access to be posted with warning signs appropriate to the current rodent control or eradication operation. The Bromethalin-100 Conservation Place Packs and Blocks products are identical in formulation to the Fastrac® Place Pacs and Blox products and contain denatonium benzoate, a bittering agent that makes the bait less palatable to humans and other non-rodent mammals.

The application methods and use sites currently allowed on the labels for the two Fastrac® products allow for direct bait placement or placement in bait stations in and within 100 feet of manmade structures. Examples of manmade structures are food processing facilities, industrial and commercial buildings, trash receptacles, agricultural and public buildings, transport vehicles (ships, trains, aircraft), docks, and port or terminal buildings. Fence and perimeter baiting beyond 100 feet from a structure is prohibited. The Fastrac® labels require the use of bait stations for outdoor, above ground use. The Fastrac® labels do not allow burrow baiting. Again, the Fastrac® formulations are identical to the Bromethalin-100 Conservation formulations and also contain denatonium benzoate.

None of the labels for the four bromethalin products that WS uses allow aerial or ground broadcast applications. The two Fastrac® labels require bait stations for all above ground use that is within, and around man-made structures and the bait stations must be tamper-resistant if the treatment area is accessible to children, pets, and nontarget species (USEPA 2017;2019). The Bromethalin-100 Conservation labels indicate that applications involving bait stations must be in tamper-resistant bait stations (USEPA 2023e;a).

The four labels require applicators and other handlers to wear long pants, shoes plus socks, and gloves (barrier laminate gloves for Bromethalin-100 Conservation products). When retrieving carcasses or unused bait, all labels require gloves, with the Bromethalin-100 Conservation labels requiring barrier laminate gloves (USEPA 2023a;e). Bromethalin's chemical properties (molecular weight of 577.93 g/mol and log K_{ow} of 7.62) indicate a low potential for dermal adsorption (USEPA 2016c). Inhalation is not expected due to the formulation (bait blocks and packs) and bromethalin's chemical properties (low volatility). Following label directions, including the use of proper personal protective equipment (PPE), will minimize worker exposure to bromethalin via inhalation and dermal contact routes.

Although oral exposure to bromethalin is acutely hazardous, label restrictions render accidental dietary exposure an incomplete exposure pathway. The four products (two formulations) all contain a bittering agent that makes them unpalatable to people. Bromethalin products are all non-food use pesticides with no anticipated drinking water exposures based on label restrictions.

Bromethalin is immobile in soil, and mobility into nearby water bodies or aquifers is not expected. In addition, use restrictions on the Bromethalin-100 Conservation labels state that no applications are allowed directly to water, areas where surface water is present, or intertidal areas below the mean high-water mark (except for elevated and floating bait stations) (USEPA 2017;2019;2023e;a). The Bromethalin-100 Conservation labels allow the use of elevated and floating bait stations in intertidal zones and subterranean spaces. Both labels restrict the use of floating bait stations to where the water is calm enough that the bait stations will not be inundated with water or capsize; the stations must be tethered or attached to a stationary object. The Bromethalin-100 Conservation labels require floating bait stations in intertidal zones to be removed if stormy weather is forecasted. Bromethalin has a low potential for volatilization due to its low vapor pressure. As a result of these label restrictions and bromethalin's environmental fate properties, surface and groundwater exposure pathways are also incomplete.

WS may monitor treatment sites for impacts to target and non-target species. Personnel that conduct posttreatment monitoring follow applicable standard operating procedures and pesticide labels that include appropriate PPE for posttreatment activities. Before monitoring, WS trains personnel in the proper handling of animals, carcasses, and the use of PPE. Monitoring does not occur during the same period as applications of bromethalin baits, so occupational exposure to bromethalin during monitoring activities would not occur. Personnel wear PPE when handling live animals and animal carcasses and when handling bait pellets in the environment. Based on these safeguards, monitoring activities are unlikely to pose health and safety concerns for personnel or the public.

Based on the expected WS use pattern and label restrictions for bromethalin bait applications, workers applying bromethalin are the most likely subgroup of the human population to be exposed to bromethalin. Exposure during transportation of bromethalin baits is not anticipated because the material is sealed in containers. Bromethalin bait formulations are ready for applicators to use with no mixing required. The potential for occupational exposure from the proposed WS use pattern is low; however, accidental exposure may occur during bait application. The risk of exposure via ingestion or inhalation is minimal due to the end-use product formulations (bait blocks and place packs), application restrictions, and PPE, which minimize exposure.

A significant direct exposure pathway to bromethalin bait formulations used by WS for the public has not been identified. The Bromethalin-100 Conservation products are Restricted Use Products that can only be used by a certified applicator or persons under their direct supervision. The Bromethalin-100 Conservation labels' application methods, except for tamper-resistant bait stations, are for use only in uninhabited areas, uninhabited vessels and manmade structures, non-crop areas, etc. The Fastrac® labels require the use of bait stations for all above-ground use; tamper-resistant bait stations are required in treatment areas accessible to people (for applications involving bait stations, the Bromethalin-100 Conservation labels only allow tamper-resistant bait stations). As a result of these use restrictions for bromethalin bait products used by WS, the public is not considered a vulnerable population for direct exposure to bromethalin baits used by WS (see Section 1.1).

4.2 Ecological Exposure Assessment

WS uses bromethalin baits to eradicate and control invasive rodents for conservation purposes, to manage rodents at airports when there are human health and safety concerns, and to control rodents that cause harm to natural resources. WS does not use bromethalin baits to manage rodents in urban and suburban residential and commercial structures.

The application methods used by WS will affect nontarget species' primary and secondary exposure potential. For most island conservation projects, WS may use Bromethalin-100

Conservation Blocks and Bromethalin-100 Conservation Place Packs. Applications under these two labels may involve the use of tamper-resistant bait stations or direct placement of bait. Tethered, floating tamper-resistant bait stations may be utilized in rodent habitat in intertidal zones or subterranean spaces where the water is sufficiently calm. For applications to unsafe or inaccessible vessels or abandoned structures, blocks or place packs (both can be grouped in sachets as well) are launched by hand or using slingshots or t-shirt cannons or delivered using a payload UAV. During canopy baiting, bait is placed directly into trees and shrubs in non-crop areas or placed in bait stations or sachets which are then placed by hand or long poles into trees or shrubs. Place packs can be used for burrow baiting. Subterranean baiting with blocks is used in subterranean infrastructure such as sewers, utility tunnels, and other underground spaces. During subterranean baiting, bait may be placed directly or placed in sachets. For subterranean spaces containing water or that could be inundated with water during baiting, blocks and sachets are securely attached to a stationary subterranean structure (USEPA 2023e;a). WS expects direct exposure to nontarget species that may consume the baits and that have access to the baits at the above treatment sites, including animals small enough to access bait stations when in use. Secondary exposure could occur if nontarget species prey or scavenge on dosed species.

WS uses Fastrac® Place Pacs and Fastrac® All-Weather Blox® products to manage rodent problems at airports and for conservation purposes to protect natural resources from rodent damage. Both labels require the use of bait stations for outdoor, above-ground use, and tamper resistant bait stations whenever children, pets, nontarget mammals, or birds may have access to the bait placement location. To date, WS has applied bromethalin in bait stations at airports to reduce aircraft bird strikes (raptors or other predators attracted to rodent prey) and damage to equipment. WS has also used bromethalin in bait stations on an island covered in man-made structures to protect a seabird colony from mammalian predators (VA DWR 2020) (See Section 1.1 Use Patterns). WS expects exposure to nontarget species that access bait stations or prey or scavenge on dosed species.

4.2.1 Aquatic Exposure Assessment

Exposure to aquatic organisms and bodies of water is expected to be minimal because labels do not allow direct applications to water bodies where surface water is present or to areas where runoff is likely. The Bromethalin-100 Conservation labels do not allow application to marshes, mangroves, wetlands, or intertidal areas below the mean high-water mark unless utilizing canopy bating or tethered, floating bait station application methods. The labels also do not allow the application of bait in floating bait stations prior to storm events.

Any bromethalin that enters the water will do so as a bait block or pack that would likely become saturated and sink to the bottom sediment where it would degrade over time.

Bromethalin has low water solubility (virtually insoluble) and environmental fate properties that suggest that residues in water would bind to suspended solids and sediment. Its low solubility and high binding affinity for soil also reduce the likelihood of leaching into any groundwater resources. The environmental fate properties of bromethalin will reduce the probability of exposure to vertebrates and invertebrates that occupy the water column. Aquatic exposures would be greatest for aquatic biota that occupy the sediment or consume benthic prey items.

The label restrictions are designed to reduce the possibility of transporting bromethalin into aquatic areas by any means, including runoff and drift. Given that product labels only allow hand deployment, and under the Bromethalin-100 Conservation labels, throwing actions and, in rare instances, UAV use, the possibility of incidental deposition of bromethalin into water resources is negligible. Thus, the expected levels in waterbodies surrounding the treatment areas would be negligible.

Bromethalin is virtually insoluble in water and environmental fate properties such as low mobility suggests that no detectable residues would occur from any incidental deposition into water. Though bromethalin is highly toxic to fish and aquatic invertebrates, there have been no incidences of bromethalin exposure in either because of treatments due to the insolubility and application methods (bait stations, hand applications and use restrictions).

4.2.2 Terrestrial Exposure Assessment

Terrestrial wildlife can be exposed to bromethalin from primary and secondary oral exposures. Terrestrial invertebrates and vertebrates may be directly exposed to bromethalin from consuming bromethalin baits. Secondary exposure will occur when nontarget terrestrial vertebrates consume invertebrate and vertebrate prey items that contain residues of bromethalin or its metabolites. These exposures can be both short- and long-term. Inhalation and dermal exposure to bromethalin are not anticipated to be a significant exposure pathway for nontarget wildlife. The formulations WS uses are in bait blocks and place packs, and the low potential for bromethalin to volatize, plus the formulations themselves, suggests a low potential for inhalation and dermal exposures to terrestrial wildlife.

USEPA (2020b) evaluated the Incident Data System (IDS) for ecological incidents involving bromethalin between 1996 and February 2020. USEPA only considered incidents classified as highly probable (9), probable (28), possible (7), exposure only, and unknown (9), totaling 53 wildlife incidents reported. Raccoons (*Procyon lotor*) and striped skunks (*Mephitis mephitis*) accounted for most of the incidents, 20 and 12 incidents, respectively. Skunk (5 incidents, Family Mephitidae), gray squirrel (4 incidents, *Sciurus carolinensis*), gray fox (2 incidents, *Urocyon cinereoargenteus*), and chipmunk (2 incidents, *Neotamias* sp.) were also reported. Only one incident for each of the following species was reported: great horned owl (*Bubo virginianus*), barn owl (*Tyto alba*), red-tailed hawk (*Buteo jamaicensis*), woodpecker (Family Picidae), cat (*Felis domesticus*), cottontail (*Sylvilagus* sp.), fox squirrel (*Sciurus niger*), rabbit (Family Leporidae), squirrel (Family Sciuridae), and turtle (Family Testudines). Several of these incidents were summarized in a study by McMillan et al. (2016); they noted that affected animals were generally found near residences and affected animals in remote locations were unlikely to be observed and reported.

WS use patterns for bromethalin baits are typically limited in location and duration. The goal of island projects using rodenticides is to eradicate or control invasive rodent species for conservation purposes. In eradication projects, the use of rodenticides, including bromethalin, would be short in duration since eradication projects are set for a specific time interval. In cases where the primary eradication effort is unsuccessful there may be longer term use of bromethalin to remove surviving rodents. There may also be longer term use in cases where control is the management goal WS also uses bromethalin baits to manage rodents at airports to reduce bird strikes and damage to equipment. To date, WS has only used bromethalin baits in tamper resistant bait stations during applications at airports. Airport use may be short- or long-term duration depending on the management goal and whether baiting with bromethalin is successful. WS may also use bromethalin baits in other natural resource management projects.

4.2.2.1 Primary Exposure

Direct exposure will be greatest for nontarget species that consume the bromethalin baits. The most relevant route of exposure to terrestrial species is through the direct consumption of bait. In addition to the use of bait stations, the two labels WS operates under for island conservation projects allow for direct bait placement (e.g., subterranean spaces and rodent burrows) and canopy baiting which makes the bait more accessible to nontarget species compared to bait stations. In island conservation uses terrestrial invertebrates, such as crabs, and vertebrates that are attracted to the baits would be exposed to bromethalin. The use of canopy baiting, bait stations, and burrow baiting on both Bromethalin-100 Conservation labels will reduce these types of exposures when compared to broadcast applications allowed for other rodenticides. In non-island conservation projects, WS uses bait stations, including tamper-resistant bait stations in areas accessible to children, pets, and nontarget species, according to label requirements. The Bromethalin-100 Conservation labels indicate only tamper-resistant bait stations may be used when bait station applications are made. Bait stations may be accessible to small nontarget vertebrate and invertebrate species. WS monitors its treatment sites for impacts on nontarget species. To date, WS has no records of nontarget take from its use of bromethalin. However, WS acknowledges that it is difficult to find all exposed animals as they can move long distances, die in underground burrows, may be difficult to find in vegetation and other landscape features, or may have been consumed by other species.

4.2.2.2 Secondary Exposure

Secondary exposure of bromethalin to scavenging and predatory birds and mammals has been noted for various species. Between March 2021 and September 2022, Murray and Cox (2023) tested raptors brought into a wildlife clinic for bromethalin (as desmethylbromethalin). Most of the birds were collected from urban and suburban areas. Only birds that died soon after admission, were euthanized due to the severity of the presenting injury or illness or were dead on arrival were tested. Of the 44 birds tested, 13 (29.5%) had detectable desmethylbromethalin in adipose tissue, and all the birds were positive for anticoagulant rodenticides. Bromethalin and desmethylbromethalin concentrations were not reported in the study. The birds were nine red-tailed hawks, two barred owls, and two eastern screech owls. Five birds showed neurological signs of bromethalin toxicosis; however, the authors could not conclude that bromethalin toxicosis was the only reason the birds were brought to the wildlife clinic. Cox et al. (2022) noted the bromethalin metabolite, desmethylbromethalin, in adipose tissue from a black bear (*Ursus americanus*) that exhibited sublethal effects and eventually died. Desmethlybromethalin residue values were not reported in the study. A recent study of rodenticides detected the bromethalin metabolite, desmethylbromethalin, in adipose tissue from a pregnant mountain lion (Rudd et al. 2024). Desmethlybromethalin residue values were not reported in the study.

Other scavenging nontarget species may also be exposed to bromethalin residues. For example, crab species and other invertebrates, may scavenge carcasses that have been exposed to bromethalin. These secondary exposures occur from consuming tissues containing bromethalin and its metabolites, or consuming undigested baits in the gastrointestinal tract of dead rodents.

5 RISK CHARACTERIZATION

This section discusses the qualitative risks associated with WS' proposed use of bromethalin baits. The evaluation of documented bromethalin health exposure data and relevant animal exposure studies applied to exposure assumption scenarios can estimate the risk of impact to human health and nontarget fish and wildlife if accidentally exposed. Deterministic methods are summarized, where appropriate, to determine if expected environmental residues exceed toxicity data suggesting possible risk. In other cases, a more qualitative discussion regarding risk may rely on literature and additional information to further elaborate on the potential for injury or harm.

5.1 Human Health

Occupational risks for applicators are anticipated to be low due to the lack of dietary exposure and label requirements regarding PPE when loading, applying, or handling products containing bromethalin. PPE requirements will minimize inhalation and dermal risks to applicators.

Risks to the public from WS uses of bromethalin baits are low. The low risk to the public is due to several factors, such as the label restrictions and WS use patterns. In past rodent eradication for island conservation, the public was not allowed on the island or there was no permanent habitation. In situations where the public may be present, there are label restrictions that reduce the risk to the public from bromethalin bait use. Bromethalin baits are not registered for use on food crops, and other resources, such as drinking water, are at low risk of contamination due to label restrictions and bromethalin's environmental fate. WS has no reports of adverse effects to the public or workers from oral, dermal, or inhalation exposures or secondary or tertiary exposures from WS uses of bromethalin baits.

5.2 Ecological Risks

Risk characterization combines information from the dose-response assessment with the exposure assessment to determine the potential adverse effects on aquatic and terrestrial species. In this risk assessment, WS uses USEPA's risk evaluations (USEPA 2020b), peer-reviewed scientific literature, product labels, and WS use patterns to characterize the ecological risks associated with WS applications of bromethalin baits.

5.2.1 Aquatic

Acute and chronic risks to aquatic vertebrates and invertebrates are anticipated to be negligible due to the lack of exposure from WS use patterns and low frequency of use. Acute toxicity to aquatic vertebrates occurs above the solubility limit for bromethalin, suggesting acute risks would be lower compared to aquatic invertebrates where acute toxicity has been noted below solubility. There is risk to aquatic invertebrates that could feed on any baits that enter the water. These risks are considered negligible based on the methods of application and avoidance of water bodies for most applications. Label restrictions state that intentional applications to water are prohibited. This includes applications to marshes, mangroves, wetlands, or intertidal areas below the mean high-water mark unless utilizing canopy baiting or tethered, floating bait station application methods. Based on the lack of aquatic exposure, label restrictions, and WS use patterns, APHIS considers the risk to aquatic species as negligible.

5.2.2 Terrestrial

Bromethalin toxicity and exposure can result in acute and chronic primary and secondary risks to most terrestrial vertebrates. As previously noted, USEPA has reported multiple incidents involving domestic animal and wildlife species through primary and secondary exposures (See Section 4.2.2).

Direct ingestion of bait by nontarget terrestrial wildlife would be expected to result in adverse acute and chronic effects depending on the dose received. The duration of primary risk to nontarget terrestrial species will depend on how long bait is available for consumption. In some cases, baits not removed by the target rodent species and any nontarget species will be recovered, but this will vary based on the feasibility of collecting unused baits. Any bait left in the environment from WS use is expected to degrade relatively quickly due to its composition and depends on environmental conditions. Bromethalin degrades slowly in the environment, with a half-life of 132 to 235 days in an aerobic soil metabolism study, but would bind to soil organic matter (USEPA 2016b). It is stable to hydrolysis (USEPA 2016b).

USEPA (2020b) conducted a screening level risk assessment to evaluate the direct risk to birds and mammals from bromethalin exposure using different body weights and food intake values. In the absence of standardized toxicity data for reptiles, the USEPA uses bird toxicity data to estimate acute risks. The exposure estimates were divided by acute toxicity values adjusted for different body weights to calculate a risk quotient (RQ) (Table 7). USEPA uses levels of concern

(LOC) to determine if there is a risk to a group of animals by comparing the RQ to the LOC. In the case of terrestrial vertebrate wildlife USEPA uses a LOC of 0.5. A RQ above 0.5 suggests an acute high risk to nontarget vertebrates. USEPA also uses an LOC of 0.1 for determining risk to federally threatened and endangered species. A RQ was estimated for three different body weights of birds and mammals.

Table 7. Estimated acute oral risk quotient (RQ) values for bromethalin in birds and mammals for a single day of bait exposure.

Exposed Wildlife	**Weight (g)**	**Adjusted LD_{50} (mg/kg-bw)[1]**	**Bromethalin intake (mg/kg-bw/day)**	**RQ[2,3]**
Passeriform Bird	20	3.27	25	**7.7**
Passeriform Bird	100	4.16	20	**4.8**
Passeriform Bird	1,000	5.88	14	**2.4**
Rodent Mammal	15	3.70	19	**5.1**
Rodent Mammal	35	3.00	13	**4.3**
Rodent Mammal	1,000	1.30	3.1	**2.4**

[1]mg/kg-bw = milligrams active ingredient per kilogram body weight
[2]Risk quotients in bold exceed the acute high-risk LOC of 0.5.
[3]RQ values based on a concentration of 100 mg/kg-bait (0.01% w/w) from structural rodent control use.
Reference: (USEPA 2020b)

The acute high-risk LOC was exceeded for all body weights for passeriform birds and rodent mammals in single-day bait exposures. These estimates are screening values that allow risk assessors to identify taxa groups that require additional risk evaluation. The endpoint used to derive the effect value is an LD_{50} based on mortality. Sublethal impacts may also occur at lower doses, and those risks are not estimated in Table 7.

Primary and secondary risks of bromethalin and its metabolites to nontarget mammals and birds will vary based on their food preferences. Bromethalin has the potential to bioconcentrate in organisms; however, it is eliminated from the blood with a half-life of 5.6 days (USEPA 2020b). Data on the half-life of bromethalin from the liver is unavailable. As previously noted, secondary exposures have been reported in birds and mammals. Secondary exposure can occur when scavengers consume tissue or undigested baits in dead rodents. The lethal and sublethal effects of secondary exposures to scavengers and predators is not well understood. In a small study no lethal or sublethal impacts to beagle dogs were noted when they were fed rat carcasses containing lethal doses of bromethalin (Jackson et al. 1982). In previous cases where scavengers or predators exhibited signs of toxicosis with detectable levels of bromethalin or desmethylbromethalin they also had detectable levels of anticoagulant rodenticides. In cases where predators and scavengers have been exposed to multiple chemical stressors its difficult to attribute toxicosis to one cause. Bromethalin is a fast-acting toxicant compared to anticoagulant rodenticides limiting opportunities for scavenger and predators to be exposed to bromethalin when compared to other rodenticides (USEPA 2020b).

Birds that consume bait or prey contaminated with bromethalin bait are at short- and long-term risk from bromethalin. Short-term primary risk is greatest immediately after treatment and will decline as bait is removed by the target rodents, some nontarget species, and as the bait degrades in the environment.

Bait blocks or place packs used for burrow baiting, subterranean baiting, canopy baiting, floating bait stations, and tamper-resistant bait stations can be used over an extended period in eradication and control efforts. These application methods can result in short- and long-term risk; however, these methods of application are typically directed towards smaller areas of treatment.

Bait removal by the target rodent species will reduce long-term primary risks to nontarget animals that consume the bait. In the case of the Bromethalin-100 Conservation labels, carcasses may be removed by workers, reducing secondary exposure to nontarget wildlife. The extent of carcass removal by workers will vary depending on site conditions. For example, collection and disposal may not be feasible if treatments occur in an area where there are high natural mortality rates and collecting and disposing of carcasses is impractical or unsafe (e.g., some breeding bird sites). No statements regarding carcass removal are required for either Fastrac® labels at this time but may be in the future. Primary and secondary risks from spilled bait are reduced by label requirements for collection and disposal for all uses.

The primary and secondary risks to mammals and birds from WS use of bromethalin is low. WS uses very little bromethalin (a total of 3 lbs of product containing 0.01% w/w bromethalin, or 0.0003 lbs active ingredient from FY 16 to FY 20 (Table 2)), reducing the potential for primary and secondary exposure, and risk, to nontarget wildlife. Future use may increase if WS expands use of bromethalin on more island conservation projects and for other uses but is still anticipated to be low. The use of rodenticides as a tool in island conservation has been shown to provide beneficial impacts to native flora and fauna on islands post eradication (Thibault 1995, Jouventin et al. 2003, Harper and Bunbury 2015, Newton et al. 2016, Graham et al. 2018, Wolf et al. 2018, Herrera-Giraldo et al. 2019, USFWS 2019). The primary and secondary adverse risks to nontarget fish and wildlife from bromethalin and other rodenticides from these types of uses can be offset by the positive impacts invasive rodent eradication and control can have on endemic island species post eradication. Other WS uses for bromethalin have also provided conservation benefits on areas other than islands and helped to ensure safety at airports.

6 UNCERTAINTIES AND CUMULATIVE IMPACTS

The uncertainties associated with this risk evaluation arise primarily from the limited toxicity information available for the two bromethalin formulations used by WS. Unpublished acute toxicology studies submitted to USEPA by registrants and individual formulation safety data sheets provide limited acute mammalian toxicity values, which can be used to make general conclusions concerning the impact of bromethalin on humans and the nontarget environment.

Other uncertainties related to chronic and sublethal effects data for some fish and wildlife and surrogacy of test organisms are typical for most pesticides. The conservative assumptions regarding the potential for exposure to human health, nontarget species, and the environment address the uncertainties to some extent. A lack of risk using these conservative assumptions supports the reasonable certainty that impacts on human health and the environment will be negligible.

Another area of potential uncertainty in this risk assessment is the potential for cumulative impacts on human health, nontarget species, and the environment from the proposed use of bromethalin in the WS program. Areas where cumulative impacts could occur are: 1) repeated worker and environmental exposures to bromethalin 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 bromethalin.

Repeated exposures that could lead to increased risks of injury from accidental bromethalin exposure by WS applications are expected to be minimal due to strict WS applicator adherence to label-required PPE.

7 PREPARERS: WRITERS, EDITORS, AND REVIEWERS

7.1 APHIS WS Methods Risk Assessment Committee

Writers for “Use of Bromethalin in Wildlife Damage Management Risk Assessment”:

Writer: Jim Warren
Position: USDA-APHIS-Policy and Program Development (PPD), Environmental and Risk Analysis Services (ERAS), Environmental Toxicologist, Little Rock, AR
Education: B.S. Forest Ecology and M.S. Entomology – University of Missouri; Ph.D. Environmental Toxicology – Clemson University
Experience: Eighteen years of experience working for APHIS preparing ecological risk assessments and providing environmental compliance support. Prior experience before joining APHIS includes other government and private sector work regarding ecological risk assessments related to various environmental regulations.

Writer: Andrea Lemay
Position: USDA-APHIS-Policy and Program Development (PPD), Environmental and Risk Analysis Services (ERAS), Biological Scientist, Raleigh, NC
Education: BS Plant and Soil Science (Biotechnology) - University of Massachusetts; MS Plant Pathology - North Carolina State University
Experience: Thirteen years of service in APHIS conducting risk analysis. Nine years of experience in preparing environmental analyses in compliance with the National Environmental Policy Act.

Editors/Contributors for “Use of Bromethalin in Wildlife Damage Management Risk Assessment”:

Editor: Shelagh DeLiberto
Position: USDA-APHIS-Wildlife Services (WS), National Wildlife Research Center (NWRC), Wildlife Biologist, Fort Collins, CO
Education: BA Biology and Environmental Science – Ithaca College; MS Wildlife Biology – Colorado State University
Experience: Sixteen years of service in APHIS conducting wildlife research. Two years of experience in preparing categorical exclusions and environmental analyses in compliance with the National Environmental Policy Act.

Editor: Emily Ruell
Position: USDA-APHIS-WS, NWRC, Registration Manager, Fort Collins, CO
Education: B.S. Zoology and Biological Aspects of Conservation – University of Wisconsin - Madison; M.S. Ecology – Colorado State University (CSU); M.A. Political Science – CSU
Experience: Ten 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: Thomas C. Hall
Position: USDA-APHIS-WS, Operational Support Staff, Staff Wildlife Biologist, Fort Collins, CO

Education: BS Biology (Natural History) and BA Psychology – Fort Lewis College; MS Wildlife Ecology – Oklahoma State University

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.

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: Tim J. Ohashi
Position: USDA-APHIS-WS Staff Wildlife Biologist – Hawaii Program
Education: BS Wildlife – University of Idaho, Moscow, ID; MS Wildlife – New Mexico State University, Las Cruces, NM
Experience: Conducted field studies on indigenous and introduced wildlife in Hawaii for various state and federal agencies. Established and supervised the Wildlife Services operational program in Hawaii, which included rodent eradication projects on Rose Atoll, American Samoa, Kure Atoll and Midway Atoll, Hawaii. Assisted in the establishment of the Brown Tree Snake control and interdiction program on Guam and the coqui frog control program on Hawaii Island. Have extensive wildlife damage management experience unique to Hawaii. As a qualified airport biologist, worked on bases in Japan, Wake Island and Alaska at the request of the Pacific Air Force command. Participated in the Wildlife Services Southwest Asia BASH mitigation program during Operation New Dawn at Joint Base Balad and Al Asad Air Base, Iraq. Holder of Dealer Representative License for sale of Restricted Use Pesticides in the State of Hawaii.

Reviewer: Aaron Shiels
Position: USDA-APHIS-WS, National Wildlife Research Center: Research Biologist and Rodents Project Leader, Fort Collins, CO
Education: BS Environmental Sciences, University of Denver; MS Biology, University of Nevada, PhD Botany/Ecology University of Hawaii
Experience: Fifteen years researching rodent damage management techniques including the use of rodenticides.

The Office of Management and Budget requires agencies to have peer review guidelines for scientific documents. The APHIS guidelines were followed to have "Minimum Risk Pesticides" peer reviewed. WS worked with the Association of Fish and Wildlife Agencies to have experts review the documents.

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

Arizona Game and Fish Department

Oregon Department of Fish and Wildlife

Minnesota Department of Natural Resources

7.3.1 Comments

1. It might be worth an added statement that toxicities in wildlife are likely under-reported. We saw multiple cases of bromethalin toxicity in terrestrial wildlife species while I was a veterinarian with Colorado Parks and Wildlife; however, we did not publish these cases or enter them into the IDS and instead reported cases through internal reports. Other states, such as California, seem to have similar internal reporting that may not always be represented in the IDS or published in peer reviewed literature. This is probably not a critical point – but just a thought as I was reviewing the paucity of available data and thinking of all the cases we've seen and not published.

Response: We appreciate this comment and agree that toxicities/exposure of wildlife to bromethalin is under-reported. 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 bromethalin, not the use of the products by the general public or other pesticide applicators. We provide the American Association of Poison Control Centers (AAPCC) National Poisoning Data System (NPDS), USEPA Ecological Incident Data System exposure information as a comparison to the exposure due to use by WS.

2. The only area I noted that could be considered for addition, might be some description of how a "tamper-resistant" bait station is assessed. We tended to see bromethalin exposure/toxicity in species that are very dexterous (raccoons, skunks), or very strong and determined (black bears). We have often wondered whether there are some species that are able to access the bait directly from tamper-resistant bait stations and that might be why toxicity is seen more frequently in those species.

Response: We have added information on EPA criteria for tamper-resistant bait stations to Section 4.1. Additionally, WS use of bromethalin is analyzed in relevant NEPA and ESA documents that assess use in areas where nontargets may access bait and methods to prevent nontarget access.

3. One additional paper that could be included in this review is below – this is a recent publication, and I suspect it was not available at the time the bromethalin document was prepared. Rudd, J.L., Poppenga, R.H., Woods, L.W., Riley, S.P., Sikich, J.A., Streitenberger, N. and Clifford, D.L., 2024. Detection of Rodenticides in Pregnant Mountain Lions (*Puma concolor*) and Their Fetuses in California. Canadian Wildlife Biology & Management (CWBM), 13(2).

Response: We have added information from the Rudd et al. (2024) paper to Section 4.2.2.2.

4. Under 4.2 it mentions that bait may be used on floating platforms in the intertidal zones- it seems like this could be risky with the toxicity to aquatic life and the potential for dispersal into the water from these stations. It does indicate that it is highly insoluble in water though. I do wonder if some aquatic studies in the lab could and should be done on a small scale.

Response: WS always follows the Bromethalin label instructions when applying Bromethalin baits. Per the Bromethalin label: "Each tethered floating bait station must be installed, tested, and proven to be durable and resistant to inundation by water for at least 24 hours prior to their use with toxic bait." We have summarized all available aquatic studies for bromethalin in Sections 2.2 and 3.2.1. Potential hazards associated with bromethalin use are summarized in Sections 4.2.2 and the specific risks associated with WS use of bromethalin in aquatic environments are summarized in Section 5.2.1. If additional studies on aquatic environments and bromethalin use become available, we will add them in future revisions of the Risk Assessment.

5. The risk to non-target species such as other mammals and birds in the area still seem like they could be high. I assume a risk assessment is done prior to application and that all non-targets found dead and ill in the area are evaluated and baiting is stopped if negative impact is too high.

Response: WS use of bromethalin is analyzed in relevant NEPA and ESA documents that assess the use of bromethalin baits in areas where nontargets may access the bait and methods to prevent nontarget access.

6. While it is clear that the water solubility of bromethalin in negligible, the use of floating bait stations is of concern, even if tethered. The report describes that such stations would only be used during calm weather. There is no mention of how long the bait stations are deployed and whether or not bait stations would be retrieved in the event of a flood or storm prediction.

Response: WS always follows the Bromethalin label instructions when applying Bromethalin baits. Per the Bromethalin label: "Each tethered floating bait station must be installed, tested, and proven to be durable and resistant to inundation by water for at least 24 hours prior to their use with toxic bait." Although there is no restriction on the amount of time floating bait stations are used, the toxic bait is removed prior to storm events as described in Section 4.1.

7. Additionally, I think that more research in the use of bromethalin around water, including the impact on aquatic organisms is warranted as well as the potential for bioaccumulation in the aquatic environment.

Response: We have summarized all available aquatic studies for bromethalin in Sections 2.2 and 3.2.1. Potential hazards associated with bromethalin use are summarized in Sections 4.2.2 and the specific risks associated with WS use of bromethalin in aquatic environments are summarized in Section 5.2.1. If additional studies on aquatic environments and bromethalin use become available, we will add them in future revisions of the Risk Assessment.

8. The risk for primary and secondary exposure of nontarget species is reasonably covered, however, there is limited data and it is likely that the number of incidents is much greater than reported. Testing of wildlife mortalities for toxicants requires first an index of suspicion that intoxication has occurred and second the resources to perform the testing. Given that the animals are infrequently observed before death and there are minimal postmortem or histopathological lesions, randomly testing for bromethalin via GC/MS is not likely to be rewarding. It is, therefore, important to observe appropriate placement and maintenance of bait stations as well as recovery of above ground carcasses to reduce nontarget species mortality.

Response: We appreciate this comment and agree that toxicities/exposure of wildlife to bromethalin is under-reported. WS always follows the Bromethalin label instructions when applying Bromethalin baits. This includes adhering to the label requirements of placement and maintenance as well as removal of carcasses.

Comments Received not requiring a response:

1. I found this to be a detailed and thorough review that adequately summarized the available information and literature on bromethalin. This review does a nice job of summarizing reports in the EPA incident data system and peer-reviewed literature; however, I suspect that many cases of wildlife toxicosis are not published or reported in IDS. The review appropriately mentions the limited toxicity information available in the 'Uncertainties and Cumulative Impacts section'.

2. This risk assessment appears to be a thorough evaluation of the human, and ecological evaluation of the risks associated with using bromethalin to control and eradicate invasive rodents for conservation purposes and around manmade structures. It adequately reviews the uncertainties associated with the use as well as mitigation protocols to reduce human exposure, and nontarget impacts.

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