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MEMORANDUM

SUBJECT: Seven Anticoagulant Rodenticides: Draft Ecological Risk Assessment for Registration Review

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The Environmental Fate and Effects Division (EFED) has completed the draft environmental fate and ecological risk assessment in support of the Registration Review of seven first- and second-generation anticoagulant rodenticides.

Draft Ecological Risk Assessment for the Registration Review of Seven Anticoagulant Rodenticides

First Generation Anticoagulants
Warfarin (PC code 086002)
Diphacinone (PC code 067701, 067705)
Chlorophacinone (PC code 067707)

Second Generation Anticoagulants
Brodifacoum (PC code 112701)
Bromadiolone (PC code 112001)
Difethialone (PC code 128967)
Difenacoum (PC code 119901)

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1 Executive Summary

This document provides the draft environmental risk assessment (ERA) for seven anticoagulant rodenticides (AR) for the registration review program. These include three first-generation ARs (FGARs; warfarin, chlorophacinone, diphacinone) and four second-generation ARs (SGARs; bromadiolone, brodifacoum, difenacoum, and difethialone). Based on previous risk assessments, the 2008 Risk Mitigation Decision (RMD), and the problem formulations for each of the 7 ARs, this ERA has been focused on risks to mammals and birds (as well as reptiles and terrestrial amphibians, for which birds serve as a proxy). This approach is formalized in the Risk Management Objectives section, below.

The nature of risk to mammals and birds from ARs is well-established and includes mortality from primary and secondary exposure, as well as chronic growth and reproduction effects. Primary exposure in this assessment is defined as consumption of treated bait by target or non-target organisms. Secondary exposure is defined as predation and consumption of exposed primary consumers. Previous assessments have concluded that SGARs present greater secondary exposure concerns than FGARs do, supported by numerous incidents in which animals too large to enter bait boxes are found to contain significant levels of AR residues in liver or other tissues. Target and non-target taxa that consume ARs via bait boxes carry residues of the persistent ARs from bait boxes into the environment, sometimes far from the treatment area because ARs do not kill immediately and some SGARs have persistent half-lives, creating secondary exposure opportunities for predators and scavengers (see the **Secondary Exposure Characterization** section for more information).

An acute-to-chronic ratio qualitative assessment of chlorophacinone and difenacoum indicates reproduction concerns for all 7 ARs. These data show that toxicity is substantially enhanced in studies that utilize repeated exposures, such as reproduction toxicity assays and subacute repeated dose dietary studies.

This ERA also conducts an analysis of wildlife incidents involving the 7 ARs, to determine if there are any meaningful trends in recent years. Since the 2008 risk mitigation decision-imposed mitigations within the United States, we have focused on reports from the US because the mitigation decision applied only to the US, although there is scientific literature on the effectiveness of similar AR mitigations from several European countries. Data sources include EPA's Incident Data System (IDS) and scientific reports that specifically addressed the question of wildlife incident trends. Literature reports were obtained from California, Kentucky and Massachusetts. The California report was done by the Department of Pesticide Regulation in response to a citizen petition.

Broadcast and floating bait station uses for two FGARs, chlorophacinone and diphacinone, were examined for aquatic risks and found not to be of concern. These uses were of concern for terrestrial organisms, however.

General Conclusions from the Incident Analysis

804 incidents (63% of incidents reported since 1971 in the Incident Data System) were reported between 2010 and 2018, indicating that exposure and wildlife incidents have continued in recent years. Two rodenticides – brodifacoum and bromadiolone – were the primary drivers of incidents, accounting together for roughly 69% of the incidents reported between 2010 and 2018. Brodifacoum and bromadiolone are both SGARs and are expected to be persistent. Based on autopsy reports of poisoned animals, exposure to two or more second-generation ARs is common (see **Section 6.4**). With regards to listed species, incidents have been reported for listed and protected species such as San Joaquin kit fox, bald eagle, and key deer. The San Joaquin kit fox (*Vulpes macrotis*) has had several recent incidents related to anticoagulant rodenticides.

Due to their robust reporting systems relative to other states, the states of California and New York account for 58 and 21% of reported incidents for the evaluated rodenticides. Open literature studies on rodenticide incidents suggest that anticoagulant rodenticides have a significant likelihood to impact non-target wildlife; exposure rates to wild animals in these studies was high, even in remote densely forested regions with no legal uses of SGARs. Anticoagulant rodenticide incidents are generally based on detection of residues in liver tissue and corroborating evidence from carcass necropsy.

The reported incident data show an apparent increase in wildlife exposure and deaths. This may be attributed to greater effort in seeking out incidents, especially in California. The report cited herein was the result of a formal petition by an NGO. The data presented in this assessment therefore do not necessarily represent an increase in incidents, but instead show that upon closer examination, incidents continue and have apparently not decreased.

1.1 Overview

This draft risk assessment is for seven anticoagulant rodenticides (ARs). Included are three FGARs (warfarin, chlorophacinone, and diphacinone) and four SGARs (bromadiolone, brodifacoum, difenacoum and difethialone). These compounds are used to control various types of rats, mice, and other small mammals such as squirrels, muskrats and prairie dogs.

All these compounds work by interfering with the role of Vitamin K in the blood-clotting process. Exposed animals die either by internal hemorrhage or for other reasons related to general weakening due to bleeding. See **Section 3.1** for more information.

Of particular concern is secondary exposure, as well as the consequent death of predatory and scavenging birds and mammals. SGARs in particular persist in the bodies of target organisms and are able, through predation and scavenging of exposed prey items, to cause effects in non-target animals.

This assessment is focused on primary and secondary exposure risks to non-target mammals and birds, and effects higher up the food chain to predators and scavengers.

EPA is taking the same combined/streamlined approach for the seven (three first generation and four second generation) anticoagulant rodenticides considered in this document, as it did with the sulfonylurea and ALS inhibitor herbicides. This streamlined approach of issuing one document covering multiple pesticides within a given class is used to conserve Agency resources and provide equity to stakeholders by ensuring a consistent approach to mitigating potential risks for chemicals in a given group. Grouping the anticoagulant rodenticides is both convenient and logical from a regulatory perspective because they exhibit a common mechanism of action and show similar effects. The first- and second-generation anticoagulant rodenticides have a common mode of action with other coumarin rodenticides: vitamin-K antagonists that disrupt normal blood-clotting mechanisms and induce capillary damage. Although the mitigation concepts for the anticoagulant rodenticides will be different from the two aforementioned example herbicide classes, the concept of streamlining for similar chemicals in a class is the same.

EFED also conducted an analysis that examines risks associated with current first-generation rodenticide (diphacinone and chlorophacinone) broadcast uses, and the chlorophacinone muskrat SLN use as “floating bait station”.

1.2 Risk Conclusions Summary

We confirm that anticoagulant rodenticides continue to be the cause of wildlife exposure and mortality in recent years. In general, exposure to SGARs is more widespread than is exposure to FGARs. There are numerous reported incidents where multiple SGAR residues were detected suggesting such exposures are common (see **Section 6.4** for more details).

Incident reports indicate that AR exposure continues to be a cause of the death of listed or protected species such as the San Joaquin kit fox, bald eagles, and golden eagles as was concluded to be likely by previous EFED Biological Evaluations (**Table 2-1**). Nationwide BEs for several of the rodenticides are scheduled as a result of a draft lawsuit settlement.

There were exceedances of both the acute (both single-day and multi-day) and chronic risk LOCs for birds and mammals exposed to anticoagulant rodenticides. A summary of the risk quotients (RQs) is presented in **Table 1-1** below. Furthermore, based on both incident data and qualitative analysis there is high risk for birds and mammals through secondary exposure to anticoagulant rodenticides. This is consistent with the findings of both the incident analysis and open literature which found through the analysis of residues in the livers of birds and mammals that they are impacted in the wild by anticoagulant rodenticide usage.

Table 1-1. Summary of Risk Quotients for Taxonomic Groups from Current Uses of the Anticoagulant Rodenticides				
Taxa	**Exposure Duration**	**Risk Quotient (RQ) Range[2]**	**RQ Exceeding the LOC for Non-listed Species**	**Additional Information/ Lines of Evidence**
Freshwater fish	acute	< 0.5	none	Exposure is not expected due to use patterns as modified by RED mitigation; acute risk below LOC for chlorophacinone and diphacinone. Incident reports include some fish mortality although exposure route is uncertain.
Estuarine/ marine fish	No meaningful exposure	Not calculated	Not calculated	Exposure is not expected due to use patterns as modified by RED mitigation
Freshwater invertebrates	acute	< 0.5	None	Exposure is not expected due to use patterns as modified by RED mitigation: Acute risk below LOC for chlorophacinone and diphacinone
Estuarine/ marine invertebrates	No meaningful exposure	Not calculated	Not calculated	Exposure is not expected due to use patterns as modified by RED mitigation
Benthic invertebrates	No meaningful exposure	Not calculated	Not calculated	Exposure is not expected due to use patterns as modified by RED mitigation
Terrestrial invertebrates	Exposure possible	Not calculated	Not calculated	For most uses, exposure to terrestrial invertebrates is not expected as bait is enclosed in tamper-proof bait stations. Tolerant terrestrial invertebrates may accumulate ARs and serve as an exposure route.
Aquatic plants	No meaningful exposure	Not calculated	Not calculated	Exposure is not expected due to use patterns as modified by RED mitigation
Terrestrial plants	No meaningful exposure	Not calculated	Not calculated	Exposure is not expected due to use patterns as modified by RED mitigation

Level of Concern (LOC) Definitions:
Terrestrial Animals: Acute=0.5; Chronic=1.0; Terrestrial invertebrates=0.4
Aquatic Animals: Acute=0.5; Chronic=1.0
Plants: 1.0

Table 1-2. Summary of Acute Risks to Birds and Mammals					
Chemical	Taxon	Primary Bait consumption, single day (RQ)	Primary Bait consumption, multiple day (RQ)	Chronic risk from Secondary exposure in birds? (**Table 9-15**)	Incidents reported to IDS thru 2019 (see **Section 6.4**)
Warfarin	Bird	0.11 - 0.34	0.62 – **2.0**	Yes	23
	Mammal	**4.02 - 8.7**	**23 – 50**	--	
Diphacinone	Bird	0.02 - 0.07	0.12 – 0.40	Yes	122
	Mammal	**0.80 - 1.7**	**4.6 – 10**	--	
Chlorophacinone	Bird	0.02 – 0.07	0.13 – 0.43	Yes	54
	Mammal	**0.80 – 1.7**	**5.1 – 11**	--	
Brodifacoum	Bird	0.01 – 0.03	**117-166**	Yes	658 (353 since 2010)
	Mammal	0.40 – **0.87**	**27 – 59**	--	
Bromadiolone	Bird	0.01 – 0.03	0.18 - **1.49**	Yes	278 (204 since 2010)
	Mammal	0.40 – **0.87**	**2.66 - 12.81**	--	
Difenacoum	Bird	0.02 – 0.07	0.12 – 0.40	Yes	12
	Mammal	**0.80 – 1.73**	**4.7– 10.2**	--	
Difethialone	Bird	0.01 – 0.03	**52 – 168**	Yes	124
	Mammal	0.40 – **0.87**	**11 – 24**	--	

Bold RQs exceed acute terrestrial animal LOC of 0.5

1.3 Environmental Fate and Exposure Summary

The available data are sufficient to characterize the fate of the seven ARs.

FGARs are considered non-persistent to slightly persistent, and moderately mobile to hardly mobile. They are not considered bio-concentrating in aquatic organisms, with the possible exception of diphacinone. SGARs are considered moderately persistent to persistent, slightly mobile to immobile, and to be bio-concentrating, including in terrestrial animals. See **Section 5** for more information.

Exposure to ARs is by primary consumption (eating of treated bait) or secondary consumption (eating of poisoned primary consumers). Persistence of AR residues in the bodies of primary consumers is often sufficient to cause mortality in secondary consumers. The first-generation anticoagulants require several days of consecutive feedings to deliver a lethal dose, whereas the second-generation anticoagulants can deliver a lethal dose in only one night of feeding, although with either type of anticoagulant, death does not occur until 5-7 days after the feeding. Exposure in water is considered negligible because of the use of bait stations.

The residue of concern in all seven cases is the parent compound only, either due to degradation to non-toxic residues (FGARs) or due to very long persistence of the parent both environmentally and *in-vivo* (SGARs).

Exposure modeling for broadcast uses (chlorophacinone and diphacinone) was done using the PWC and T-REX models. Otherwise, exposure to primary consumers was estimated based on active ingredient concentration in the applied product, or to secondary consumers by concentration in wildlife food items (e.g., rodents consuming ARs).

1.4 Ecological Effects Summary

The seven ARs are all classified as very highly toxic to mammals on an acute oral (or acute dietary) exposure basis. While data are lacking on chronic toxicity to mammals for some of the ARs, sublethal effects (e.g. internal bleeding, lethargy) seen in acute tests are relevant to reproductive toxicity.

Although there is overlap in their properties, SGARs tend to be more acutely toxic than the FGARs, and SGARs are retained in body tissues longer compared to the FGARs. The retention in the body tissues increases the likelihood that non-target wildlife will encounter SGARs via secondary exposure, typically through the predation of target pests.

In birds, the FGARs range from slightly toxic to moderately toxic on an acute oral exposure basis. On a subacute dietary exposure basis, the FGARs range from highly toxic (chlorophacinone) to moderately toxic (warfarin and diphacinone) to birds. While chronic toxicity data are not available for warfarin or diphacinone, exposure to chlorophacinone reduced the mean 14-day survivor weights in a reproductive toxicity study in mallard ducks (*Anas platyrhynchos*) (NOAEC=0.046 mg ai/kg-diet; LOAEC=0.096 mg ai/kg-diet).

In contrast, the SGARs are much more toxic to birds on acute oral exposure basis. For the SGARs, acute oral toxicity in birds ranges from very highly toxic (brodifacoum, difethialone) to moderately toxic (difenacoum, bromadiolone). While chronic toxicity data for birds are not available for all ARs, LOAECs for 6 ARs were estimated based on the toxicity data for chlorophacinone.

2 Introduction

This Draft Risk Assessment (DRA) examines the potential ecological risks associated with labeled uses of seven first- and second-generation anticoagulant rodenticides on non-target organisms. These chemicals include warfarin, chlorophacinone, diphacinone (1st gen), and brodifacoum, bromadiolone, difethialone, and difenacoum (2nd gen). After review of the Problem Formulations and considering risk mitigations imposed during the Reregistration Eligibility Decision (RED) process and Notice of Intent to Cancel proceedings, this DRA quantitatively addresses only acute risk to birds and mammals. Acute and chronic risks to mammals, as the target organisms, have been well-documented in previous risk assessments. Acute risks to birds, especially via secondary poisoning, have also been previously established. This DRA extends this analysis to chronic effects on birds with new reproductive data for

chlorophacinone, coupled with a qualitative comparison to acute effect levels for the other 6 ARs.

This DRA also addresses incident reports since the time of the RED mitigation, including reports of adverse effects in listed and protected species. This analysis is intended to determine whether there are any discernable trends in incident reports since the mitigations, and whether there are any products or use patterns that are significant in the data.

2004 Comparative Risk Assessment. "Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: A Comparative Approach" (USEPA 2004) evaluated primary and secondary exposure of anticoagulant rodenticides to birds and mammals. The assessment determined that the greatest risk of rodenticide use to non-target animals is via primary and secondary exposure to mammals. The 2004 assessment also specified factors contributing to uncertainty in assessing anticoagulant rodenticides.

Risk Mitigation Decision for Rodenticides. In 2008, EPA released the Risk Mitigation Decision for Ten Rodenticides (RMD) (EPA 2008, Docket ID EPA-HQ-OPP-2006-0955 at www.regulations.gov). The focus of the decision was: 1) To minimize children's exposure to rodenticide products used in homes by requiring that all rodenticide bait products marketed to general and residential consumers be sold only with bait stations, with loose bait (e.g., pellets and meal) as a prohibited bait form and, 2) to reduce wildlife exposures and ecological risks, by requiring sale and distribution limits intended to prevent general consumers from purchasing residential use bait products containing four of the ten rodenticides that pose the greatest risk to wildlife (the second-generation anticoagulants – brodifacoum, bromadiolone, difenacoum, and difethialone). Moreover, bait stations were to be required for all outdoor, above-ground uses of these second-generation anticoagulants in order to reduce exposure.

Endangered Species Assessments. Several of the anticoagulant rodenticides have been the subject of Biological Evaluations for selected listed species. These assessments and their conclusions are listed in Table 2-1. Most of these were prompted by lawsuits specific to California. The chlorophacinone and diphacinone assessments for use on black-tailed prairie dogs were the result of FIFRA section 3 new use registrations, and related ESA litigation.

Table 2-1. Summary of Endangered & Threatened Species Assessments

Active Ingredient	Listed Species	Risk Conclusion	Reference
Warfarin	Salt Marsh Harvest Mouse, Alameda Whipsnake	May Affect, Likely to Adversely Affect. Adverse Habitat Modification.	USEPA 2011. In: Warfarin PF, 2015
Chlorophacinone	Salt Marsh Harvest Mouse, Alameda Whipsnake, San Joaquin Kit Fox, California Tiger Salamander	May Affect, Likely to Adversely Affect. Adverse Habitat Modification.	USEPA 2011. In: Chlorophacinone PF, 2015

Chlorophacinone (later extended to Diphacinone)	8 mammals 8 birds 2 Invertebrates 2 amphibians 1 reptile	Risks mitigated in consultation with USFWS for registration of Rozol for use on black tailed prairie dogs; Bulletins issued	USEPA 2010. In: Chlorophacinone PF, 2015
Diphacinone	Salt Marsh Harvest Mouse, Alameda Whipsnake, San Joaquin Kit Fox, California Tiger Salamander	May Affect, Likely to Adversely Affect. Adverse Habitat Modification.	USEPA 2011. In: Diphacinone PF, 2015
Difenacoum	Salt Marsh Harvest Mouse, Alameda Whipsnake, San Joaquin Kit Fox,	May Affect, Likely to Adversely Affect. Adverse Habitat Modification.	USEPA, 2012. In: Difenacoum PF, 2016

Scope of Work

Final Work Plans (FWPs) were completed for the first-generation anticoagulant rodenticides in May/June 2016, and for the second-generation anticoagulant rodenticides in September 2016 (**Table 2-2**). Problem Formulations and past risk assessments for the anticoagulant rodenticides concluded that these chemicals have the potential to pose risks to non-target animals through primary exposure via granular/bait applications and secondary exposure to predators or scavengers feeding on target pests who have consumed the bait. The anticoagulant rodenticides can become concentrated in the animal's liver leading to bioaccumulation in non-target wildlife. Risk mitigation during registration review will therefore focus on continued efforts to reduce exposure of non-target species.

On a risk management basis, the registration review team in EPA's Pesticide Re-evaluation Division has determined that with consideration of benefits and the potential risk exceedances to non-target species, the appropriate risk mitigation will likely be exposure reduction based on the *2008 Risk Mitigation Decision (RMD) for Ten Rodenticides (Commensal Uses Only)*. The RMD was signed on May 28, 2008 and revised June 24, 2008. However, the June revisions did not affect the risk conclusions, the risk management decision, or the rationale behind the decision, and the requirements imposed by the decision were unchanged.

All anticoagulant rodenticide field uses were required to be Restricted Use Products (RUP) as a result of the *1998 Rodenticide Cluster RED (All Uses)*. The 2008 RMD then required that all residential consumer use products be in securable bait form, in a tamper resistant bait station, within 50 ft of a building, and ≤1 lb of bait. Above ground uses must also be made within 100 ft of structures and fence line baiting is prohibited. The Agency's focus in registration review is on evaluating the effects of these mitigation measures. Furthermore, EPA has reviewed available data and incident reporting to inform the risk management decision.

Table 2-2. Anticoagulant rodenticides to be included in group assessment

Chemical (PC code)	*Registration Review Docket*
First generation anticoagulant rodenticides	
Chlorophacinone (067707)	EPA-HQ-OPP-2015-0778
Diphacinone (067701)	EPA-HQ-OPP-2015-0777
Warfarin (086002)	EPA-HQ-OPP-2015-0481
Second generation anticoagulant rodenticides	
Brodifacoum (112701)	EPA-HQ-OPP-2015-0767
Bromadiolone (112001)	EPA-HQ-OPP-2015-0768
Difenacoum (119901)	EPA-HQ-OPP-2015-0769
Difethialone (128967)	EPA-HQ-OPP-2015-0770

3 Problem Formulation Update

The purpose of problem formulation is to provide the foundation for the environmental fate and ecological risk assessment being conducted for the labeled uses of the seven FGARsSGARs. The problem formulation identifies the objectives for the risk assessment and provides a plan for analyzing the data and characterizing the risk. As part of the Registration Review (RR) process, detailed Problem Formulations (D426286, D426557, D426576, D429381, D429375, D429384, D429400) for each of the anticoagulant rodenticides were completed and are published in EPA's docket between December 2015 and March 2016 (**Table 2-2**). The following sections summarize the key points of the Problem Formulations and discusses key differences between the analysis outlined there and the analysis conducted in this DRA.

The risk conclusions summarized that the FGARs (warfarin, chlorophacinone, and diphacinone) present mortality risk to mammals and birds via primary and secondary exposure. Based on the use patterns (bait boxes, broadcast, floating bait stations), and specifically the lack of a spray application, the rodenticides posed little to no risk to aquatic taxa, or terrestrial plants. The SGARs (brodifacoum, bromadiolone, difethialone, and difenacoum) require that their use patterns are limited to a bait box, which excludes risk to aquatic taxa and terrestrial plants, as well. Of the rodenticides, warfarin was the only rodenticide that did not pose a risk to birds via secondary exposure, based on toxicity tests. An avian reproduction study was requested for all the rodenticides, except warfarin, since currently no data are available to assess the effects of long-term, low-dose exposure on avian reproduction.

Avian chronic (reproduction) studies were submitted for chlorophacinone and difenacoum. This DRA will use that data to qualitatively characterize reproductive risks to birds for the other five active ingredients.

3.1 Mode of Action for Target Pests

FGARs (warfarin, chlorophacinone and diphacinone) work by uncoupling oxidative phosphorylation, depressing hepatic synthesis of prothrombin and clotting factors VII, IX and X and cause direct damage to capillary permeability. The ultimate effect is widespread internal hemorrhage (World Health Organization, 2010). ARs are vitamin-K antagonists that disrupt normal blood-clotting mechanisms and induce capillary damage. Typically, death is delayed for four to ten or more days after a lethal dose is ingested, and animals may continue to feed and move about until shortly before death. Death results from hemorrhage, and exposed animals may exhibit behavior that may make them more susceptible to predation (Cox and Smith, 1992). This may result in secondary exposure to predatory animals.

FGARs tend to be less toxic and less persistent in biological tissue than SGARs, and usually require several days of consecutive feedings to deliver a lethal dose. SGARs tend to be more

acutely toxic than are the FGARs, and they are retained longer in body tissues of primary consumers. The greater potency and duration of action of long-acting ARs is attributed to their: (i) greater affinity for vitamin K(1)-2,3-epoxide reductase; (ii) ability to disrupt the vitamin K(1)-epoxide cycle at more than one point; (iii) hepatic accumulation; and (iv) unusually long biological half-lives due to high lipid solubility and enterohepatic circulation (Watt et al. 2005).

The first-generation anticoagulants require several days of consecutive feedings to deliver a lethal dose, whereas the second-generation anticoagulants can deliver a lethal dose in only one night of feeding, although with either type of anticoagulant, death does not occur until 5-7 days after the feeding. Because it takes several days for the rodent to die, animals may return to feed on the bait, thus acquiring multiple doses and allowing for higher than lethal concentrations of the rodenticide to accumulate. SGARs become concentrated in the animal's liver, with liver half-lives of up to a year. If an animal that consumes a SGAR is eaten by a predator or scavenger, then that animal can become secondarily exposed and affected by the rodenticide. Because SGARs are very persistent in the environment), these rodenticides have been shown to bioaccumulate in non-target wildlife.

3.2 Label and Use Characterization

3.2.1 Label Summary

Summaries of the labeled uses of the seven ARs are given in their respective problem formulations. All of these uses are for the control of rats, mice, or other small mammals. In accordance with the 2008 RMD, nearly all above-ground uses require tamper-resistant bait stations. Loose product (pellets, tracking powder, treated grain) are allowed for use in animal burrows only. Bait blocks are allowed for use in sewers. All of these use patterns are intended to limit primary exposure to the target rodents. Other exposure pathways are discussed below.

Broadcast Applications. Chlorophacinone and diphacinone have outdoor broadcast applications. Chlorophacinone may be broadcast at up to 40 lb/acre/year to control voles in orchards, non-crop areas, nurseries and tree and forestry plantations. Diphacinone may be broadcast at a rate of up to 20 lbs/acre on CRP lands and forests (as well as ships, boats and shipholds) to control Norway rats, roof rats, Polynesian rats, house mice, meadow voles and other invasive rodents. It may also be broadcast at a rate of 70 grams per burrow to control California ground squirrel. Warfarin is registered for use in controlling wild hogs in Texas. These uses pose a greater chance of non-target and secondary exposure and will be considered in detail later.

Floating Bait Stations. Chlorophacinone is used in a floating bait station to control muskrats, under SLN CA890023 (California Reg. No. 10965-500004ZA). This is a 0.005% treated grain, restricted-use product for use only in California, and sold only through the county agricultural commissioners. Up to 5 pounds of bait in an enclosed bait station is secured to a small raft

and anchored to the bottom or bank of the water body. This use poses some potential for exposure in aquatic systems and will be considered later.

3.2.2 Usage Summary

As the use patterns for rodenticides are not necessarily related to agriculture, OPP's Biological and Economic Analysis Division (BEAD) has not provided usage estimates for the ARs except for warfarin which was not sufficient to create a comparative usage analysis.

Limited information on usage of the 7 ARs is available from California's investigation of AR incidents (CDPR, Nov. 16, 2018). The CDPR document provides incomplete information on sale and use in California for 2005 to 2017. The greatest reported usage was for diphacinone (up to 120 pounds in 2013), followed by bromadiolone (about 75 pounds in 2016), and chlorophacinone (about 30 pounds in 2011). All the others were below 20 pounds per year from 2005 to 2017. Sales over the same period were highest again for diphacinone (nearly 250 pounds in 2017), followed by chlorophacinone (as much as 130 pounds in 2012), and bromadiolone (just over 100 pounds in 2012). Others were below 50 pounds per year from 2005 to 2017.

In Massachusetts, AR use by pest control services was tracked and reported to the Massachusetts Department of Agriculture to determine the frequency of use of specific rodenticides by pest management professionals in the state between 2008-2015. To estimate chemical rodenticide usage within a year, the study authors examined a list of active pesticide license holders in 2015. License holders for which company names denoted tree, landscape, solely insect-related, or other services clearly unrelated to structural rodent control were excluded, resulting in approximately 1300 individual licenses remaining. This number could be an overestimate of the total sampling population due to inability to ascertain whether each of these license holders definitely offered rodent control services in that year. For each of the years 2008, 2009, 2013, 2014, and 2015, random selections of 100 PURs filed by PMPs employing rodenticides for structural use were reviewed to evaluate the frequencies of use of specific rodenticides by PMPs in each year. The percentages recorded represented the number of reports of each toxicant per 100 pesticide usage reports that indicated structural use of chemical rodenticides. There was overall increase of AR use within the evaluated time period. The majority of reporting users employed more than one type of AR in each year. In all years evaluated, bromadiolone was the most frequently reported AR. 2015 was also the only year for which reports of use of all three of the most frequently employed SGARs, bromadiolone, brodifacoum, and difethialone, were over 50% for each SGAR (Murray 2017).

4 Residues of Concern

In this risk assessment, the stressors are those chemicals that may exert adverse effects on non-target organisms. Collectively, the stressors of concern are known as the Residues of Concern (ROC). The residues of concern usually include the active ingredient, or parent chemical, and may include one or more degradates that are observed in laboratory or field environmental fate studies. Degradates may be included in, or excluded from, the ROC based on submitted toxicity data, percent formation relative to the application rate of the parent compound, modeled exposure, and structure-activity relationships (SARs). Structure-activity analysis may be qualitative, based on retention of functional groups in the degradate, or they may be quantitative, using programs such as ECOSAR, the OECD Toolbox, ASTER, or others.

According to the problem formulations, the residue of concern is parent-only for all seven anticoagulant rodenticides: warfarin, chlorophacinone, diphacinone, brodifacoum, bromadiolone, difenacoum, and difethialone.

5 Environmental Fate Summary

Summaries of the physical properties and environmental fate parameters for the 7 ARs are given in their respective problem formulations. Selected fate parameters are given in Table 5-1 below. Based on these data, the FGARs can be characterized as non-persistent (<15 days) to slightly persistent (15-45 days) on the Goring (1975) scale, moderately mobile (Koc 100 –1000) to hardly mobile (Koc 10,000 – 100,000) (Food and Agricultural Organization of the United Nations (FAO) scale), and not bioconcentrating in aquatic organisms (logP <3), with the possible exception of diphacinone.

The SGARs may be characterized as moderately persistent (45 – 180 days) to persistent (>180 days) based on soil half-life (Goring 1975), slightly mobile (Koc 1,000 to 10,000) to immobile (Koc > 100,000) (FAO scale), and potentially bioconcentrating in fish (BCF > approx. 1,000).

Because the residue of concern in each case is parent-only, and because the exposure pathways are predominantly terrestrial, aquatic modeling is not performed except for broadcast uses of chlorophacinone and diphacinone. Modeling parameters for diphacinone and chlorophacinone will be given in the Aquatic Exposure section below.

Table 5-1. Fate characterization of Anticoagulant Rodenticides					
Chemical	Soil Half-life (days)	Hydrolysis Half-life pH 7	Aq. Photolysis half-life	Koc, L/g-oc	BCF (whole fish)
First generation					
Warfarin	5 (a)	stable	Not significant (a)	174 (a)	LogP <3
Chlorophacinone	17 - 47	stable	No data	20,999	LogP <3
Diphacinone	28 - 32	stable	stable	1700 - 2100	LogP = 4.85
Second generation					
Bromadiolone	128	stable	0.1d @pH7	1850 - 4750	1658
Brodifacoum	157	stable	No data	9155 (a)	2450
Difenacoum	>108 - 439	stable	8.1hr @pH7	170,700 (a)	9010 (a)
Difethialone	204 – 635 (a)	62min @pH7	No data	1E+8 – 5.3E+9	555
(a) data found in Footprint database https://sitem.herts.ac.uk/aeru/footprint/index2.htm					

The problem formulations for the four SGARs also indicated some concern for bioaccumulation via terrestrial foodchains. All four SGARs are believed to accumulate in the livers of primary consumers over multiple feedings, which may lead to a fatal dose for secondary consumers. The measured bioconcentration factors in fish (555 to 9010 for the SGARs) provide support for this concern. These effects are considered below in the sections on risks to birds and mammals.

6 Ecotoxicity Summary

Ecological effects data are used to estimate the toxicity of the ARs to surrogate species. The ecotoxicity data for the seven ARs have been reviewed previously in multiple ecological risk assessments (Rodenticide Cluster, USEPA, 1998; Risk Management Decision, USEPA, 2008) and most recently in Problem Formulations for Registration Review. These data are summarized in Section 3.

6.1 Aquatic Toxicity

Information on the toxicity of the seven ARs to aquatic organisms is given in the respective problem formulations. Exposure of aquatic organisms is generally not expected due to the use patterns as modified by the 2008 RMD, which requires the use of bait stations or application directly into animal burrows. None of the problem formulations anticipated carrying out an aquatic exposure analysis.

The FGARs, chlorophacinone and diphacinone still have broadcast applications that could result in aquatic exposure via runoff or erosion. Data cited in the problem formulations indicate that chlorophacinone is "highly toxic" to freshwater fish (rainbow trout (*Oncorhynchus mykiss*), LC_{50} = 0.452 mg ai/L) and invertebrates (daphnid (*Daphnia magna*), EC_{50} = 0.640 mg ai/L). In contrast, diphacinone is "moderately toxic" to the same species (rainbow trout, LC_{50} = 2.6 mg ai/L and *Daphnia*, EC_{50} = 1.8 mg ai/L). Therefore, in the aquatic risk assessment (**Section 9.2**), risks are quantified for chlorophacinone and are considered inclusive and protective of any potential risks to aquatic organisms from diphacinone which has similar use patterns, fate parameters and application rates as chlorophacinone.

Preliminary Tier 1 ecological modeling (using GENEEC) in the PFs indicated low risk concerns, however the modeled application rates were far below the maximum labeled rates (chlorophacinone, 40 lb/acre and diphacinone, 20 lb/acre). This analysis will be repeated at Tier 2 in this assessment.

6.2 Terrestrial Toxicity

Information on the toxicity of the seven ARs to terrestrial organisms was obtained from the respective problem formulations. The ARs are all classified very highly toxic to mammals on an acute exposure basis. While data are generally lacking on chronic toxicity to mammals, sublethal effects (e.g. internal bleeding, lethargy) seen in acute tests are relevant to reproductive toxicity.

Although there is overlap in their metabolic and toxicological properties, SGARs tend to be more acutely toxic than the FGARs, and they are retained in body tissues longer compared to the FGARs. The retention in the body tissues increases the likelihood that non-target wildlife will encounter SGARs via secondary exposure, typically through the predation of target pests.

In birds, the FGARs (warfarin, diphacinone, chlorophacinone) range from slightly toxic to moderately toxic on an acute oral exposure basis. On a subacute dietary exposure basis, the FGARs range from highly toxic (chlorophacinone) to moderately toxic (warfarin and diphacinone) to birds. While chronic toxicity data are not available for warfarin or diphacinone, chlorophacinone reduced the mean 14-day survivor weights in a reproductive toxicity study in mallard ducks (NOAEC=0.046 mg ai/kg-diet; LOAEC=0.096 mg ai/kg-diet).

In contrast, the SGARs are much more toxic than FGARs to birds on acute oral exposure basis. For the SGARs, acute oral toxicity in birds ranges from very highly toxic (brodifacoum, difethialone) to moderately toxic (difenacoum, bromadiolone). While chronic toxicity data for birds are not available for all of the ARs, we have made estimates of the possible LOAEC for 6 ARs based on the chlorophacinone toxicity data.

Toxicity to Birds

1st Generation Rodenticides: Diphacinone, Chlorophacinone and Warfarin

Diphacinone

On an acute oral exposure basis, diphacinone is classified as slightly toxic to birds. An acute oral study (MRID 42245201) that assessed toxicity to the bobwhite quail (*Colinus virginianus*) determined the LD_{50} value was 1630 mg ai/kg-bw. An acute dietary study that assessed the toxicity to mallard ducks (*Anas platyrhynchos*) determined the LC_{50} to be 906 mg ai/kg-diet (MRID 42408802). There are currently no chronic avian studies available for diphacinone.

Also for diphacinone, an LD_{50} of 96.8 mg ai/kg-bwt is available for one raptor species (American kestrel, *Falco sparverius*) (Rattner *et al*. 2011). This study suggests that American kestrels may be more sensitive than the standard test species (*i.e.,* based on the available studies, 17 to 21 times more sensitive than bobwhite quail and 33 times more sensitive than mallard ducks). None of the other evaluated rodenticides have data for which an LD_{50} for raptors, or, more generally, predatory birds is available. If the sensitivity of the American kestrel to diphacinone is representative of other species of raptors, this information suggests that raptors may be more sensitive to diphacinone than either bobwhite quail or mallard duck. For consistency, the acute oral bobwhite quail endpoint will be used for risk assessment.

Chlorophacinone

On an acute oral exposure basis, chlorophacinone is classified as moderately toxic to birds. An acute oral study (MRID 41513101) that assessed toxicity to the bobwhite quail determined the oral LD_{50} value to be 258 mg ai/kg-bw. An acute dietary study that assessed the toxicity to northern bobwhites determined the LC_{50} to be 56 mg ai/kg-diet (MRID 41513102). A chronic study of the mallard duck determined the NOAEC to be 0.046 mg ai/kg-diet (MRID 48994002). The NOAEC is based on the reduction in the mean 14-day survivor weights at 0.096 and 0.96 mg ai/kg-diet treatment levels.

Warfarin

On an acute oral exposure basis, warfarin is classified as slightly toxic to birds. An acute oral study (MRID 00248782) that assessed toxicity to the mallard duck determined the LD_{50} value was 621 mg ai/kg-bw. An acute dietary study that assessed the toxicity to bobwhite quail determined the LC_{50} to be 625 mg ai/kg-diet (MRID 00153365), and classified warfarin as moderately toxic on this basis. There are currently no chronic avian studies available for warfarin.

2nd Generation Rodenticides: Bromadiolone, Brodifacoum, Difenacoum, Difethialone

Bromadiolone

An acute oral study (MRID 00143279) that assessed toxicity of bromadiolone to bobwhite quail determined the LD_{50} value was 170 mg ai/kg-bw. An acute dietary study that assessed the

toxicity to bobwhite quails determined the LC_{50} to be 37.6 mg ai/kg-diet (MRID 00143280). There are currently no chronic avian studies available for bromadiolone.

Brodifacoum

On an acute oral and subacute dietary exposure basis, brodifacoum is classified as highly toxic to birds. An acute oral study (MRID 41563303) that assessed toxicity to the mallard duck determined the LD_{50} value was 0.26 mg ai/kg-bw. A sub-acute dietary study that assessed the toxicity to bobwhite quails determined the LC_{50} to be 0.8 mg ai/kg-diet (MRID 00124477). In addition to lethal effects observed in toxicity studies, birds were observed to have sublethal effects including hemorrhaging, weight loss, decreased activity levels, wing droop, loss of equilibrium, and lethargy and other sublethal effects. There are currently no chronic avian studies available for brodifacoum.

Difenacoum

On an acute oral exposure basis, difenacoum is classified as moderately toxic to birds. An acute oral study (MRID 46750922) that assessed toxicity to the bobwhite quail determined the LD_{50} value was 67 mg ai/kg-bw. Sublethal effects noted in the acute oral study in live test birds that were euthanized and subsequently subjected to necropsy, included hemorrhaging and lethargy in all birds, and there was 40% mortality even at the lowest treatment group of 50 mg/kg bw. An acute dietary study that assessed the toxicity to the mallard duck determined the LC_{50} to be 14.1 mg ai/kg-diet (MRID 46750926), classifying difenacoum as very highly toxic on this basis. Post-mortem examinations indicated evidence of hemorrhaging and blood clots in the liver and other organs for birds exposed to the ≥0.75 mg/kg treatment diets in the sub-acute dietary study. There are currently no chronic avian studies available for difenacoum.

Difenacoum exhibited high levels of toxicity to birds via the drinking water exposure route in a 6-week one-generation reproductive effects study on Japanese quail (*Coturnix coturnix japonica*) (MRID 50623624). Difenacoum could not be measured in feed at low enough levels to measure the dose levels, so the exposure route was switched to water. Based on the study author's results, no mortality was observed in the control or in the lowest treatment group (58 µg ai/kg bw). Treatment-related mortalities were noted in the 115 and 241 µg ai/kg bw treatment groups (female birds in each pair). The ratio of acute (67 mg ai/kg-bw) and chronic (58 µg ai/kg bw) endpoints is 1,155, similar to that for chlorophacinone (1,796).

Difethialone

On an acute oral exposure basis, difethialone is classified as highly toxic to birds. An acute oral study (MRID 40696901) that assessed toxicity to the bobwhite quail determined the LD_{50} value was 0.26 mg ai/kg-bw. An acute dietary study that assessed the toxicity to the bobwhite quail determined the LC_{50} to be 0.56 mg ai/kg-diet (MRID 40696902), classifying difethialone as very highly toxic. In these studies sublethal effects included lethargy, subcutaneous hemorrhaging, weakness, bloody diarrhea or urine and reduced food consumption and body weight loss. There are currently no chronic avian studies available for difethialone.

Toxicity to Mammals

1st Generation Rodenticides: Diphacinone, Chlorophacinone and Warfarin

Diphacinone

On an acute oral exposure basis, diphacinone is classified as very highly toxic to mammals. An acute study (MRID 05002272) that assessed toxicity to laboratory rats (*Rattus norvegicus*) determined the LD_{50} value was 1.9 mg ai/kg-bw. A mammalian acute dietary study (Teeters, 1981) set the LC_{50} at 2.08 mg ai/kg-diet, indicating that diphacinone is very highly toxic on an acute dietary exposure basis. There are currently no chronic studies available for diphacinone.

Chlorophacinone

On an acute oral exposure basis, chlorophacinone is classified as very highly toxic to mammals. An acute oral study (Ashton, et al., 1986) that assessed laboratory rats (*Rattus norvegicus*) through multiple doses determined the LD_{50} value was 0.8 mg ai/kg-bw. A mammalian acute dietary study (Teeters 1981) set the LC_{50} at 1.14 mg ai/kg-diet, indicating that chlorophacinone is very highly toxic on an acute dietary exposure basis. A 2-generation reproduction study with rabbits (MRID 43570801) indicated that the developmental NOAEL for mammals was 10 µg/kg-bw/day. The endpoint was derived from the lack of sufficient fetuses at the end of the test, as there was high maternal mortality in the higher test levels.

Warfarin

On both an acute oral and dietary exposure basis, warfarin is classified as very highly toxic to mammals. An acute oral study with rats (MRID 05002272) determined the LD_{50} value was 3.0 mg ai/ kg-bw. A mammalian acute dietary study (Teeters 1981, TMN 126) set the LC_{50} at 4.41 mg ai/kg-diet. There are no chronic mammalian studies for warfarin.

2nd Generation Rodenticides: Bromadiolone, Brodifacoum, Difenacoum, Difethialone

Bromadiolone

On an acute oral exposure basis, bromadiolone is classified as very highly toxic to mammals. An acute study (MRID 00241703) determined the LD_{50} value was 0.6 mg ai/ kg-bw. A 2-generation mammalian study with rats (MRID 92196014) determined the NOAEL to be 0.035 mg ai/kg-bw, and the LOAEL to be 0.070 mg ai/kg-bw. Sublethal effects included vaginal bleeding, hypotonicity, and pale eyes.

Brodifacoum

On an acute oral exposure basis, brodifacoum is classified as very highly toxic to mammals. In addition to lethal effects observed in toxicity studies, mammals were observed to have sublethal effects, including hemorrhaging, weight loss, decreased activity levels, loss of equilibrium, and lethargy, among other sublethal effects. An acute oral study (MRID 42687501) determined the LD_{50} value was 0.42 mg ai/kg-bw; the study classified brodifacoum as “highly toxic”. A mammalian acute dietary study (USEPA, TN110) set the LC_{50} at 0.55 mg ai/kg-diet. A wild mammal acute dietary study conducted by the USFWS (MRID 00080237) set the LC_{50} at 1.4

mg ai/kg-diet. Both acute dietary study endpoints indicated that brodifacoum is very highly toxic. No chronic data are available for brodifacoum.

Difenacoum

Difenacoum is very highly toxic to mammals on an acute oral exposure basis, based on the rat data (male acute oral LD50 = 1.8 mg/kg-bw, MRID 46750935). Additionally, MRID 46766206 shows that the *cis* isomer may be more toxic than the *trans* isomer and the house mouse may be more sensitive than the rat, with male mice exposed to the *cis* isomer having an LD50 of 0.45 mg ai/kg-bw (female mice exposed to the *cis* isomer in the same study had an LD50 of 1.0 mg ai/kg-bw), while the *trans* isomer was approximately 2-3 times less toxic (male and female LD50s of 1.18 and 2.75, respectively). EFED typically averages the male and female LD50 values if a difference exists between them. In the risk assessment, male mouse data with the *cis* isomer will be used for risk characterization. No acceptable acute dietary or chronic mammalian data are available for difenacoum.

Difethialone

Difethialone is very highly toxic to mammals. In addition to lethal effects observed in toxicity studies, mammals were observed to have sublethal effects that included lethargy, subcutaneous hemorrhaging, weakness, bloody diarrhea or urine, reduced food consumption, and body weight loss. On an acute oral exposure basis, difethialone is classified as very highly toxic to mammals. An acute study (MRID 40268903, 42687704) determined the LD_{50} value was 0.55 mg ai/kg-bw. There are no chronic mammalian data available for difethialone.

Table 6-1. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Warfarin (1st Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Mallard duck *Anas platyrhynchos*	LD_{50}=621 mg ai/kg-bw Slightly toxic	00248782 (Acceptable)
Sub-acute dietary	Bobwhite quail *Colinus virginianus*	LD_{50}=625 mg ai/kg-diet Moderately Toxic	00153365 (Acceptable)
Mammals			

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=3.0 mg ai/kg-bw Very Highly Toxic	05002272 (Acceptable)
Acute Dietary		LC_{50}=4.41 mg ai/kg-diet Very Highly Toxic	Teeters 1981 (TMN 126) (Supplemental)

Table 6-2. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Chlorophacinone (1st-Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Bobwhite quail *Colinus virginianus*	LD_{50}=258 mg ai/kg-bw Slope = 2.88	41513101 (Acceptable)
Sub-acute dietary		LC_{50}=56 mg ai/kg-diet Slope=1.49	41513102 (Acceptable)
Chronic	Mallard duck *Anas platyrhynchos*	NOAEC=0.046 mg ai/kg-diet LOAEC=0.096 mg ai/kg-diet (based on mean 14-day survivor weight)	48994002 (Acceptable)
Mammals			
Acute Oral	Black-tailed Prairie dogs *Cynomys ludovicianus*	LD_{50}=1.94 mg ai/kg-bw Very Highly Toxic	47333601 (Supplemental)
Acute Oral	Laboratory rat *Rattus norvegicus*	5-day LD_{50}=0.8 mg ai/kg-bw[1] Very Highly Toxic	Ashton et al (1986) (Supplemental/ Qualitative)
Acute Dietary		LC_{50}=1.14 mg ai/kg-diet Slope=7.19 Very Highly Toxic	Teeters 1981 (TNM 117) (Supplemental)
Chronic (2-gen. repro)	Rabbit *Oryctolagus cuniculus*	Developmental NOAEL=10 µg ai/kg-bw/day	43570801 (Acceptable)

1. A dose of 0.16 mg ai/kg-bw was given every day for 5 days

Table 6-3. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Diphacinone (1st Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Bobwhite quail *Colinus virginianus*	LD_{50}=1630 mg ai/kg-bw Slightly Toxic	42245201 (Acceptable)
Sub-acute dietary	Mallard duck *Anas platyrhynchos*	LC_{50}=906 mg ai/kg-diet Slope=0.5 Moderately Toxic	42408802 (Acceptable)
Reptiles			
Acute Oral	Brown tree Snake *Boiga irregularis*	LD_{50}=20.75 mg ai/kg-bw Slope=4.2 Highly Toxic	Brooks et al 1998 (Supplemental /Quantitative)
Mammals			
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=1.9 mg ai/kg-bw Very Highly Toxic	05002272 (Supplemental)
Acute Dietary		LC_{50}=2.08 mg ai/kg-diet Very Highly Toxic Slope=4.2	Teeters 1981 (TNM 75) (Supplemental)

Table 6-4. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Bromadiolone (2nd-Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Bobwhite quail, *Colinus virginianus*	LD_{50}=170 mg/kg-bw (95% CI: 115-261) Highly Toxic	00143279 (Acceptable)
Sub-acute dietary		LC_{50}=37.6 mg ai/kg-diet (95% CI: 8.9-84.5) Slope=0.83 (95% CI: 0.42-1.23) Highly Toxic	00143280 (Acceptable)
Sub-acute dietary	Mallard duck *Anas platyrhynchos*	LC_{50}=158 mg ai/kg-diet (95% CI: 7-762) Slope=0.46 (95% CI: 0.11-0.81) Highly Toxic	00143278 (Acceptable)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Mammals			
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=0.6 mg ai/kg-bw Very Highly Toxic	00241703 (Supplemental)
Chronic (2-generation reproduction)	Laboratory rat *Rattus norvegicus*	NOAEL=0.035 mg ai/kg-bw LOAEL=0.070 mg ai/kg-bw	92196014 (Acceptable)

Table 6-5. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Brodifacoum (2nd-Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Mallard duck *Anas platyrhynchos*	LD_{50}=0.26 mg ai/kg-bw (95% CI: 0-0.8) Very Highly Toxic	41563303 (Acceptable)
Sub-acute dietary	Bobwhite quail, *Colinus virginianus*	40-Day LC_{50}=0.8 mg ai/kg-diet (95% CI: 0.1-4.7) Very Highly Toxic	00124477 (Acceptable)
Mammals			
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=0.42 mg ai/kg-bw (females) Highly Toxic	42687501 (Acceptable)
Acute Dietary		LC_{50}=0.55 mg ai/kg-diet (95% CI: 0.45-0.68) Very Highly Toxic	Test No. 110 USEPA Beltsville, MD
Acute Dietary	Wild vole *Vole Microtus sp.*	LC_{50}=1.4 mg ai/kg-diet (95% CI: 0.77-2.0) Very Highly Toxic	00080237 USFWS Denver Lab

Table 6-6. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Difenacoum (2nd-Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Bobwhite quail *Colinus virginianus*	LD_{50}=67 mg ai/kg-bw (95% CI: 3.5-150.7) Slope=1.22 Moderately Toxic	46750922 (Acceptable)
Sub-acute dietary	Mallard duck *Anas platyrhynchos*	LC_{50}=14.1 mg ai/kg-diet (95% CI: 6.9-88.2) Slope=1.13 Very Highly Toxic	46750926 (Supplemental)
Mammals			
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=1.8 mg ai/kg-bw (95% CI: 1.5-2.1) Very Highly Toxic	46750935 46750936 (Acceptable)

Table 6-7. Summary of Most Sensitive Endpoints from Terrestrial Toxicity Studies for Difethialone (2nd-Generation AR)

Study Type	Test Species	Toxicity Value	MRID or ECOTOX No./ Classification
Birds (Surrogates for Terrestrial Amphibians and Reptiles)			
Acute Oral	Bobwhite quail, *Colinus virginianus*	30-Day LD_{50}=0.26 mg ai/kg-bw (95% CI: 0.17-4.0) Very Highly Toxic	40696901 (Acceptable)
Sub-acute dietary		30-Day LC_{50}=0.56 mg ai/kg-diet (95% CI: 0.16-1.9) Very Highly Toxic	40696902 (Acceptable)
Mammals			
Acute Oral	Laboratory rat *Rattus norvegicus*	LD_{50}=0.55 mg ai/kg-bw Very Highly Toxic	40268903 42687704 (Acceptable)

6.3 ECOSAR Analysis

ECOSAR analysis was performed for the aquatic assessment of chlorophacinone broadcast uses. Toxicity estimates for freshwater fish 96h LC_{50} (0.22 mg/L) and *Daphnia* 48h LC_{50} (0.17 mg/L) from the Neutral Organics class were within the "good" range, i.e., matched within a factor of 5 of the measured results (0.452 and 0.640 mg/L, respectively). The ECOSAR estimates for toxicity to freshwater fish (chronic), *Daphnia* (chronic), green algae (acute), saltwater fish (acute and chronic), and *Mysid* (acute and chronic) all exceeded exposure estimates by several orders of magnitude. It is therefore presumed that these taxa are not at risk from chlorophacinone, and by extension diphacinone, broadcast uses.

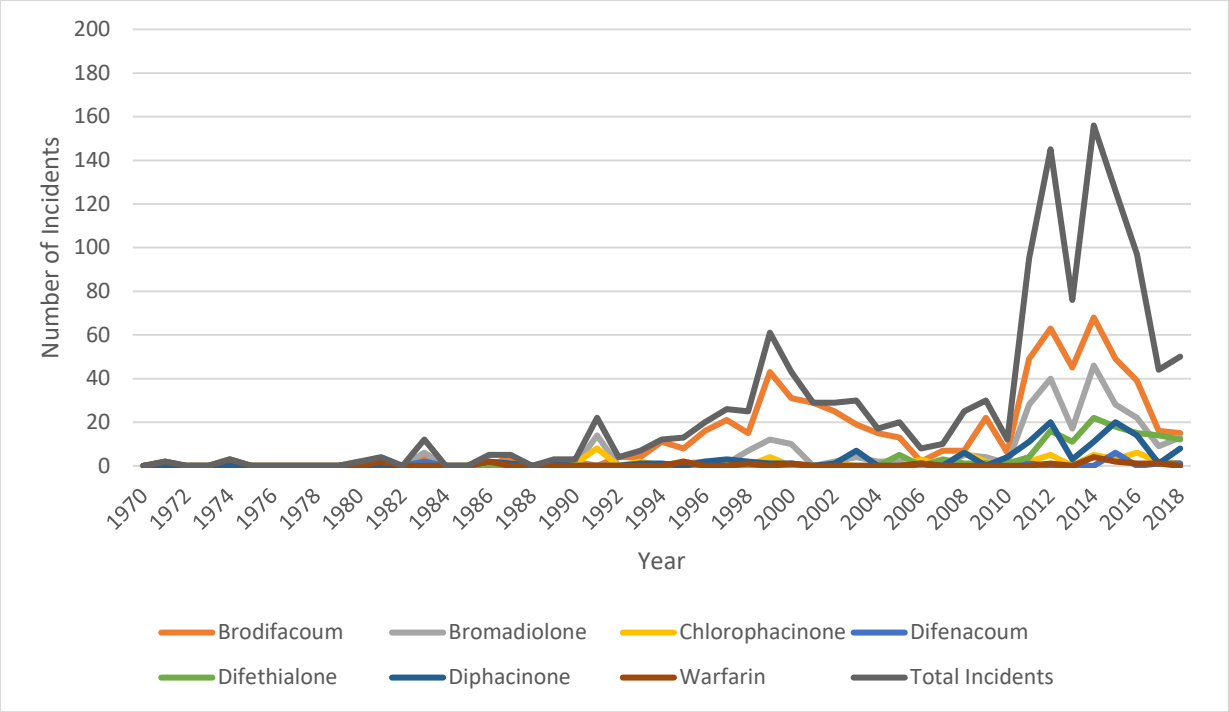
6.4 Incident Data

The Incident Data System (IDS) is an OPP database that houses ecological incidents that have been reported to the Agency. When available, IDS includes the date and location of an incident, type and magnitude of effects observed in various species, use(s) of pesticides known or suspected of contributing to the incident, and results of any chemical residue analysis or other analyses conducted during incident investigation. IDS incidents are categorized according to the certainty that the incident resulted from pesticide exposure. The current report summarizes the available incident information as of August 2019. This search excluded incidents classified as 'unlikely', 'unspecified', or 'unrelated' and only includes incidents with the certainty categories of 'exposure only', 'possible', 'probable', and 'highly probable'. The number of actual incidents associated with anticoagulant rodenticides may be higher than what is reported to the Agency. Incidents may go unreported since side effects may not be immediately apparent or readily attributed to the use of a chemical. Although incident reporting is required under FIFRA Section 6(a)(2), the absence of reports in IDS does not indicate that the chemical has no effects on wildlife; rather, it is possible that incidents are unnoticed and unreported.

Over 1200 incidents have been reported for the seven evaluated rodenticides (brodifacoum, bromadiolone, chlorophacinone, difenacoum, difethialone, diphacinone, and warfarin) since 1971. Of the 1271 reported incidents, 804 (63%) were reported between 2010 and 2018, subsequent to the 2009 implementation of restricted use and bait box requirements imposed by the Agency, indicating that exposure and wildlife incidents have continued at an increased reporting rate since 2010. This increase in reported incidents is largely driven by two rodenticides in particular – brodifacoum and bromadiolone, which have 353 and 204 reported incidents between 2010 and 2018, respectively, accounting for roughly 69% of the incidents for all evaluated rodenticides during that time period, even though they have no broadcast uses. One possible explanation for the high numbers of brodifacoum and bromadiolone incidents is that these chemicals are more persistent, which may play a role in their residues' frequent appearances in animal livers relative to the other rodenticides. Notably, the FGARs with broadcast uses do not seem to be comparatively major causes of incidents. It is difficult to determine if apparent trends in incidents are meaningful or not given that very few of the total

incidents that occur are actually observed or reported to regulatory agencies. **Figure 6-1** shows the number of incidents reported for each rodenticide since 1971 and does not include incidents without a specified year. The increase in the number of reported incidents over time may be due in part to more systematic reporting or other factors.

Figure 6-1. Rodenticide Incident Occurrence Since 1970



The likelihood that an incident is caused by a particular pesticide is classified with various certainty criteria based on the availability of a residue analysis of carcasses, visual verification of gross pathological observations such as hemorrhaging, or other evidence. **Table 6-8** shows the number of incidents that fell into each certainty index for each evaluated rodenticide as of 2019.

As expected for rodenticides, observed incidents among the evaluated chemicals impacted primarily mammals and birds. Few incidents were reported among the fish, invertebrate, and reptile taxa.

Table 6-8. The Number of Incidents per Certainty Category for Evaluated Rodenticides

	Residue Exposure Only[1]	Highly Probable[2]	Possible[3]	Probable[4]	Unlikely[5]	Unrelated[6]	Unspecified[7]
Brodifacoum	81	302	120	155	51	64	31
Bromadiolone	56	67	76	79	37	35	21
Chlorophacinone	8	21	11	14	8	8	4
Difenacoum	1	2	6	3	4	0	0
Difethialone	14	41	38	31	13	12	18
Diphacinone	24	29	54	15	22	18	5
Warfarin	1	11	7	4	3	2	0
Total Incidents	185	473	312	301	138	139	79

[1] Pesticide was detected in live animal and an incident report was submitted to document the exposure
[2] Pesticide confirmed as cause through residue analysis or other reliable evidence, or circumstances and the pesticide's toxicity or history of previous incidents give strong support that pesticide was the cause
[3] Pesticide could have caused the incidents, but there are other possible plausible explanations
[4] Circumstances of the incident and properties of the pesticide indicate that this pesticide was the cause, but confirming evidence is lacking
[5] Evidence exists that a stressor other than exposure to this pesticide caused the incident, but that evidence is not conclusive
[6] Conclusive evidence exists that a stressor other than exposure to this given pesticide is what caused the incident
[7] No information on the certainty category was available for the incident

Anticoagulant incidents are based on detection of residue or residues in liver tissue and corroborating evidence from carcass necropsy. Such analyses are expensive, and insufficient funding limits the extent of analyses and incident reporting. Furthermore, most incidents are not reported for a variety of reasons. For example, most animal carcasses are never found by humans, scavengers quickly remove and consume carcasses, carcasses or ill animals discovered by humans are not always reported to the proper authorities, and carcasses discovered and reported are not typically analyzed for rodenticides. Additionally, although most of the reported wildlife incidents involve animals found dead, there are several rodenticide incidents that involve incapacitated animals (most of which died after being found). They demonstrate that animals exposed to rodenticides may be incapacitated in ways that would almost certainly make them more vulnerable to predators and accidental death (e.g., car or window strikes). If an animal dies due to predation or an accident, their death may not necessarily be attributed to a pesticide, even if it is a contributing factor.

Birds. Incidents involving anticoagulants have been observed in over 70 species of birds, including owls, diurnal raptors and vultures, corvids, and others. In **Table 6-9** below, the total numbers of incidents for birds involving SGARs and FGARs since 1971 are reported alongside the number of incidents involving SGARs and FGARs since 2010 in parentheses. Overall the results demonstrate that significant numbers of incidents are being reported for birds for both SGARs and FGARs, with over half of all reported incidents for birds coming within the 2010 to

2018 time frame, possibly due to an increase in incident reporting and not necessarily due to an increase in actual incident occurrence. Of the 656 incidents in which anticoagulant rodenticides were involved, SGARs were detected in 90% and FGARs in 10%. Brodifacoum was detected in 60% of the bird-related incidents, bromadiolone in 19%, difethialone in 11%, difenacoum in 1.2%, chlorophacinone in 3.2%, diphacinone in 5.0%, and warfarin in 1.5%.

Table 6-9. Anticoagulant Rodenticide Incidents in Birds

Species	Total Number of Incidents	SGARs	FGARs
Owls			
Long-Eared Owl (*Asio otus*)	2	2	0
Burrowing Owl (*Athene cunicularia*)	1	1	0
Snowy Owl (*Bubo scandiacus*)	1	0	1
Great Horned Owl (*Bubo virginianus*)	123 (69)	113 (60)	10 (9)
Eastern Screech-Owl (*Megascops asio*)	12 (1)	12 (1)	0
Screech-Owl (*Megascops* sp.*)*	4	4	0
Owl (*Strigidae*)	8 (5)	8 (5)	0
Saw-Whet Owl (*Aegolius acadicus*)	1	1	0
Spotted Owl (*Strix occidentalis*)	3 (3)	2 (2)	1 (1)
Barred Owl (*Strix varia*)	4 (3)	4 (3)	0
Barn Owl (*Tyto alba*)	91 (78)	83 (73)	8 (5)
Diurnal Raptors			
Red-Tailed Hawk (*Buteo jamaicensis*)	145 (77)	137 (73)	8 (4)
Cooper's Hawk (*Accipiter cooperii*)	24 (3)	23 (2)	1 (1)
Golden Eagle (*Aquila chrysaetos*)[1]	14 (2)	13 (2)	1
Bald Eagle (*Haliaeetus leucocephalus*)[1]	15 (9)	6 (4)	9 (5)
Red-Shouldered Hawk (*Buteo lineatus*)	19 (16)	18 (15)	1 (1)
Broad-Winged Hawk (*Buteo platypterus*)	2	2	0
Sharp-Shinned Hawk (*Accipiter striatus*)	2 (1)	2 (1)	0
Unidentified Eagle (*Buteoninae*)	2	1	1
American Kestrel (*Falco sparverius)*	4 (2)	3 (1)	1 (1)
Peregrine Falcon (*Falco peregrinus*)	3	1	2
Turkey Vulture (*Cathartes aura*)	20 (14)	16 (13)	4 (1)
Black Vulture (*Coragyps atratus*)	1	1	0
Unidentified Hawk (*Accipitridae*)	37 (16)	35 (14)	2 (2)
Buzzard (*Buteo* sp.)	2	1	1
Northern Harrier (*Circus cyaneus*)	1	1	0
Others			
Auklet (*Alcidae*)[2]	1	1	0
Mallard (*Anas platyrhynchos*)[2]	1	1	0
Duck/Swan (*Anatidae*)[2]	2	2	0

Species	Total Number of Incidents	SGARs	FGARs
Black Noddy (*Anous minutus*)[2]	2	1 (1)	0
Goose (*Anserinae*)[2]	2 (1)	2 (1)	0
Great Blue Heron (*Ardea herodias*)	1	1	0
Egret/Heron (*Ardeidae*)	3	3	0
Ruddy Turnstone (*Arenaria interpres*)[2]	1 (1)	1 (1)	0
Canada Goose (*Branta canadensis*)[2]	6 (1)	4 (1)	2
Lapland Longspur (*Calcarius lapponicus*)[2]	1	1	0
Rock Sandpiper (*Calidris ptilocnemis*)[2]	1	1	0
Pigeon Guillemot (*Cepphus columba*)[2]	1	1	0
Plover (*Charadriidae*)[2]	1	1	0
New Zealand Dotterel (*Charadrius obscurus*)[2]**	1	1	0
Emperor Goose (*Chen canagica*)[2]	1	1	0
Bobwhite Quail (*Colinus virginianus*)[2]	1	0	1
Rock Dove (*Columbia livia*)[2]	2	1	1
Pigeon (*Columbidae*)[2]	1	0	1
American Crow (*Corvus brachyrhynchos*)	18 (2)	18 (2)	0
Common Raven (*Corvus corax*)	3 (2)	3 (2)	0
Fish Crow (*Corvus ossifragus*)	1	1	0
Tufted Puffin (*Fratercula cirrhata*)[2]	1	1	0
Finch (*Fringillidae*)[2]	1	1	0
Northern Fulmar (*Fulmarus glacialis*)	1	1	0
Crane (*Gruidae*)	1	1	0
Pied Stilt (*Himantopus himantopus)*[2]**	1	1	0
Harlequin Duck (*Histrionicus histrionicus*)[2]	1	1	0
Glaucous-Winged Gull (*Larus glaucescens*)	1	1	0
Franklin's Gull (*Larus pipixcan*)	1	1	0
Laughing Gull (*Leucophaeus articilla*)	1	1	0
Turkey (*Meleagridinae*)[2]	2 (1)	1	1 (1)
Wild Turkey (*Meleagris gallopavo*)[2]	2	0	2
Thrasher (*Mimidae*)[2]	1 (1)	1 (1)	0
Bristle-Thigh Curlew (*Numenius tahitiensis*)[2]	1 (1)	1 (1)	0
Sooty Tern (*Onychoprion fuscatus*)[2]	1 (1)	1 (1)	0
Sparrow (*Passeroidea*)[2]	1	0	1
Pelagic Cormorant (*Phalacrocorax pelagicus*) [2]	1	1	0
Snow Bunting (*Plectrophenax nivalis*)[2]	1	1	0
Pacific Golden Plover (*Pluvialis fulva*)[2]	1 (1)	1 (1)	0
Pukeko (*Porphyrio melanotus*) [2]**	1	1	0
Parakeet/Parrot (*Psittacidae*)[2]**	1 (1)	1 (1)	0

Species	Total Number of Incidents	SGARs	FGARs
Avocet (*Recurvirostra*)[2]	1	1	0
Common Eider (*Somateria mollissima*)[2]	1	1	0
Western Meadowlark (*Sturnella neglecta*)[2]	2 (1)	1	1 (1)
Starling (*Sturnus vulgaris*)[2]	2 (2)	2 (2)	0
Red-Footed Booby (*Sula sula*)[2]**	1 (1)	1 (1)	0
Robin (*Turdidae*)[2]	1	1	0
Spur-Winged Plover (*Vanellus miles novaehollanidae*)[2]**	1	1	0
Mourning Dove (*Zenaida macroura*)[2]	1	1	0
Golden-Crowned Sparrow (*Zonotrichia atricapilla*)[2]	1	1	0
White-Crowned Sparrow (*Zonotrichia leucophrys*)[2]	1	1	0
Unknown Bird	16 (8)	14 (7)	2 (1)
Unknown Waterfowl	2 (1)	1	1 (1)
Total Birds	**654 (341)**	**590 (306)**	**64 (34)**

[1] Listed (endangered or threatened) or protected species

[2] Species' exposure may occur via terrestrial invertebrate consumption rather than mammal/bird consumption due to their diet

**Non-North American species

Numbers in parentheses () are the number of incidents that species had from 2010 to 2018, after the implementation of the RMD.

Mammals. Anticoagulant rodenticide incidents have been recorded in over 40 species, including the endangered San Joaquin kit fox, key deer, and lynx. As above, in **Table 6-10** below, the total numbers of mammal incidents involving SGARs and FGARs since 1971 are reported alongside the number of incidents involving SGARs and FGARs since 2010 in parentheses. Overall the results demonstrate that significant numbers of incidents are being reported for mammals for both SGARs and FGARs with over half of all reported incidents for mammals coming within the 2010 to 2018 time frame, possibly due to an increase in incident reporting and not necessarily due to an increase in actual incident occurrence. With respect to listed species, one incident was reported for the endangered lynx (1991) and two for the endangered key deer (2008), and no other incidents have been reported with those species in the time since. In contrast, incidents with another listed species, the San Joaquin kit fox, have continued recently; the kit fox has had 35 of its 38 total incidents occur in 2011 or later. SGARs were detected in 78% of the incidents and FGARs in 22%. By rodenticide, brodifacoum was detected in 43%, bromadiolone in 26%, difethialone in 8.6%, difenacoum in 0.66%, chlorophacinone in 5.4%, diphacinone in 14%, and warfarin in 2.1%. Brodifacoum and bromadiolone residues were detected together in some incidents, especially bobcats and mountain lions but also several coyotes and kit foxes.

Table 6-10. Anticoagulant Rodenticide Incidents in Mammals

Species	Total Number of Incidents	SGARs	FGARs
Canids			
Fox (*Canidae*)	7 (2)	7 (2)	0
Dog (*Canis familiaris*)	6 (4)	4 (2)	2 (2)
Coyote (*Canis latrans*)	54 (43)	39 (33)	15 (10)
Gray Fox (*Urocyon cinereoargenteus*)	19 (18)	15 (14)	4 (4)
Red Fox (*Vulpes fulva*)	65 (58)	60 (54)	5 (4)
Kit Fox (*Vulpes macrotis*)	9 (8)	7 (7)	2 (1)
San Joaquin Kit Fox (*Vulpes macrotis mutica*)[1]	38 (35)	37 (35)	1
Felids			
Mountain Lion (*Felis concolor*)	61 (57)	42 (39)	19 (18)
Lynx (*Lynx canadensis*)[1]	1	1	0
Bobcat (*Lynx rufus*)	79 (64)	54 (47)	25 (17)
Cat (*Felis domesticus*)	1	0	1
Other carnivores			
Raccoon (*Procyon lotor*)	46 (39)	40 (34)	6 (5)
Black Bear (*Ursus americanus*)	7 (7)	5 (5)	2 (2)
American Marten (*Martes americana*)	3 (2)	2 (2)	1
Stone Marten (*Marten foina*)	1	1	0
Fisher (*Martes pennati*)	6 (4)	6 (4)	0
Weasel (*Mustela* sp.)	1	1	0
Mink (*Mustela vison*)	1 (1)	1 (1)	0
Badger (*Taxidea taxus*)	7 (4)	3 (2)	4 (2)
Others			
Beaver (*Castor canadensis*)[2]	2 (2)	2 (2)	0
Deer (*Cervidae*)[2]	3	3	0
Opposum (*Didelphimorphia*)	19 (15)	17 (13)	2 (2)
Virginia Opossum (*Didelphis marsupialis*)	4 (3)	4 (3)	0
Kangaroo rat (*Dipodomys* sp.)[1], [3]	1	0	1
Horse (*Equus caballus*)[2]	1 (1)	0	1 (1)
Rabbit/Hare (*Leporidae*)[2]	9 (3)	6 (3)	3
Skunk (*Mephitidae*)	29 (27)	23 (21)	6 (6)
Striped Skunk (*Mephitis mephitis*)	17 (15)	13 (11)	4 (4)
Mountain Vole (*Microtus montanus*)[3]	1	0	1
Chipmunk (*Neotamias* sp.)	3 (2)	3 (2)	0

Species	Total Number of Incidents	SGARs	FGARs
White-Tailed Deer (*Odocoileus virginianus*)[2]	7	5	2
Key Deer (*Odocoileus virginianus clavium*)[1, 2]	2	2	0
Norway Rat (*Rattus norvegicus*)	1	1	0
Black Rat (*Rattus rattus*)	2 (2)	2 (2)	0
Rat (*Rattus* sp.)	6 (5)	3 (3)	3 (2)
Squirrel (*Sciuridae*)	25 (13)	22 (13)	3
Gray Squirrel (*Sciurus carolinensis*)	44 (4)	31 (2)	9 (2)
Eastern Fox Squirrel (*Sciurus niger*)	4 (4)	2 (2)	2 (2)
Ground Squirrel (*Spermophilus* sp.)	1	0	1
Pig (*Suidae*)[2]	2 (1)	0	2 (1)
Boar (*Sus scrofa*)[2]	2	1	1
Eastern Chipmunk (*Tamias striatus*)[3]	1	1	0
Unknown Mammal	4 (4)	2 (2)	2 (2)
Total Mammals	**607 (452)**	**474 (363)**	**133 (89)**

[1] Listed (endangered or threatened) or protected species

[2] Species' route of exposure is uncertain due to a diet which excludes mammal/bird/terrestrial invertebrate consumption

[3] Species' exposure may occur via terrestrial invertebrate consumption rather than mammal/bird consumption due to their diet

**Non-North American species

Numbers in parentheses () are the number of incidents that species had from 2010 to 2018, after the implementation of the RMD.

Other Taxa. Anticoagulant rodenticides have also been detected in incidents involving fish (mullet, dolly varden, and puffer fish), invertebrates (land crab and hermit crab), and reptiles (unknown species) (**Table 6-11**). All fish and invertebrate incidents, as well as two of the three reptile incidents, involved the SGAR brodifacoum. One of the three reptile incidents involved an accidental misuse of the FGAR diphacinone. The route of exposure for these incidents is unknown and may represent misuse, or poor disposal practices. Neither of the FGARs still labeled for broadcast use had a reported incident.

A single state, California, accounts for a majority (51%) of reported incidents of all evaluated rodenticides. New York accounts for the second most incidents (26%) among evaluated rodenticides, and the two states combined contain approximately 77% of reported incidents. This is due to the fact that these two states have more robust reporting systems through the California Department of Fish and Game (Pesticides Investigation Unit) and the New York State Department of Environmental Conservation (Wildlife Pathology Unit), respectively, and does not reflect that fewer incidents were necessarily occurring in other states, just that fewer were investigated or reported to the Agency by the other 23 states which reported incidents. Though

25 states did not report any incidents for evaluated rodenticide uses, this should not be considered as a lack of incidents within those states, but more a lack of processes to document incidents and report them to federal regulators. It should be noted that this is probably an underestimate of nationwide impact as 2 states reported 979 of these incidents (California and New York). For each evaluated rodenticide, the incidents reported from 1971 to 2018 were analyzed and summarized regarding the species involved and the certainty of chemical exposure causing effects that were observed.

Table 6-11. Anticoagulant Rodenticide Incidents in Fish, Reptiles, and Invertebrates

Species	No. Incidents	SGAR	FGAR
Fish			
Mullet (*Mugilidae*)	2	2	0
Dolly Varden (*Salvelinus malma*)	1	1	0
Puffer Fish	2	2	0
Total Fish	**3 (2)**	**3 (2)**	**0**
Invertebrates			
Land Crab (*Cardisoma* sp.)	2	2	0
Hermit Crab (*Coenobita perlatus*)	2	2	0
Unknown Crustacean	1 (1)	1 (1)	0
Total Invertebrates	**3 (3)**	**3 (3)**	**0**
Reptiles			
Unknown Reptile	3 (3)	2 (2)	1 (1)
Total Reptiles	**3 (3)**	**2 (2)**	**1 (1)**

Numbers in parentheses () are the number of incidents that species had from 2010 to 2018, after the implementation of the RMD.

"Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: A Comparative Approach" (USEPA 2004) evaluated primary and secondary exposure of anticoagulant rodenticides to birds and mammals. The assessment determined that the greatest risk of rodenticide use to non-target animals is via primary and secondary exposure to mammals. The 2004 assessment also specified factors contributing to uncertainty in assessing anticoagulant rodenticides. Those factors that contributed the most uncertainty were: (1) missing data, including acute, chronic, and secondary toxicity as well as data regarding retention of some active ingredients in the liver, blood, and other body tissues; (2) the variable quality and quantity of existing data on metabolism and retention times in rodents and non-target species; (3) specific use information by formulation, including typical amounts applied by use site, seasonally, and annually; distances applied from buildings; amounts used in rural versus urban areas; use by Certified Applicators versus homeowners and other non-certified applicators; and other such relevant information; (4) information on the number and species of birds and non-target mammals frequenting baited areas and the likelihood of their finding and consuming bait

or poisoned primary consumers in the various use areas; (5) methods to determine liver concentration(s) and total body burdens of rodenticide that would corroborate death or even if such a cause-effect relationship is appropriate (e.g., the "threshold of toxicity" concentration); (6) not accounting for the impacts of sub-lethal effects on reproduction and non-target mortality (e.g., clotting abnormalities, hemorrhaging, stress factors including environmental stressors, such as adverse weather conditions, food shortages, and predation); (7) not accounting for bioaccumulation of repeated sub-lethal exposures to bait or poisoned rodents utilized as food by predators and scavengers; and (8) lack of incident reporting.

Incident data were also obtained from literature reports. In a 2018 investigation of anticoagulant rodenticide data, the California Department of Pesticide Regulation concluded that the FGAR chemicals (diphacinone, chlorophacinone, and warfarin) are less toxic, less persistent, and less bioaccumulative than the SGARs (brodifacoum, bromadiolone, difethialone, and difenacoum), demonstrating that the inherent risk of the FGARs is lower (CDPR, 2018). The investigation also concluded that exposure rates among non-target animals are lower for FGARs than for SGARs, citing a study which observed that owls that were fed rats exposed to FGARs showed no mortalities nor sublethal effects (USEPA, 2004). As a result, the investigators found that current uses of FGARs are unlikely to have a significant adverse impact on non-target wildlife. However, they also concluded that SGARs are more toxic, persistent, and bioaccumulative with the potential to cause population-level adverse effects. For example, Serieys et al. (2015) found statistically significant associations between SGARs and mange, but did not find the same association for FGARs. Sublethal effects such as mange can impact fitness and have population level effects (Serieys et al. 2015). A severe mange outbreak in a population of bobcats in Southern California caused a genetic bottleneck (Serieys et al. 2015). It is conceivable that other predator populations may be similarly negatively impacted by exposure to SGARs. The California investigation agrees with EFED's conclusions that brodifacoum may have the highest level of risk within the SGARs due to its higher exposure rates that are disproportionate to its use (CDPR, 2018). Ultimately the investigation concludes that due to the physiochemical properties, high exposure rates, and population-level impacts of SGARs that they have a significant likelihood to impact non-target wildlife (CDPR, 2018).

A study by the Kentucky Department of Fish and Wildlife Resources investigated the exposure of barn owls in Kentucky to anticoagulant rodenticides by testing the liver tissue of 48 barn owl carcasses collected from 2012 to 2016 (KY DFWR, 2019). The investigators confirmed exposure to one or more anticoagulant rodenticides in 33% of the birds examined, including brodifacoum and bromadiolone. The study found that the prevalence of detected exposure to brodifacoum for after-hatch-year birds (65%) was significantly ($p=0.012$) higher than hatch-year birds (22%) (KY DFWR, 2019). The report provides another line of evidence that brodifacoum is having outsized exposure relative to its usage with its finding that brodifacoum was the most commonly detected anticoagulant rodenticide, found in 88% of AR-positive birds (KY DFWR, 2019). Furthermore, the implications of one third of examined carcasses having confirmed exposure to anticoagulant rodenticides is a further line of evidence that there is significant secondary exposure to non-target animals occurring through the use of these pesticides.

A 2017 evaluation of anticoagulant rodenticide exposure in four species of birds of prey was conducted from 2012 to 2016 in Massachusetts in order to evaluate the efficacy of the recently implemented 2011 restrictions on SGARs in the United States (Murray, 2017). The study analyzed liver tissue from four species of birds of prey admitted to a wildlife clinic in Massachusetts for residues of anticoagulant rodenticides. Of the 94 birds that were analyzed, 16 were symptomatic for AR toxicosis and 78 asymptomatic; however, when residues in the liver were measured, 96% of all birds tested were positive for SGARs (Murray, 2017). This serves as a line of evidence that asymptomatic wildlife is not proof of a lack of exposure; anticoagulant rodenticide poisoning may be more widespread than it appears. 66% of all tested birds contained residues of two or more SGARs (Murray, 2017). A significant increase in exposures to multiple SGARs occurred in later years in the study which coincides with the overall spike in reported incidents (**Figure 6-1**). The study found that three SGARs (bromadiolone, brodifacoum, and difethialone) were present in combination in the majority of birds, with increases in multiple exposures driven by increased detections of bromadiolone and difethialone (Murray 2017). This study is further evidence that secondary exposure of non-target organisms to anticoagulant rodenticides is a widespread issue.

Brodifacoum

In a recent 2019 query of the IDS system 658 wildlife incident reports were obtained for brodifacoum use which far outnumbers incidents reported for any other currently registered rodenticide. For brodifacoum exposure certainty 302 were considered highly probably, 155 were considered probable and 120 were considered possibly attributable to brodifacoum uses. 81 were reports of living animals exposed to residues of brodifacoum.

A number of the individual incidents observed which involved brodifacoum in Massachusetts were summarized in a published study (Murray, 2011). This study documented residue analysis conducted on 80 Red tailed hawks, 40 Barred owls, 23 Eastern screech owls, and 18 Great horned owls which were found dead or which subsequently died after showing adverse behavioral reactions and were brought to the Wildlife Clinic of Tufts Cummings School of Veterinary Medicine in North Grafton, MA. Of the 161 birds analyzed, 139 displayed residues of anticoagulant rodenticides in liver samples. Brodifacoum residues were found in the livers of 98% of these birds (136 of the 139 birds analyzed), thus indicating that widespread secondary exposure to poisoned prey was evident in the area from which the birds were found.

Brodifacoum is the largest driver of incidents among the evaluated rodenticides. Brodifacoum accounted for over 50% of total reported incidents among the evaluated rodenticides with 658 identified since 1980, the first year with a brodifacoum incident. Furthermore, 350 incidents involving brodifacoum have been reported since 2010. This represents roughly 44% of the total incidents reported during that time frame (2010-2018) for evaluated rodenticides.

Avian species suffering mortality by either primary exposure to the baits or by secondary exposure to contaminated carcasses or living organisms that had previously ingested brodifacoum baits include multiple species of hawks, eagles, seabirds, owls, vultures, geese,

and passerine species. Mammalian poisoning incidents have involved predatory mammals such as bear, bobcat, mountain lion, coyote, fox, and badger as well as non-predators such as raccoon, beaver, opossum, skunk, squirrels, non-target rodents, rabbits, and deer. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving brodifacoum include the bald eagle (4 incidents), San Joaquin kit fox (20), golden eagle (12), and key deer (1).

Bromadiolone

In a recent 2019 query of the IDS system 278 wildlife incident reports were obtained for bromadiolone, representing the second highest number of incidents among the evaluated rodenticides and a significant (22%) portion of the total. All but one involved either birds or mammals. It appears likely that some mortalities were caused by primary exposure to bromadiolone bait and others by secondary exposure through the consumption of exposed birds, mammals, or terrestrial invertebrates. Those incidents were classified as possible (76), probable (79), or highly probably (67) in terms of the certainty of the association with bromadiolone exposure. 56 were reports of living animals exposed to residues of bromadiolone. The incidents occurred between 1983 and 2018 (note: dates are not available for all incidents). These incidents include reports of residues in animals. Although some of these residue data were associated with the incidents, residue data were also reported for animals that were not dead or moribund at the time of sampling (e.g., some samples were collected as part of a long-term genetics and population study).

Avian species suffering mortality by either primary exposure to the baits or by secondary exposure to contaminated carcasses or living organisms that had previously ingested bromadiolone baits include multiple species of hawks, eagles, seabirds, owls, and passerine species. Mammalian poisoning incidents have involved predatory mammals such as bear, bobcat, mountain lion, coyote, fox, and badger as well as non-predators such as raccoon, opossum, skunk, squirrels, non-target rodents, rabbits, and deer. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving bromadiolone include the bald eagle (1 incident), lynx (1), and San Joaquin kit fox (12).

Chlorophacinone

In a recent 2019 query of the IDS system 54 wildlife incident reports were obtained for chlorophacinone. Those incidents were classified as possible (11), probable (14), or highly probably (21) in terms of the certainty of the association with chlorophacinone exposure. Eight were reports of living animals exposed to residues of chlorophacinone. The incidents occurred between 1990 and 2018 (note: dates are not available for all incidents).

The reported avian species include herbivorous geese, granivorous/insectivorous quail and turkeys, as well as carnivore/scavenger birds that include the barn owl, turkey vulture, bald eagle, and red-tailed hawk. The reported mammalian species include herbivorous and granivorous squirrels. Omnivorous mammals such as raccoon and boar as well as carnivores including the badger, bear, coyote, and bobcat were also cited in the reported incidents. These incidents involve federally listed and non-listed species; listed and protected species with

observed incidents involving chlorophacinone include the bald eagle (4 incidents), San Joaquin kit fox (1), and golden eagle (1).

Difenacoum

In a recent 2019 query of the IDS system 12 wildlife incident reports were obtained for difenacoum. Those incidents were classified as possible (6), probable (3), or highly probably (2) in terms of the certainty of the association with difenacoum exposure. One was a report of living animals exposed to residues of difenacoum. The incidents occurred between 1983 and 2018 (note: dates are not available for all incidents).

The reported avian species include red-tailed hawk and turkey vulture. The reported mammalian species include dog, rabbit, raccoon, and striped skunk. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving difenacoum include the bald eagle (1 incident).

Difenacoum, which was first registered in 2007, has not been registered for as long as other second-generation anticoagulant rodenticides (e.g. brodifacoum) which have comparatively greater reporting of incidents associated with their use. The lack or low occurrence of reported incidents does not, therefore, necessarily indicate the actual frequency with which incidents related to the use of difenacoum may occur.

Difenacoum exhibited high levels of toxicity to birds in a 6-week one-generation reproductive effects study on Japanese quails (*Coturnix coturnix japonica*) (MRID 50623624). Based on the study author's results, no mortality was observed in the control or in the lowest treatment group (58 µg ai/kg bw). Treatment-related mortalities were noted in the 115 and 241 µg ai/kg bw treatment groups (female birds in each pair). Observed hematomas and hemorrhages in birds that died were believed to have been treatment-related. Dose-dependent, statistically significant decreases in female mean liver weight in the 115 and 241 µg ai/kg bw treatment groups were observed. Dose-dependent, statistically significant increases in female mean spleen weight were observed in the 241 µg ai/kg bw treatment group. A significant reduction (23%) was detected in eggs laid/pen at the highest treatment level (241 µg ai/kg bw) and in hatchling weight (8.4% inhibition) at all treatment levels; therefore, the overall NOAEL was <58 µg ai/kg bw. However, while the effect on hatchling weight was statistically significant at all treatment levels, it was not dose-dependent, as the percent inhibition decreased to 6.5% at the highest treatment level. Therefore, the effect on hatchling weight may not be biologically significant. Regardless, a NOAEL of 115 µg ai/kg bw based on the egg laid/pen effect would indicate a very high toxicity to avian species.

Difethialone

Numerous incident investigations have detected difethialone residues in liver tissues of necropsied birds and mammals which had no direct contact with baits, supporting the hypothesis that secondary exposure via feeding on baited prey animals is leading to the deaths of predators.

In a recent 2019 query of the IDS system 124 wildlife incident reports were obtained for difethialone. Those incidents were classified as possible (38), probable (31), or highly probably (41) in terms of the certainty of the association with difethialone exposure. 14 were reports of living animals exposed to residues of difethialone. The incidents occurred between 1999 and 2018 (note: dates are not available for all incidents).

The reported avian species include barn owl, barred owl, Eastern screech owl, starling, and turkey vulture. The reported mammalian species include coyote, dog, fox, opossum, raccoon, rat, squirrel, and skunk. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving difethialone include the golden eagle (1 incident), key deer (1), and San Joaquin kit fox (5). Incidents with red-tailed hawks, a Cooper's hawk, red fox, and black bear showed difethialone concentrations in the liver ranging from 10 to 861 ppb.

Diphacinone

In a recent 2019 query of the IDS system 122 wildlife incident reports were obtained for diphacinone. Those incidents were classified as possible (54), probable (15), or highly probably (29) in terms of the certainty of the association with diphacinone exposure. 24 were reports of living animals exposed to residues of diphacinone. The incidents occurred between 1986 and 2018 (note: dates are not available for all incidents).

The reported avian species include American kestrel, barn owl, Canada goose, fisher, rock dove, turkey, and turkey vulture. The reported mammalian species include badger, coyote, dog, squirrel, fox, kangaroo, opossum, pig, rabbit, raccoon, rat, skunk, and deer. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving diphacinone include the bald eagle (2 incidents), and kangaroo rat (1).

Warfarin

In a recent 2019 query of the IDS system 23 wildlife incident reports were obtained for warfarin. Among those incidents, 22 were classified as possible (7), probable (4), or highly probably (11) in terms of the certainty of the association with warfarin exposure. One was a report of living animals exposed to residues of warfarin. The incidents occurred between 1971 and 2017 (note: dates are not available for all incidents).

The reported avian species include barn owl, bobwhite quail, and sparrow. The reported mammalian species include cat, coyote, squirrel, fox, mountain vole, and skunk. These incidents involve federally listed and non-listed species; listed and protected species with observed incidents involving warfarin include the bald eagle (3 incidents). Warfarin was detected at concentrations in the liver ranging from 0.22 to 1.48 ppm.

7 Analysis Plan

7.1 Overall Process

This assessment uses a weight of evidence approach that relies heavily, but not exclusively, on a risk quotient (RQ) method. RQs are calculated by dividing an estimate environmental concentration (EEC) by a toxicity endpoint (*i.*e., EEC/toxicity endpoint). This is a way to determine if an estimated concentration is expected to be above or below the concentration associated with the effects endpoint. The RQs are compared to regulatory levels of concern (LOCs). The LOCs for non-listed species are meant to be protective of community-level effects. For acute and chronic risks to vertebrates, the LOCs are 0.5 and 1.0, respectively, and for plants, the LOC is 1.0. The acute and chronic risk LOCs for bees are 0.4 and 1.0, respectively. In addition to RQs, other available data (*e.g.*, incident data) can be used to help understand the potential risks associated with the use of the pesticide.

Based on the problem formulations, the primary risks of concern are to birds and mammals (bird are surrogates for reptiles and terrestrial amphibians). Exposures of concern are both primary (consumption of AR-treated baits or granular forms) and secondary (consumption of poisoned primary consumers). Risks that have been quantified in previous assessments include acute risks to mammals and birds, and chronic risks to mammals.

In this assessment, risk to birds and mammals will be quantified through assessing AR levels in non-target taxa through the consumption of bait based on both one-day consumption and consumption over six days. These effects will be divided by the exposure of the ARs to calculate the acute toxicity RQs. The chronic risk to birds via secondary exposure will be quantified for chlorophacinone. A reproductive study on chlorophacinone will be used to qualitatively estimate lowest-observed-adverse-effect-concentrations (LOAEC), using 5-day dietary LC_{50} data on the other 6 ARs.

Analysis of risks to aquatic organisms will be limited to chlorophacinone and diphacinone, based on the above-ground broadcast use patterns for each. Based on their similar fate properties and use patterns, the quantification of aquatic risk will be limited to chlorophacinone, since it is more toxic to the tested organisms (rainbow trout and Daphnia magna) than is diphacinone. Exposures will be quantified with the Pesticides in Water Calculator (PWC), using scenarios representing orchard, nursery, turf and tree plantation use sites.

Risks of consumption of treated bait applied by broadcast methods (chlorophacinone and diphacinone) will be examined using the T-REX model.

Risks to all other taxa will not be examined due either to lack of exposure (such as for bees and other terrestrial invertebrates) and/or lack of effects data.

Incident data will be used to qualitatively characterize the risk conclusions that are based on toxicity data and primary and secondary exposure estimates. The incident data will be examined to determine if there have been any trends since the 2008 RMD, or whether any particular active ingredients are involved in a large number of incidents.

7.2 Modeling

Various models are used to calculate aquatic and terrestrial EECs. In this assessment, PWC version 1.52 was used for aquatic exposure, and TREX version 1.5.2 was used for terrestrial exposure. Other exposures were assessed as the concentration in baits, or for secondary exposure, residues in primary consumers.

8 Aquatic Organisms Risk Assessment

8.1 Aquatic Exposure Assessment

8.1.1 Modeling

According to the problem formulations, aquatic exposure for most ARs is unlikely due to the use patterns as modified by the 2008 RMD. Almost all outdoor uses are required to be in bait stations or underground, limiting exposure to non-target organisms. However, the broadcast use of chlorophacinone and diphacinone (treated bait) on the soil surface could potentially lead to runoff or erosion.

Chlorophacinone and diphacinone are the only two ARs that have broadcast use patterns that may result in aquatic exposure through runoff. Chlorophacinone baits may be broadcast at a maximum application rate of 20 lb/A in bait form (4.4 lb ai/acre; 0.005% active ingredient by weight), twice per season (30-day re-application interval), to control voles in orchards, nurseries, non-crop areas, and tree and forestry plantations. Diphacinone may be broadcast at up to 20 lb/A in bait form (4.4 lb ai/acre; 0.005% active ingredient by weight), twice per season (30-day re-application interval), to control voles, mice and various types of rats.

The floating bait station use for chlorophacinone to control muskrats does not lend itself to aquatic exposure modeling, which typically is for agricultural use. Exposures are expected to be lower and less widespread than the broadcast uses of chlorophacinone. Effects to mammals or birds that are primary and secondary consumers of the treated bait are expected to be the same as for other use patterns. Acute effects to freshwater fish and invertebrates are expected to be lower and less widespread than for the broadcast uses.

Tier 2 exposure modeling is performed here to quantify exposure from the broadcast uses. Because the rates and application patterns are similar, and because chlorophacinone is much

more toxic than diphacinone on an acute basis to freshwater fish and *Daphnia magna*, its exposure is modeled as a conservative estimate of exposure by both chemicals. **Table 8.1** provides the model input parameters as presented in the problem formulations for the ARs. A number of PWC modeling scenarios were run, representing nurseries, orchards, turf, and tree plantations.

The maximum 1-in-10 year peak EEC was obtained for the Michigan cherry scenario (0.065 ppb). This is well below the most sensitive endpoint (fish acute) of 452 ppb. Therefore, there are no acute aquatic risks of concern for freshwater organisms.

Due to the lack of data, chronic risks to fish and invertebrates, and risks to aquatic plants cannot be assessed. ECOSAR analysis suggests that these taxa are not at risk.

Table 8.1. Aquatic Modeling Input Parameters for Chlorophacinone

Parameter (units)	Value (s)	Source	Comments
K_{OC} (mL/g)	20,299	MRID 42666001 42205503	Slope of line of Kd vs. Fraction OC (PF)
Water Column Metabolism Half-life (days) at 20°C	156 d	PF D426557	2x soil metabolism input, per guidance
Benthic Metabolism Half-life (days) at 20°C	Assumed stable	--	No data
Aqueous Photolysis Half-life (days)@ pH 7	Assumed stable	PF D426557	Previous study now Unacceptable (PF)
Hydrolysis Half-life (days)	stable	MRID 42205501	No significant degradation observed at 25°C.
Soil Half-life (days) at 20°C	78 d	MRID 43159801	Represents the 90 percent upper confidence bound on the mean of 2 representative half-life values from aerobic soil metabolism studies.
Foliar Half-life	--	--	No Data
Molecular Weight (g/mol)	374.81	--	--
Vapor Pressure (Torr) at 25°C	3.58E-6	MRID 42237401	--
Solubility in Water (mg/L)	3.43	MRID 42237401	25°C

[1] Other input parameters for the applications tab are shown in **Table 8.2**

Pesticide in Water Calculator Scenarios are used to specify soil, climatic, and agronomic inputs in PRZM, and are intended to result in higher water concentrations associated with a particular crop and pesticide within a geographic region. Each PWC scenario is specific to a vulnerable area where the crop is commonly grown. Soil and agronomic data specific to the location are built into the scenario, and a specific climatic weather station providing 30 years of daily weather values is associated with the location. **Table 8.2** identifies the use sites associated with each PRZM scenario, and **Table 8.3** presents surface water EEC's?.

Table 8.2. Aquatic Modeling (PWC) Input Parameters Specific to Use Patterns for Chlorophacinone

Run Name	Use Site	PWC Scenario	Date of Initial App.	App. Rate in (kg ai/ha)	# App. per Year	App. Interval (days)	App Method	Application Efficiency/ Spray Drift
MI Cherry	Orchard	MICherries	Apr 1	22.4 x 0.005% ai = 0.112 kg/ha	2	30	Above crop	1.0 (bait) Zero drift

Table 8.3. Surface Water EECs for Chlorophacinone (Estimated Using PWC version 1.52)

Run Name	Use	PWC Scenario	Annual App Rate Kg/ha, App type	1-in-10 year EEC (1 – day)
MI Cherry	Orchard	MICherriesSTD	0.112, bait	0.65

8.2 Monitoring

The Agency is not aware of any water monitoring conducted by Federal and state agencies. A search of the Water Quality Portal was conducted on August 19, 2019. No results were found. These monitoring programs do not typically analyze for vertebrate control agents such as the anticoagulant rodenticides.

8.3 Aquatic Organism Risk Characterization

8.3.1 Aquatic Vertebrates

The highest modeled exposure was for the Michigan cherry scenario. Comparison of the acute, 1-day average exposure (0.65 ppb) to the acute endpoints in rainbow trout (452 ppb) and Daphnia magna (640 ppb) yield RQs that are well below the LOC. This analysis is considered to be protective of the floating bait station use as well.

The aquatic risks of chlorophacinone and diphacinone based on the broadcast use pattern are quantified and summarized below. Limited data are available to assess aquatic toxicity for the ARs (see Section 6.1). As shown in Tables 8-4 and 8-5, acute risks are well below the Agency's levels of concern.

Table 8-4. Acute and Chronic Vertebrate Risk Quotients for Chlorophacinone

Use Sites	1-in-10 Yr EEC µg/L		Risk Quotient			
			Freshwater		Estuarine/Marine	
	Daily Ave	60-day Ave	Acute[1]	Chronic	Acute[1]	Chronic
			LC_{50} = 452 µg ai/L	NOAEC = no data	LC_{50} = no data	NOAEC = no data
MI Cherry	0.65	0.20	0.0014	--	--	--

Bolded values exceed the LOC for acute risk to non-listed species of 0.5 or the chronic risk LOC of 1.0. The endpoints listed in the table are the endpoint used to calculate the RQ.

[1] The EECs used to calculate these RQs are based on the 1-in-10-year peak 1-day average value from **Table 8-3.**

8.3.2 Aquatic Invertebrates

The acute risk quotient for the aquatic invertebrate Daphnia magna is presented in Table 8-5. The RQ is below the level of concern.

Table 8-5. Acute and Chronic Aquatic Invertebrate Risk Quotients (Chlorophacinone)

Use Scenario	1-in-10 Yr EEC µg/L		Risk Quotient			
			Freshwater		Estuarine/Marine	
	Daily Ave	21-day Ave	Acute[1]	Chronic	Acute[1]	Chronic
			LC_{50} = 640 µg ai/L	NOAEC = no data	LC_{50} = no data	NOAEC = no data
MI Cherry	0.65	0.24	0.001	--	--	--

Bolded values exceed the LOC for acute risk to non-listed species of 0.5 or the chronic risk LOC of 1.0. The endpoints listed in the table are the endpoint used to calculate the RQ.

[1] The EECs used to calculate this RQ are based on the 1-in-10-year peak 1-day average value from **Table 8-3**. Error! Reference source not found..

9 Terrestrial Vertebrates Risk Assessment

9.1 Terrestrial Vertebrate Exposure Assessment

EFED's exposure assessment for the rodenticides differs from that for most other pesticides. For a rodenticide, the bait itself is the potential food item of concern. Thus, the amount of active ingredient in the formulated bait is used as an EEC in risk estimation.

For this assessment, it was assumed that terrestrial animals could be exposed in two different pathways: 1) Animals may directly consume bait ("primary consumption"), or 2) animals may consume contaminated carcasses either killed or scavenged by the consumer ("secondary consumption"). Both approaches and the expected exposure levels are detailed below.

This information is used to estimate the amount of bait that birds and mammals of various sizes need to consume to obtain a dose expected to be lethal to 50% of the individuals in the population (i.e., LD_{50} dose). Estimates of food-ingestion rates (g dry matter per day) are determined from established allometric equations presented in the Wildlife Exposure Factors Handbook (USEPA 1993). The concentration of the first generation ARs in grain bait is also used to estimate initial dietary exposure (mg ai per kg in bait) which in turn is used to calculate avian and mammalian dietary RQs. All second generation ARs are labeled for use only in tamper-proof bait stations.

In this assessment, primary consumption for non-target organisms (birds and mammals) is calculated for a single day of exposure as well as for multiple days of feeding.

9.1.2. Calculation of a Single Day of Bait Intake

Exposure to terrestrial birds and mammals through bait consumption is calculated as mg ai/kg-bw, where kg-bw is the kilograms body weight of the consuming individual for three standard weight classes of passeriform birds and rodents. Exposure (food dry weight consumption) estimates were derived using allometric equations from USEPA (1993). The allometric equations for passeriform birds and rodent mammals were used as these would best approximate those individuals with high potential for consuming grain and they would give the most conservative exposure estimates. Food dry weight was assumed equivalent to food wet weights as the expected water content of the bait would be minimal.

Formulas for calculation of dose estimates are provided in **Table 9-1**, and AR exposure estimates (on a dose basis) are provided in **Table 9-2 and 9-3**.

RQs are generated by dividing these exposure estimates of ARs (mg ai/kg-bw) for a given weight class by the most conservative toxicity endpoint for the relevant taxa adjusted for the default body weights. RQs using these exposure estimates were generated for acute bird and mammal (using LC_{50} data) non-targets.

Table 9-1. Formulas for Calculation of Daily AR Intake based on Consumption of Bait.

Passeriform bird food intake (g, dry weight): FI (g dry-wt/day) = 0.398 * $Wt(g)^{0.850}$

Rodent mammal food intake (g, dry weight): FI (g dry-wt/day) = 0.621 * $Wt(g)^{0.564}$

AR intake (mg ai/kg-bwt/day) = FI (g dry-wt/day) * mg ai/kg-bait / Wt(g) (from Table 9-3)

Where: Wt (g) = weight (in grams) of the bird or mammal consumer

Table 9-2. AR Concentration in Bait.

Anticoagulant Rodenticide	Concentration in Bait (mg ai/kg-bait)
Diphacinone	50
Chlorophacinone	50
Warfarin	50
Bromadiolone	25
Brodifacoum	25
Difenacoum	50
Difethialone	25

9.1.2 Expected AR Accumulation through Multiple Feedings of Bait

ARs typically cause mortality several days to weeks after ingestion, which may allow target animals to consume bait for several days before dying. This delayed effect can lead to doses that far exceed the acute lethal dose. A compound that accumulates in body tissues may pose greater risk to primary and secondary consumers, especially if repeated sublethal exposure results in the accumulation of a lethal dose or if additional exposures occur before the lethal dose has taken its effect (*i.e.,* leading to a dose that is beyond what is sufficient to cause mortality). Available AR data on elimination from blood and liver is presented in Table **9-4.**

Table 9-3. Expected Daily AR Intake for Default Bird and Mammal Weights based on Consumption of Bait.

Taxa	Weight (g)	Food intake (g dry-wt/day)	AR intake (mg ai/kg-bw/day)
Diphacinone (Bait concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	12.70
	100	19.95	9.97
	1000	141.22	7.06
Rodent Mammals	15	2.86	9.53
	35	4.61	6.59
	1000	30.56	1.53
Chlorophacinone (Bait concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	12.70
	100	19.95	9.97
	1000	141.22	7.06
Rodent Mammals	15	2.86	9.53
	35	4.61	6.59
	1000	30.56	1.53
Warfarin (Bait concentration = 250 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	12.70
	100	19.95	9.97
	1000	141.22	7.06
0.Rodent Mammals	15	2.86	9.53
	35	4.61	6.59
	1000	30.56	1.53
Bromadiolone (Bait Concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	6.35
	100	19.95	4.99
	1000	141.22	3.53
Rodent Mammals	15	2.86	4.77
	35	4.61	3.29
	1000	30.56	0.76
Brodifacoum (Bait concentration = 25 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	6.35
	100	19.95	4.99
	1000	141.22	3.53
Rodent Mammals	15	2.86	4.77

	35	4.61	3.29
	1000	30.56	0.76
Difenacoum (Bait concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	12.70
	100	19.95	9.97
	1000	141.22	7.06
Rodent Mammals	15	2.86	9.53
	35	4.61	6.59
	1000	30.56	1.53
Difethialone (Bait concentration = 25 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	6.35
	100	19.95	4.99
	1000	141.22	3.53
Rodent Mammals	15	2.86	4.77
	35	4.61	3.29
	1000	30.56	0.76
*surrogate for reptiles and terrestrial-phase amphibians			

Table 9-4. Retention of ARs in Blood and Liver (Mammals)					
Diphacinone					
Species	**Dose (mg ai/kg)**	**# doses**	**Blood half-life (days)**	**Liver retention (days)**	**Reference (MRID)**
Pig	12.5	3 or 5	NA	Half-life = 5.43 days	Fisher 2006
Pig	1.5	1	NA	Half-life = 12.4 days	Crowell et al. 2013
Rat	1.5	1	NA	Half-life = 3 days	Fisher et al. 2003 (48190801)
Rat	0.18 or 0.4	1	NA	20% of dose in body tissues at 8 days, highest concentrations in liver (1.4 and 1.0 mg ai/kg-liver, respectively)	Yu et al. 1982
Mouse	0.6	1	NA	30% of dose in body tissues at 4 days, highest concentrations in liver (0.6 mg/kg-liver)	Yu et al. 1982
Cattle	1.0 (injection)	1	NA	Half-life > 90 days	Bullard et al. 1976
Cattle	1.5	1	NA	*Trial 1*: Initial (day 0 to 30): 9.4 days: Terminal (day 30 onwards): 25.2 days Trial 2: Initial(day 0 to 30): 4.1 days; *Terminal (day 30 onwards): 35.4 days*	Crowell et al. 2013
Red deer	1.5	1	NA	Half-life = 6 days	Crowell et al. 2013
Chlorophacinone					
Mouse	336 µg/mouse	1	11.7	35.4	Vandenbroucke et al. 2008

Rat	4-5 mg ai/kg	1	0.4	NA	Belleville 1981 (00155540)
Black-tailed prairie dog	23 mg/prairie dog	1	NA	5.9	Witmer, et al., 2015
Warfarin					
Mouse	5985 µg/mouse	1	14.9	66.8	Vandenbroucke et al. 2008
Rat	unknown	unknown	0.7 (male) 1.2 (female)	NA	Pyrola 1968
Rat	1.0	1	NA	26.2	Fisher et al. 2003 (48190801)
Rabbit	unknown	unknown	0.2	NA	Breckenridge et al 1985
Possum	unknown	unknown	0.5	NA	Eason et al. 1999
Pig	unknown	unknown	NA	30-40	O'Brien et al 1987
Brodifacoum					
Mouse	6.44 µg/mouse	1	91.7	307.4	Vandenbroucke et al. 2008
Rat	0.02 or 0.15 0.35	1 1	NA	350 128	Batten and Bratt 1990 (42007502)
Rat	0.2	1	NA	282	Hawkins et al. 1991 (42596801)
Rat	0.25	1	NA	150-200	Bratt and Hudson 1979 (00080235)
Rat	0.06	4 (at weekly intervals)	NA	136	Belleville 1991 (42065009)
Rat	0.35	1	NA	130	Parmar et al. 1987

Rat	unknown	unknown	6.5	>80	Backmann and Sullivan 1983
Rat	0.1	1	NA	113.5 ($t_{1/2}$)	Fischer et al. 2003 (48190801)
Possum	0.1	1	20-30	>252	Eason et al. 1996
Rabbit	unknown	unknown	2.5	NA	Brechenridge et al. 1985
Sheep	0.2 or 2.0	1	NA	>128	Laas et al. 1985
Dog	unknown	unknown	6	NA	Woody et al. 1992
Dog	unknown	unknown	0.9-4.7	NA	Robben et al. 1998
Difenacoum					
Mouse	12.88 µg/mouse	1	20.4	61.8 ($t_{1/2}$)	Vandenbroucke et al., 2008
Rat	1.2 mg/kg	1	--	118 ($t_{1/2}$)	Bratt, 1987 (46750957)
Difethialone					
Mouse	20 µg/mouse	1	38.9	28.5 ($t_{1/2}$)	Vandenbroucke et al. 2008
Rat	0.50	1	2.3	108 ($t_{1/2}$)	Belleville 1986 (42065010) Lechevin and Poche 1988
Rat	0.06	4 (at weekly intervals)	NA	74 ($t_{1/2}$)	Belleville 1991 (42065009)

Cumulative rodenticide doses for animals consuming bait for six consecutive days were also calculated using formulae (**Table 9-5)**. Expected AR accumulation through multiple feedings of bait analysis assumed that 100% of the daily diet of the birds and mammals is represented by the rodenticide bait and that they eliminate the AR, based on the maximum liver half-life value of that AR, provided in the problem formulation of the respective ARs (**Table 9-6**)**.** In the formula, the variable "C" represents the concentration of the pesticide in the bait. The elimination rate constant (k) was calculated using the maximum estimated of the AR half-life, and food intake (FI) was calculated according to the allometric equation for birds and mammals (**Table 9-5**). The resulting cumulative body burden concentrations of each AR are presented in **Table 9-7**.

Table 9-5. Formulas for Calculation of FGAR Body Burden based on Consumption of Bait for Six Consecutive Days.
$$D_t = D_{(t-1)} * e^{-k} + FI * C$$ $$k = \ln(2) / t_{1/2}$$

Table 9-6. Elimination half-lives for rodenticides. Values based on elimination rates from liver in mammals.

Rodenticide	**Elimination half-life (days)**
Diphacinone	12.4[1]
Chlorophacinone	35.4[1]
Warfarin	66.8[1]
Bromadiolone	318.0[2]
Brodifacoum	307.4[1]
Difenacoum	118[1]
Difethialone	28.5[1]
1. Values reported in previous risk assessments from a study on mice by Vandenbroucke et al. (2011). 2. Values reported in previous risk assessment on rats (MRID 42596801)	

Table 9-7. Expected Six Day AR Intake for Default Bird and Mammal Weights based on Consumption of Bait.

Species	Weight (g)	Food intake (g dry-wt/day)	AR intake (mg ai/kg-bwt/day)
Diphacinone (Bait Concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	73.70
	100	19.95	57.90
	1000	141.22	41.00
Rodent Mammals	15	2.86	55.30
	35	4.61	38.20
	1000	30.56	8.90
Chlorophacinone (Bait concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	80.60
	100	19.95	63.30
	1000	141.22	44.80
Rodent Mammals	15	2.86	60.50
	35	4.61	41.80
	1000	30.56	9.70
Warfarin (Bait concentration = 250 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	371.20
	100	19.95	291.60
	1000	141.22	206.40
Rodent Mammals	15	2.86	278.70
	35	4.61	192.80
	1000	30.56	44.70
Bromadiolone (Bait Concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	6.35
	100	19.95	4.99
	1000	141.22	3.53
Rodent Mammals	15	2.86	4.77
	35	4.61	3.29
	1000	30.56	0.76
Brodifacoum (Bait concentration = 25 mg ai/kg-bait)			

Passeriform Birds*	20	5.08	76.00
	100	19.95	60.00
	1000	141.22	42.00
Rodent Mammals	15	2.86	57.00
	35	4.61	39.00
	1000	30.56	9.00
Difenacoum (Bait concentration = 50 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	75.10
	100	19.95	59.00
	1000	141.22	41.70
Rodent Mammals	15	2.86	56.40
	35	4.61	39.00
	1000	30.56	9.00
Difethialone (Bait concentration = 25 mg ai/kg-bait)			
Passeriform Birds*	20	5.08	36.00
	100	19.95	28.00
	1000	141.22	20.00
	15	2.86	27.00
	35	4.61	19.00
	1000	30.56	4.00
*surrogate for reptiles and terrestrial-phase amphibians			

9.1.1.1 Risks from Direct Bait Consumption

In the case of primary exposure, it is assumed the bait containing the AR is ingested by non-target animals and evokes a toxic response. For toxic response elicited from gavage exposure route, exposure is measured as mg ai/kg-bw (**Tables 9-8 and 9-9**). The six day dose-based exposure assessment utilized the same toxicity information discussed above, but in this assessment RQs were calculated by estimating body burden based on the assumption that bait was consumed exclusively for six days. Body burden concentrations (mg ai/kg-bwt) were based on feeding rates and elimination rates from liver half-life estimates. For the diet-based primary exposure assessment, EPA evaluated the concentration of ai in the bait and the dietary LC_{50}. The LC_{50} (mg ai/kg-diet) is obtained from 5-day exposure dietary toxicity studies. RQs are calculated as a ratio of ai concentration and the LC_{50}. Risk results that agree between this method and the multiple day accumulated dose method described above provide an enhanced degree of confidence in risk conclusions for a given chemical. Toxicity is measured by the LD_{50} obtained from the single-gavage studies for birds and mammals. The LD_{50}'s are adjusted for the weight of the assessed animals (birds: 20, 100, 1000 g; mammals: 15, 35, 100 g) (**Table 9-9**). For birds (passerine and ge~~neric~~ class) with a single day exposure, the LOCs were not exceeded. For mammals (both the rodent class and generic mammals), the acute LOCs were

exceeded for all three weight classes after a single day of exposure and after six consecutive days of exposure.

Table 9-8. Formulas for Calculation of Weight-adjusted Avian and Mammalian Chlorophacinone LD_{50}s.

Adjusted avian LD_{50}: $Adj.\ LD_{50} = LD_{50} * \left(\frac{AW}{TW}\right)^{(0.25)}$ where:

Adj. LD_{50} = adjusted LD_{50} (mg/kg-bw)
LD_{50} = endpoint reported from bird study (mg/kg-bw)
TW = body weight of tested animal (178g bobwhite)
AW = body weight of assessed animal (20g, 100g, and 1000g)
x = Mineau scaling factor for birds; EFED default 1.15

Adjusted mammalian LD_{50}: $Adj.LD_{50} = LD_{50} * \left(\frac{AW}{TW}\right)^{(0.25)}$ where:

Adj. LD_{50} = adjusted LD_{50} (mg/kg-bw)
LD_{50} = endpoint reported from mammal study (mg/kg-bw)
TW = body weight of tested animal (938g prairie dog)
AW = body weight of assessed animal (15g, 35g, 1000g)

Table 9-9. Bird and Mammal Acute Gavage RQs based on consumption of AR bait						
	Weight (g)	**Adjusted LD50 (mg ai/kg-bw)[2]**	**Single day of bait exposure**		**Six consecutive days of bait exposure**	
			AR intake (mg ai/kg-bwt)[1]	**RQ[3]**	**AR body burden (mg ai/kg-bwt)[4]**	**RQ[3]**
Diphacinone (50 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	12.70	0.07	73.70	0.40
	100	236.6	9.97	0.04	57.90	0.24
	1000	334.2	7.06	0.02	41.00	0.12
Rodent Mammals	15	5.5	9.53	**1.73**	55.30	**10.05**
	35	4.4	6.59	**1.50**	38.20	**8.68**
	1000	1.9	1.53	**0.80**	8.90	**4.68**
Chlorophacinone (50 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	12.70	0.07	80.60	0.43
	100	236.6	9.97	0.04	63.30	0.27
	1000	334.2	7.06	0.02	44.80	0.13
Rodent Mammals	15	5.5	9.53	**1.73**	60.50	**11.00**
	35	4.4	6.59	**1.50**	41.80	**9.50**
	1000	1.9	1.53	0.80	9.70	**5.11**
Warfarin (250 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	63.48	0.34	371.20	**2.00**
	100	236.6	49.87	0.21	291.60	**1.23**
	1000	334.2	35.30	0.11	206.40	**0.62**
Rodent Mammals	15	5.5	47.67	**8.67**	278.70	**50.67**
	35	4.4	32.95	**7.49**	192.80	**43.82**
	1000	1.9	7.64	**4.02**	44.70	**23.53**
Bromadiolone (25 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	6.35	0.03	33.24	0.18
	100	236.6	4.99	0.02	100.47	0.42
	1000	334.2	3.53	0.01	499.54	**1.49**
Rodent Mammals	15	5.5	4.77	**0.87**	14.63	**2.66**
	35	4.4	3.29	**0.75**	16.20	**3.68**

	1000	1.9	0.76	0.40	24.34	**12.81**
Brodifacoum (25 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	6.35	0.03	76	**117**
	100	236.6	4.99	0.02	60	**135**
	1000	334.2	3.53	0.01	42	**166**
Rodent Mammals	15	5.5	4.77	**0.87**	57	**59**
	35	4.4	3.29	**0.75**	39	**51**
	1000	1.9	0.76	0.40	9	**27**
Difenacoum (50 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	12.70	0.07	75.10	0.40
	100	236.6	9.97	0.04	59.0	0.25
	1000	334.2	7.06	0.02	41.7	0.12
Rodent Mammals	15	5.5	9.53	**1.73**	56.4	**10.25**
	35	4.4	6.59	**1.50**	39.0	**8.86**
	1000	1.9	1.53	**0.80**	9.0	**4.74**
Difethialone (25 mg ai/kg-bait)						
Passeriform Birds*	20	185.9	6.35	0.03	36	**168**
	100	236.6	4.99	0.02	28	**104**
	1000	334.2	3.53	0.01	20	**52**
Rodent Mammals	15	5.5	4.77	**0.87**	27	**24**
	35	4.4	3.29	**0.75**	19	**21**
	1000	1.9	0.76	0.40	4	**11**

*surrogate for reptiles and terrestrial-phase amphibians
1 See Table 9-5 for derivation.
2 See Table 9-8 for derivation.
3 Bolded RQs exceed Acute Risk LOC (0.50).
4 See Table 9-5 for derivation.

T-REX analysis for broadcast uses.

Upper-bound Kenaga nomogram values are used to derive EECs for chlorophacinone and diphacinone exposures to terrestrial mammals and birds on the field of application based on a 1-year time period. Consideration is given to different types of feeding strategies for mammals, including herbivores, insectivores and granivores. Dose-based exposures are estimated for three weight classes of birds (20 g, 100 g, and 1,000 g) and three weight classes of mammals (15 g, 35 g, and 1,000 g). A summary of EECs is found in **Table 9-10**.

Table 9-10. Summary of Dietary (mg ai/kg-diet) and Dose-based EECs (mg ai/kg-bw) as Food Residues for Birds, Reptiles, Terrestrial-Phase Amphibians and Mammals from Labeled Uses of Chlorophacinone and Diphacinone (T-REX v. 1.5.2, Upper Bound Kenaga)

Food Type	Dietary-Based EEC (mg/kg-diet)	Dose-Based EEC (mg/kg-body weight)					
		Birds			Mammals		
		Small (20 g)	Medium (100 g)	Large (1000 g)	Small (15 g)	Medium (35 g)	Large (1000 g)
Chlorophacinone (4.4 lb ai/acre, 1x interval)							
Short grass	1044.38	1189.45	678.27	303.67	233.53	199.48	106.93
Tall grass	478.68	545.16	310.88	139.18	107.04	91.43	49.01
Broadleaf plants/small insects	587.47	669.06	381.53	170.82	131.36	112.21	60.15
Fruits/pods/(seeds, dietary only)	65.27	74.34	42.39	18.98	14.60	12.47	6.68
Arthropods	409.05	465.87	265.66	118.94	91.47	78.13	41.88
Seeds (granivore)	NA	16.52	9.42	4.22	3.24	2.77	1.49
Diphacinone (10 lbs ai/A, 1x, 5 day-interval)							
Short grass	4523.43	5151.73	2937.73	1315.26	4312.74	2980.68	691.08
Tall grass	2073.24	2361.21	1346.46	602.83	1976.67	1366.15	316.75
Broadleaf plants/small insects	2544.43	2897.85	1652.48	739.84	2425.92	1676.63	388.73
Fruits/pods/(seeds, dietary only)	282.71	321.98	183.61	82.20	269.55	186.29	43.19
Arthropods	1771.68	2017.76	1150.61	515.14	1689.16	1167.43	270.67
Seeds (granivore)	NA	71.55	40.80	18.27	59.90	41.40	9.60

Bolded values exceed the LOC for acute risk to non-listed species of 0.5 or the chronic risk LOC of 1.0.

RQ values are generated based on the upper bound EECs discussed above and toxicity values contained in **Section 6**. These values are found in Tables **9-11** and **9-12**.

Table 9-11. Acute RQ values for Birds, Reptiles, and Terrestrial-Phase Amphibians from Labeled Uses of Chlorophacinone and Diphacinone (T-REX v. 1.5.2, Upper Bound Kenaga)

Food Type	Acute Dose-Based RQ			Acute Dietary-Based RQ
	Small (15 g)	Medium (35 g)	Large (1000 g)	
Chlorophacinone (4.4 lb ai/acre, 1x interval)				
Short grass	**6.40**	**2.87**	**0.91**	**18.65**
Tall grass	**2.93**	**1.31**	0.42	**8.55**
Broadleaf plants	**3.60**	**1.61**	**0.51**	**10.49**
Fruits/pods/seeds	0.40	0.18	0.06	**1.17**
Arthropods	**2.51**	**1.12**	0.36	**7.30**
Seeds	**0.09**	**0.04**	0.01	N/A
Diphacinone (10 lbs ai/A, 1x, 5 day-interval)				
Short grass	**4.39**	**1.97**	**0.62**	**4.99**
Tall grass	**2.01**	**0.90**	0.29	**2.29**
Broadleaf plants	**2.47**	**1.11**	0.35	**2.81**
Fruits/pods/seeds	0.27	0.12	0.04	0.31
Arthropods	**1.72**	**0.77**	0.24	**1.96**
Seeds	0.06	0.03	0.01	N/A

Bolded values exceed the LOC for acute risk to non-listed species of 0.5.

Table 9-12. Acute RQ values for Mammals from Labeled Uses of Chlorophacinone and Diphacinone (T-REX v. 1.5.2, Upper Bound Kenaga)

Food Type	Acute Dose-Based RQ			Acute Dietary-Based RQ
	Small (15 g)	Medium (35 g)	Large (1000 g)	
Chlorophacinone (4.4 lb ai/acre, 1x interval)				
Short grass	**233.53**	**199.48**	**106.93**	**916.13**
Tall grass	**107.04**	**91.43**	**49.01**	**419.89**
Broadleaf plants	**131.36**	**112.21**	**60.15**	**515.32**
Fruits/pods/seeds	**14.60**	**12.47**	**6.68**	**57.26**
Arthropods	**91.47**	**78.13**	**41.88**	**358.82**
Seeds	**3.24**	**2.77**	**1.49**	N/A
Diphacinone (10 lbs ai/A, 1x, 5 day-interval)				
Short grass	**1032.77**	**882.19**	**472.89**	**2174.72**
Tall grass	**473.35**	**404.34**	**216.74**	**996.75**
Broadleaf plants	**580.94**	**496.23**	**266.00**	**1223.28**
Fruits/pods/seeds	**64.55**	**55.14**	**29.56**	**135.92**
Arthropods	**404.50**	**345.52**	**185.21**	**851.77**
Seeds	**14.34**	**12.25**	**6.57**	N/A

Bolded values exceed the LOC for acute risk to non-listed species of 0.5.

Chronic Risk Analysis for Broadcast Uses

For toxic response elicited from the dietary exposure route extended over several days, exposure is measured as mg ai/kg-bait (**Table 9-13**). Toxicity is measured by the LC_{50} obtained from the dietary studies (5 days on treated diet) for birds and mammals. While a single day dose risk assessment suggests only a risk to small passeriforms from the highest concentration formulation, accounting for the potential for multiple day accumulation on a dose basis expands the concerns to include passeriforms and other small and medium sized birds at all

formulation concentrations assessed. Acute dietary RQs were calculated for diphacinone. Toxicity is measured by the LC_{50} obtained from the dietary studies (5 days on treated diet) for birds and mammals. Avian and mammalian RQs based on dietary studies are provided in **Tables 9-13 and 9-14**. While risks for birds did not exceed EFED's LOC, acute risks to mammals exceeded LOCs.

Table 9-13. Bird and Mammal Acute Dietary RQs based on a 5-day Exposure to Diphacinone in the Diet (consumption of bait)

	Diphacinone concentration in bait (mg ai/kg-bait)	LC_{50} (mg ai/kg-diet)	RQ[1]
Birds*	50	906	0.06
Mammals	50	2.08	**24.00**

*surrogate for reptiles and terrestrial-phase amphibians
[1] Bolded RQs exceed acute Risk LOCs.

Chronic dietary RQs were calculated for chlorophacinone, since it is the more toxic than diphacinone based on bait concentration (mg ai/kg-bait) and the avian and mammalian NOAECs were based on reproduction endpoints. The chronic RQs were 1090 and 270 for birds and mammals, respectively; both exceeded the Chronic LOC (=1.0).

Table 9-14. Bird and Mammal Acute Dietary RQs based on a 5-day Exposure to Chlorophacinone in the Diet (consumption of bait)

	Chlorophacinone concentration in bait (mg ai/kg-bait)	LC_{50} (mg ai/kg-diet)	RQ[1]
Birds*	50	56	**0.89**
Mammals	50	1.14	**43.9**

*surrogate for reptiles and terrestrial-phase amphibians
[1] Bolded RQs exceed Acute Risk LOCs.

Table 9-15. Bird and Mammal Chronic RQs based on Consumption of Bait Containing Chlorophacinone

	Chlorophacinone concentration in bait (mg ai/kg-bait)	NOAEC (mg ai/kg-diet)	RQ[1]
Birds*	50	0.046	**1090**
Mammals	50	0.185	**270**

*surrogate for reptiles and terrestrial-phase amphibians
[1] Bolded RQs exceed Chronic Risk LOCs.

Secondary Exposure Characterization

Risk from secondary exposure of ARs has been assessed on a qualitative basis extensively in past assessments. The previous assessments concluded that SGARs present greater secondary exposure concerns than FGARs do. Based on the varying measurements of residue levels in carcasses, secondary exposure will be assessed qualitatively in this assessment. Target and non-target taxa that consume ARs via bait boxes carry residues of the persistent ARs from the bait boxes into the environment, creating secondary exposure opportunities for predators and scavengers such as raptors, vultures, and owls. See **Section 6.4** for more information on AR incidents. The likely route of transport is within the bodies of animals which feed on the bait. Because these poisoned animals are not killed immediately, they may travel a significant distance before dying, thereby potentially exposing other animals away from the application site. This hypothesis is supported by numerous incidents in which animals too large to enter the bait boxes are found to contain significant levels of residues in liver or other tissues upon post mortem examinations. In addition, insects such as ants or cockroaches are sometimes attracted to the bait and may feed on it or transport it outside of the bait boxes where they, as well as the bait particles, may be consumed by insectivorous wildlife.

The impaired rodent populations also serve as attractants for predators, which increases risk of secondary exposure. A California study found that red-tailed hawks were more likely to forage in prairie dog colonies that were treated with Rozol Prairie Dog Bait (0.005% chlorophacinone) because the poisoned prairie dogs were easier to capture, due to lethargy and decreased awareness (CDPR, 2018). The persistent half-lives of the second-generation rodenticides increase potential for exposure.

Exposure has also occurred when non-target taxa have home ranges that include illegal cannabis cultivation sites (CDPR, 2018). In the quoted study, a sub-population of fishers (*Pekania pennanti*) in California were necropsied to determine the cause of death. Anticoagulant rodenticide exposure was the cause of death of 11/167 fishers. The fishers that died because of AR exposure were located near illegal cannabis cultivation sites. These sites potentially use rodenticides out of compliance with the labels. This introduces uncertainty of the actual amount of rodenticide exposure to non-target taxa.

Labels that restrict second-generation rodenticide use to bait boxes increases the likelihood that non-target taxa's route of exposure to rodenticides is through secondary exposure. Based on incident data, and reviews of the open literature (CDPR, 2018), brodifacoum and bromadiolone are the anticoagulant rodenticides that non-target taxa are most likely exposed to. Although there is a decrease in incidents over recent time for all ARs (See **Section 6.4**), because incident reporting is not standardized and is potentially subject to error in reporting, results from incident data should be interpreted with caution.

Estimation of Avian Chronic LOAEC for Several ARs

For chronic risk to birds, the relationship between acute and chronic endpoints observed for chlorophacinone and difenacoum was used to estimate chronic toxicity for all rodenticides. The gap between the mallard duck LC_{50} and LOAEC (1792-fold) was calculated by dividing the LC_{50} from the acute dietary mallard study (MRID's 41513101) by the LOAEC of chronic mallard duck study (MRID 48994002) in the following equation:

172 mg ai/kg-diet / 0.096 mg ai/kg-diet = 1792

The corresponding estimated LOAECs for each rodenticide based on the mallard relationship are listed in Table 9-16. The method for calculating the chronic endpoint for each rodenticide is a method typically used to determine toxicity to aquatic organisms, and its use for terrestrial organisms is subject to review for quantitative use in the risk assessment of terrestrial taxa. Currently, the calculated LOAECs can add to the weight of evidence of effects of the rodenticides on avian species. The results should not be interpreted as precise toxicity thresholds, and this analysis was conducted in this case due to the similar mode of action across the ARs and the corroborating studies for two of the ARs.

Difenacoum exhibited high levels of toxicity to birds via the drinking water exposure route in a 6-week one-generation reproductive effects study on Japanese quails (*Coturnix coturnix japonica*) (MRID 50623624). Based on the study author's results, no mortality was observed in the control or in the lowest treatment group (58 µg ai/kg bw). Treatment-related mortalities were noted in the 115 and 241 µg ai/kg bw treatment groups (female birds in each pair). The ratio of acute (67 mg ai/kg-bw) and chronic (58 µg ai/kg bw) endpoints is 1,155, similar to that for chlorophacinone (1,792).

Previous risk assessments for the anticoagulant rodenticides (ARs) have raised the issue of reproductive effects in avian species (birds and their surrogates, reptiles). In registration review, avian reproduction data was submitted for one first-generation AR (FGAR), chlorophacinone, and one second generation AR (SGAR), difenacoum. EPA was able to use this data to estimate reproduction endpoints (Lowest Observed Adverse Effect Level, LOAEL) for the other two FGARs and three SGARs, by comparing the 5-day acute dietary LC50s for chlorophacinone and difenacoum to the LOAELs from the submitted reproduction studies. The ratio of the LC50s to the LOAELs, approximately 1200x to 1800x, was applied to the acute dietary endpoint for the other ARs to estimate their LOAELs for avian reproduction. There is uncertainty in applying factors developed using these two AR rodenticides to the other AR rodenticides. EPA believes that the estimated LOAELs are sufficient to support a registration review decision. However, EPA plans to conduct biological evaluations for rodenticides with the first draft BEs due in 2023 for warfarin, brodifacoum, bromadiolone, and zinc phosphide. The BEs are expected to require greater certainty with respect to the level of exposure associated with reproductive effects to make effects determinations and to set the action area

for endangered species. If a reproduction study is not available to allow EPA to use in the BE, then EPA will use conservative assumptions to estimate a reproduction NOAEC and/or LOAEC.

Table 9-16. Estimated Mallard Duck LOAECs (mg/kg-diet)		
Anticoagulant	**Mallard Dietary LC_{50}**	**Estimated LOAEC (1 sig.fig.)**
Diphacinone	906	0.5
Warfarin	890	0.5
Brodifacoum	2.7	0.002
Bromadiolone	158	0.09
Difenacoum	14.1	0.008
Difethialone	1.96	0.001

9.1.1.2 Risks from Secondary Exposure through Consumption of Contaminated Carcasses

Based on the avian chronic toxicity calculated for chlorophacinone, risk from secondary exposure through consumption of contaminated carcasses was assessed. The determination of chlorophacinone intake for individuals consuming chlorophacinone poisoned animals or carcasses is calculated in a manner similar to the approach for individuals consuming bait (Section 9.1.2). Empirical residue data was used instead of bait concentration of chlorophacinone (Table 9-15). Chlorophacinone body burdens were determined in deceased mammals from field and laboratory studies after exposure to chlorophacinone bait.

Data from several studies were available in which deceased mammals were collected from treated fields and analyzed for residues or in which deceased laboratory animals dosed with chlorophacinone were analyzed for chlorophacinone residues. For all studies, it was assumed the concentrations were reported using wet weights of the mammals. Mean concentrations ranged from 0.122 to 1.58 mg ai/kg-bw, with reported individual values ranging from <LOD to 4.1 mg ai/kg-bw. Field collected data are subject to a number of uncertainties including (but not limited to) possible partial decomposition of bodies in field, missing carcasses with highest body burdens during collection, missing individuals during collection that were rapidly predated, died off site, or died underground.

Because there is a lack of data on chlorophacinone residues in birds, amphibians and reptiles, it was assumed the mammal body burden data would be relevant for all the evaluated taxonomic groups. Due to the uncertainties regarding adequate sampling to capture the full distribution of carcass residue values, the maximum reported individual whole body value, 4.1 mg ai/kg-carcass, will be used for this assessment. The RQ, calculated by dividing the whole body value by the LOAEC of the chronic mallard duck study (MRID 48994002), is 43, exceeding the chronic LOC of 1.0 (**Table 9-12**).

Table 9-17. Avian Chronic RQs based on Consumption of Contaminated Carcasses.

	Chlorophacinone concentration in bait (mg ai/kg-carcass)	LOAEC (mg ai/kg-diet)	RQ[1]
Birds*	4.1	0.096	**43**

*surrogate for reptiles and terrestrial-phase amphibians
[1] Bolded RQs exceed Chronic Risk LOCs.

Based on the estimated LOAECs calculated using the acute-to-chronic ratio, avian chronic exposure-to-endpoint ratios for each AR were calculated. The highest body burden of each AR in mammalian carcasses reported in previous risk assessments were divided by the estimated

avian chronic LOAECs of each AR. Ratio values ranged from 5.90 to 12,985, all exceeding the LOC of 1.0. The considerably large risk quotient exceedance of brodifacoum aligns with the ecotoxicity observed both in laboratory settings and reported wildlife incidents in Section 6 of this document. These calculations can be used qualitatively in the weight of evidence approach to risk.

Table 9-18. Avian Chronic Hazard based on Mallard Duck Acute-Chronic Analysis.

AR	Bait Concentration (mg ai/kg-carcass)	Test Species	LOAEC (mg ai/kg-diet)	Ratio of exposure to effect level
Chlorophacinone	4.1	*Anas platyrhynchos*	0.096	**43**
Diphacinone	3.4	*Anas platyrhynchos*	0.5	**7**
Warfarin	2.95	*Anas platyrhynchos*	0.5	**6**
Bromadiolone	1.83	*Anas platyrhynchos*	0.09	**20**
Brodifacoum	25.97	*Anas platyrhynchos*	0.002	**13,000**
Difenacoum	0.74	*Anas platyrhynchos*	0.008	**93**
Difethialone	2.67	*Anas platyrhynchos*	0.001	**2700**

9.2 Terrestrial Vertebrate Risk Characterization

A number of studies have also been conducted where AR residues in wildlife were monitored. A summary of reports from three states – Massachusetts, Kentucky, and California are presented below.

California

The California Department of Pesticide Regulations (CDPR) assessed liver samples of necropsied animals for the presence of ARs from 2014 to 2018. In summary, these studies showed an overall increase in exposure to ARs over time, especially second generation ARs. The results for these studies can be found in **Appendix E.**

Kentucky

The University of Kentucky tested 51 barn owl carcasses found in western and central Kentucky for the presence of ARs, between January 2012 and December 2016. Thirty-three % (16/48) of the barn owls sampled contained residues of at least one anticoagulant rodenticide in their liver. Of the birds that tested positively for anticoagulant rodenticides, 31% (5/16) tested positive for more than one anticoagulant rodenticide in its liver. Brodifacoum was the most commonly detected anticoagulant rodenticide, found in 88% (14/16) of the birds that tested positively. Bromadiolone was detected in 38% (6/16) of the birds that tested positively. The

researchers found that the prevalence of detected exposure to brodifacoum for after-hatch-year birds was significantly higher than hatch-year birds.

Massachusetts

The Massachusetts Department of Agriculture evaluated specimens of four species of avian wildlife: red-tailed hawks (*Buteo jamaicensis*), barred owls (*Strix varia*), Eastern screech-owls (*Megascops asio)*, and great horned owls [*Bubo virginianus*]) that were diagnosed with AR toxicosis to evaluate the extent to which residues of ARs favored by pest management professionals are present in those species. Of the 100 reports collected per year, most reports employed more than one type of AR in each year, and bromadiolone was the most frequently reported AR. Of all birds tested, 90 (96%) were positive for ARs (97% of red-tailed hawks, 88% of barred owls, 100% of great horned owls, 100% of eastern screech owls). All birds suspected of suffering from AR toxicosis were positive. Of the 78 asymptomatic birds, 74 (95%) were positive. All positive birds had residues of second-generation anticoagulant rodenticides (SGARs). Brodifacoum was found in all positive birds except one (99%), a great horned owl which was positive for bromadiolone only. Two birds had residues of first-generation anticoagulant rodenticides (FGARs): an eastern screech owl with residues of both diphacinone and brodifacoum and a great horned owl with residues of chlorophacinone along with brodifacoum, bromadiolone, and difethialone.

Overall, we find that both first and second generation ARs continue to pose risks to wildlife, especially to secondary consumers. The risk is considerably greater from SGARs, as documented in the incident analysis section (6.4).

10 Terrestrial Invertebrate Risk Assessment

Exposure of soil-dwelling terrestrial invertebrates is possible, from some outdoor uses of the ARs, particularly use in animal burrows and the broadcast uses of chlorophacinone and diphacinone. However, the exposure is not expected to be widespread. Table 10-1 below summarizes 14-day LC50 acute toxicity data for the earthworm *Eisenia foetida* found in the Footprint database (ref). The data have not been reviewed by EFED, but taken at face value indicate that the ARs are minimally toxic to earthworms.

Table 10-1. Earthworm Acute Toxicity Data found in Footprint Database
https://sitem.herts.ac.uk/aeru/footprint/index2.htm

Rodenticide	*Eisenia foetida* 14-d LC_{50} (mg/kg soil)	Data cited in problem formulation	MRID
Warfarin	> 10		
Chlorophacinone	> 300	> 1000 (NOAEC 309) NOAEC < 95 (weight)	47383001
Diphacinone	No data		
Brodifacoum	> 994	450 (Liu et al. 2015)	

Bromadialone	> 4.74		
Difenacoum	No data		
Difethialone	> 1000		

Exposure of honey bees is not expected, given the allowed use patterns. Toxicity data on honey bees has not been submitted, and was not requested in the problem formulations, due to the lack of expected exposure.

Alomar et al. (Sci Total Environ. 610-11 (2018) 576-582) have shown that slugs (*Deoceras reticulatum*) accumulate the active ingredient when exposed to bromadiolone, brodifacoum and chlorophacinone. Accumulation of brodifacoum in field-collected slugs was sufficient to serve as a route of exposure and a risk of secondary effects to predators, including hedgehog, European starling and common shrew.

11 Terrestrial Plant Risk Assessment

Based on the use patterns as modified by the 2008 RMD, meaningful exposure of terrestrial plants to the 7 ARs is not expected. No terrestrial plant toxicity data (vegetative vigor and seedling emergence) has been submitted, nor was any requested at the time of the problem formulations. Risk to terrestrial plants is considered minimal, based on lack of exposure and the anticoagulant mode of action.

12 Conclusions

Mammals and birds are at risk of mortality and reproduction effects from the use of the seven anticoagulant rodenticides, both by primary and secondary exposure routes. Other terrestrial vertebrates (reptiles, amphibians) may also be at risk based on surrogacy.

Incident reports indicate that non-target exposures to ARs are continuing. Exposures to brodifacoum and to a lesser extent difethialone and bromadiolone (all of which are SGARs) are more predominant than other AR rodenticides.

Incident reports also indicate that listed and protected species such as the San Joaquin kit fox, bald eagles, and golden eagles have been adversely affected by exposure to (list of ARs) as concluded earlier for the San Joaquin kit fox in EFED Biological Evaluations.

Chronic or reproductive risks to birds were previously unquantified due to a lack of reproductive toxicity data. Toxicity thresholds for the 7 ARs have been qualitatively estimated, supported by literature data. These data show that studies that utilize a prolonged exposure

regimen result in substantially lower LOAEC values, which is consistent with bioaccumulative properties. LOAEC estimates are in the microgram per kilogram diet range.

Both previous risk assessments and risk quotients presented in this risk assessment indicate that aquatic organisms are not at risk from the use of the ARs, either due to lack or exposure or exposure well below acute toxic thresholds. There are reported aquatic incidents, though it is unclear whether these incidents are due to misuse or poor disposal techniques.

Risk to terrestrial invertebrates is not expected either due to lack of exposure (honey bees and other pollinators) or practical non-toxicity (earthworms). Exposure of predators through invertebrates that accumulate ARs is possible. Risk to terrestrial plants is not generally expected due to lack of exposure, although some exposure via the roots is possible from underground or broadcast uses.

Table 12-1. Potential Environmental Fate Concerns Identified for Seven Anticoagulant Rodenticides

Aquatic Bioconcentration/ Bioaccumulation[1]	Groundwater Contamination	Sediment	Persistence[2]	Residues of Concern	Secondary Exposure	Volatilization
Warfarin No, log K_{ow}<3	No	No	Non-Persistent	Parent	Yes	No
Chlorophacinone No, log Kow < 3	No	No	Slightly persistent	Parent	Yes	No
Diphacinone Possible, log Kow = 4.85	No	No	Slightly persistent	Parent	Yes	No
Brodifacoum Possible, log Kow = 6.12 fish BCF = 2450	No	No	Moderately persistent	Parent	Yes	No
Bromadiolone Possible, log Kow = 4.07 fish BCF = 1658	No	No	Moderately persistent	Parent	Yes	No
Difenacoum Possible, log Kow = 7.6 fish BCF = 9010	No	No	Moderately persistent to persistent	Parent	Yes	No
Difethialone Possible, log Kow = 6.29	No	No	Persistent	Parent	Yes	No

fish BCF = 555						

[1] Based on K_{ow} Based Aquatic Bioaccumulation Model (KABAM) for chemicals with a log K_{ow} >3.

[2] Persistence classification consistent with Goring *et al* (1975) applied to aerobic soil metabolism studies.

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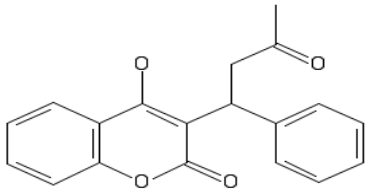
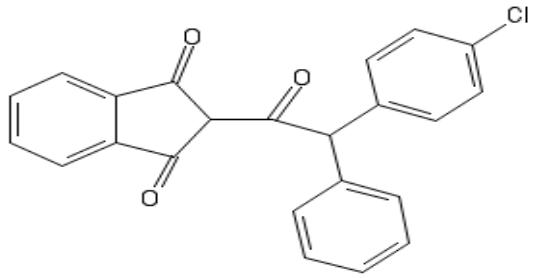
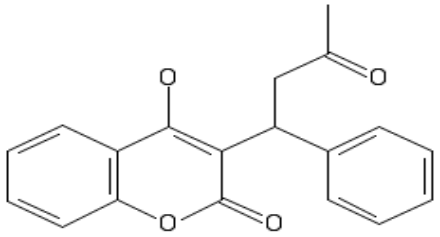
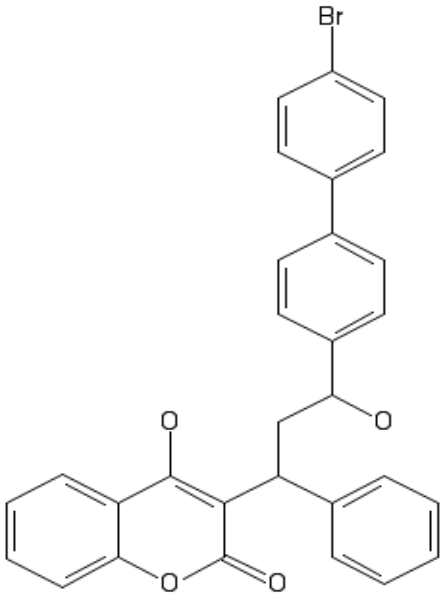
Appendix A. Structures and Formulas of the Seven Anticoagulant Rodenticides

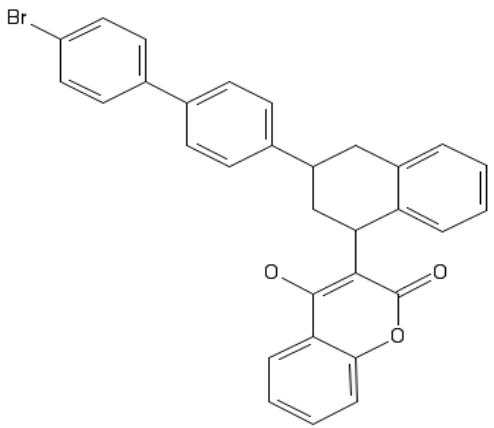
Table B1. Chemical Names and Structures of Seven Anticoagulant Rodenticides

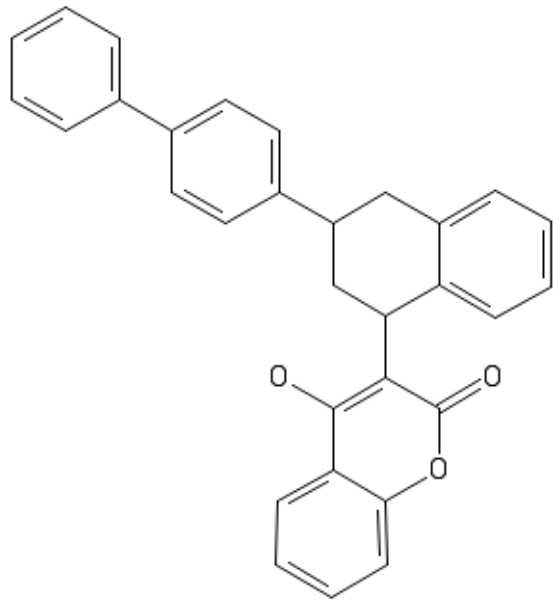
Chemical	Chemical Name	Chemical Structure
First Generation ARs		
Warfarin	4-hydroxy-3-(3-oxo-1-phenylbutyl)chromen-2-one **CAS No.:** 81-81-2 **Formula:** C19H16O4 **MW:** 308.33 g/mol **SMILES:** c1ccc2C(O)=C(C(c3ccccc3)CC(=O)C)C(=O)Oc2c1	

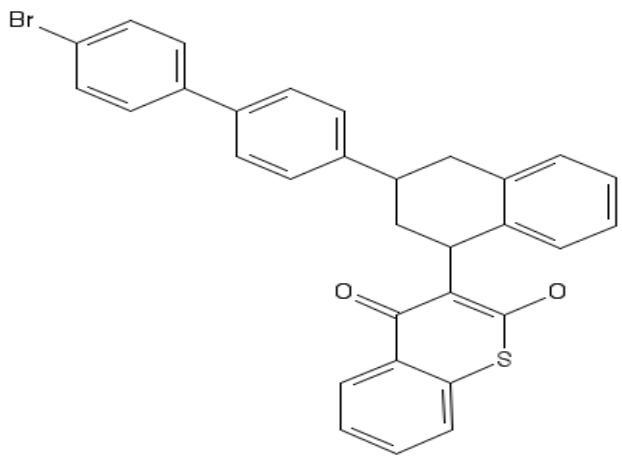
Chlorophacinone	2-[(RS)-2-(4-chlorophenyl)-2-phenylacetyl]indan-1,3-dione **Formula:** C23H15ClO3 **MW:** 374.82 g/mol **SMILES:** C1=CC=C(C=C1)C(C2=CC=C(C=C2)Cl)C(=O)C3C(=O)C4=CC=CC=C4C3=O	

Diphacinone	2-(diphenylacetyl)indan-1,3-dione **Formula:** C23H16O3 **MW:** 340.3735.75 g/mol **SMILES:** C1=CC=C(C=C1)C(C2=CC=CC=C2)C(=O)C3C(=O)C4=CC=CC=C4C3=O	
Second Generation ARs		
Bromadiolone	3-[(1RS,3RS;1RS,3SR)-3-(4'-bromobiphenyl-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxycoumarin Formula: C30H23BrO4 MW: 527.40 g/mol SMILES: C1=CC=C(C=C1)C(CC(C2=CC=C(C=C2)C3=CC=C(C=C3)Br)O)C4=C(C5=CC=CC=C5OC4=O)O	

		
Brodifacoum	3-[(1RS,3RS;1RS,3SR)-3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin **Formula**: $C_{31}H_{23}BrO_3$ **MW: 523.4** g/mol **SMILES:** C1C(CC2=CC=CC=C2C1C3=C(C4=CC=CC=C4OC3=O)O)C5=CC=C(C=C5)C6=CC=C(C=C6)Br	

		
Difenacoum	3-((1RS,3RS;1RS,3SR)-3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycoumarin **Formula:** C31H24O3 **MW:** 444.52 g/mol **SMILES:** C1C(CC2=CC=CC=C2C1C3=C(C4=CC=CC=C4OC3=O)O)C5=CC=C(C=C5)C6=CC=CC=C6	

Difethialone	3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzothiopyran-2-one **Formula**: C31H23BrO2S **MW**: 539.48 g/mol **SMILES:** C1C(CC2=CC=CC=C2C1C3=C(SC4=CC=CC=C4C3=O)O)C5=CC=C(C=C5)C6=CC=C(C=C6)Br	

Appendix B. Example Aquatic Modeling Output and Input Batch Files

Summary of Water Modeling of chlorophacinone and the USEPA Standard Pond

Estimated Environmental Concentrations for chlorophacinone are presented in Table 1-B for the USEPA standard pond with the MICherriesSTD field scenario. A graphical presentation of the year-to-year peaks is presented in Figure 1. These values were generated with the Pesticide Water Calculator (PWC), Version 1.52. Critical input values for the model are summarized in Tables 2-B and 3-B.

This model estimates that about 1% of chlorophacinone applied to the field eventually reaches the water body. The main mechanism of transport from the field to the water body is by erosion (96.5% of the total transport) followed by runoff (3.51%).

In the water body, pesticide dissipates with an effective water column half-life of 276.6 days. (This value does not include dissipation by transport to the benthic region; it includes only processes that result in removal of pesticide from the complete system.) The main source of dissipation in the water column is metabolism (effective average half-life = 428 days) followed by volatilization (781.6 days).

In the benthic region, pesticide dissipation is negligible (1032.1 days). The main source of dissipation in the benthic region is burial (effective average half-life = 1032.1 days). The vast majority of the pesticide in the benthic region (99.95%) is sorbed to sediment rather than in the pore water.

Table 1-B. Estimated Environmental Concentrations (ppb) for chlorophacinone.

Peak (1-in-10 yr)	0.651
4-day Avg (1-in-10 yr)	0.385
21-day Avg (1-in-10 yr)	0.236
60-day Avg (1-in-10 yr)	0.196
365-day Avg (1-in-10 yr)	0.178
Entire Simulation Mean	0.130

Table 2-B. Summary of Model Inputs for chlorophacinone.

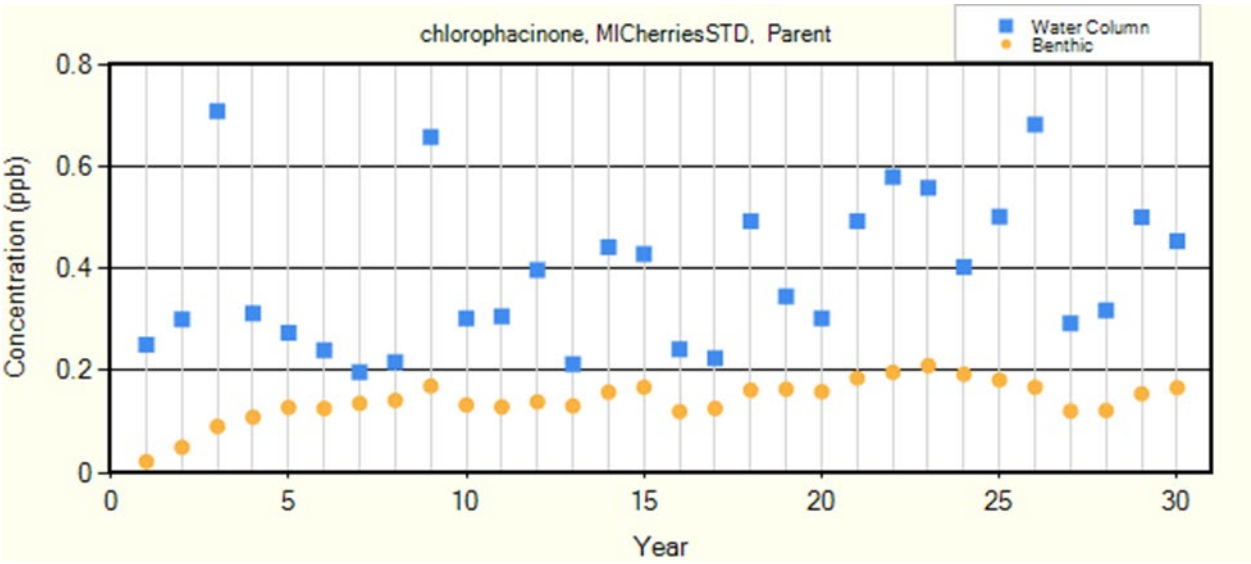
Scenario	MICherriesSTD
Cropped Area Fraction	1
Koc (ml/g)	20299

Water Half-Life (days) @ 25 °C	156
Benthic Half-Life (days) @ 25 °C	0
Photolysis Half-Life (days) @ 40 °Lat	0
Hydrolysis Half-Life (days)	0
Soil Half-Life (days) @ 25 °C	78
Foliar Half-Life (days)	0
Molecular Weight	374.81
Vapor Pressure (torr)	3.58E-6
Solubility (mg/l)	3.43
Henry's Constant	2.1E-05

Table 3-B. Application Schedule for chlorophacinone.

Date (Mon/Day)	Type	Amount (kg/ha)	Eff.	Drift
04/01	Ground	0.112	1.0	0
05/01	Ground	0.112	1.0	0

Figure 1. Yearly Peak Concentrations



Appendix C. T-REX Analysis for Chlorophacinone and Diphacinone

Upper Bound Kenaga Residues For RQ Calculation

Chemical Name:	Chlorophacinone
Use	0
Formulation	0
Application Rate	4.3516 lbs a.i./acre
Half-life	35 days
Application Interval	1 days
Maximum # Apps./Year	1
Length of Simulation	1 year
Variable application rates?	no

Acute and Chronic RQs are based on the Upper Bound Kenaga Residues.

The maximum single day residue estimation is used for both the acute and reproduction RQs.

RQs reported as "0.00" in the RQ tables below should be noted as <0.01 in your assessment. This is due to rounding and significant figure issues in Excel.

Endpoints

Avian	Bobwhite quail	LD50 (mg/kg-bw)	258.00
	Bobwhite quail	LC50 (mg/kg-diet)	56.00
	Bobwhite quail	NOAEL(mg/kg-bw)	0.00
	Bobwhite quail	NOAEC (mg/kg-diet)	0.00
Mammals		LD50 (mg/kg-bw)	1.94
		LC50 (mg/kg-diet)	1.14
		NOAEL (mg/kg-bw)	0.00
		NOAEC (mg/kg-diet)	0.00

Dietary-based EECs (ppm)	Kenaga Values
Short Grass	1044.38
Tall Grass	478.68
Broadleaf plants	587.47
Fruits/pods/seeds	65.27
Arthropods	409.05

Avian Results

Avian Class	Body Weight (g)	Ingestion (Fdry) (g bw/day)	Ingestion (Fwet) (g/day)	% body wgt consumed	FI (kg-diet/day)
Small	20	5	23	114	2.28E-02
Mid	100	13	65	65	6.49E-02
Large	1000	58	291	29	2.91E-01
Granivores	20	5	5	25	5.06E-03
	100	13	14	14	1.44E-02
	1000	58	65	6	6.46E-02

Avian Body Weight (g)	Adjusted LD50 (mg/kg-bw)
20	185.87
100	236.62
1000	334.24

Dose-based EECs (mg/kg-bw)	Avian Classes and Body Weights (grams) small 20	mid 100	large 1000
Short Grass	1189.45	678.27	303.67
Tall Grass	545.16	310.88	139.18
Broadleaf plants	669.06	381.53	170.82
Fruits/pods	74.34	42.39	18.98
Arthropods	465.87	265.66	118.94
Seeds	16.52	9.42	4.22

Dose-based RQs (Dose-based EEC/adjusted LD50)	Avian Acute RQs Size Class (grams) 20	100	1000
Short Grass	6.40	2.87	0.91
Tall Grass	2.93	1.31	0.42
Broadleaf plants	3.60	1.61	0.51
Fruits/pods	0.40	0.18	0.06
Arthropods	2.51	1.12	0.36
Seeds	0.09	0.04	0.01

Dietary-based RQs (Dietary-based EEC/LC50 or	RQs Acute	Chronic
Short Grass	18.65	#DIV/0!
Tall Grass	8.55	#DIV/0!
Broadleaf plants	10.49	#DIV/0!
Fruits/pods/seeds	1.17	#DIV/0!
Arthropods	7.30	#DIV/0!

Note: To provide risk management with the maximum possible information, it is recommended that both the dose-based and concentration-based RQs be calculated when data are available

Chlorophacinone 0 Upper bound Kenaga Residues

Mammalian Results

Mammalian Class	Body Weight	Ingestion (Fdry) (g bwt/day)	Ingestion (Fwet) (g/day)	% body wgt consumed	FI (kg-diet/day)
Herbivores/ Insectivores	15	3	14	95	1.43E-02
	35	5	23	66	2.31E-02
	1000	31	153	15	1.53E-01
Grainvores	15	3	3	21	3.18E-03
	35	5	5	15	5.13E-03
	1000	31	34	3	3.40E-02

Mammalian Class	Body Weight	Adjusted LD50	Adjusted NOAEL
Herbivores/ Insectivores	15	4.26	0.00
	35	3.46	0.00
	1000	1.49	0.00
Granivores	15	4.26	0.00
	35	3.46	0.00
	1000	1.49	0.00

Dose-Based EECs (mg/kg-bw)	Mammalian Classes and Body weight (grams) 15	35	1000
Short Grass	995.74	688.19	159.56
Tall Grass	456.38	315.42	73.13
Broadleaf plants	560.10	387.11	89.75
Fruits/pods	62.23	43.01	9.97
Arthropods	390.00	269.54	62.49
Seeds	13.83	9.56	2.22

Dose-based RQs (Dose-based EEC/LD50 or	Small mammal 15 grams Acute	Chronic	Medium mammal 35 grams Acute	Chronic	Large mammal 1000 grams Acute	Chronic
Short Grass	233.53	#DIV/0!	199.48	#DIV/0!	106.93	#DIV/0!
Tall Grass	107.04	#DIV/0!	91.43	#DIV/0!	49.01	#DIV/0!
Broadleaf plants	131.36	#DIV/0!	112.21	#DIV/0!	60.15	#DIV/0!
Fruits/pods	14.60	#DIV/0!	12.47	#DIV/0!	6.68	#DIV/0!
Arthropods	91.47	#DIV/0!	78.13	#DIV/0!	41.88	#DIV/0!
Seeds	3.24	#DIV/0!	2.77	#DIV/0!	1.49	#DIV/0!

Dietary-based RQs (Dietary-based EEC/LC50 or NOAEC)	Mammal RQs Acute	Chronic
Short Grass	916.13	#DIV/0!
Tall Grass	419.89	#DIV/0!
Broadleaf plants	515.32	#DIV/0!
Fruits/pods/seeds	57.26	#DIV/0!
Arthropods	358.82	#DIV/0!

Note: To provide risk management with the maximum possible information, it is recommended that both the dose-based and concentration-based RQs be calculated when data are available

Upper Bound Kenaga Residues For RQ Calculation

Chemical Name:	Diphacinone
Use	1
Formulation	0
Application Rate	9.89 lbs a.i./acre
Half-life	35 days
Application Interval	5 days
Maximum # Apps./Year	2
Length of Simulation	1 year
Variable application rates?	no

Acute and Chronic RQs are based on the Upper Bound Kenaga Residues.

The maximum single day residue estimation is used for both the acute and reproduction RQs.

RQs reported as "0.00" in the RQ tables below should be noted as <0.01 in your assessment. This is due to rounding and significant figure issues in Excel.

Endpoints

Avian	Bobwhite quail	LD50 (mg/kg-bw)	1630.00
	Mallard duck)	LC50 (mg/kg-diet)	906.00
	Bobwhite quail	NOAEL(mg/kg-bw)	0.00
	Bobwhite quail	NOAEC (mg/kg-diet)	0.00
Mammals		LD50 (mg/kg-bw)	1.90
		LC50 (mg/kg-diet)	2.08
		NOAEL (mg/kg-bw)	0.00
		NOAEC (mg/kg-diet)	0.00

Dietary-based EECs (ppm)	Kenaga Values
Short Grass	4523.43
Tall Grass	2073.24
Broadleaf plants	2544.43
Fruits/pods/seeds	282.71
Arthropods	1771.68

Avian Results

Avian Class	Body Weight (g)	Ingestion (Fdry) (g bw/day)	Ingestion (Fwet) (g/day)	% body wgt consumed	FI (kg-diet/day)
Small	20	5	23	114	2.28E-02
Mid	100	13	65	65	6.49E-02
Large	1000	58	291	29	2.91E-01
Granivores	20	5	5	25	5.06E-03
	100	13	14	14	1.44E-02
	1000	58	65	6	6.46E-02

Avian Body Weight (g)	Adjusted LD50 (mg/kg-bw)
20	1174.30
100	1494.94
1000	2111.66

Dose-based EECs (mg/kg-bw)	Avian Classes and Body Weights (grams) small 20	mid 100	large 1000
Short Grass	5151.73	2937.73	1315.26
Tall Grass	2361.21	1346.46	602.83
Broadleaf plants	2897.85	1652.48	739.84
Fruits/pods	321.98	183.61	82.20
Arthropods	2017.76	1150.61	515.14
Seeds	71.55	40.80	18.27

Dose-based RQs (Dose-based EEC/adjusted LD50)	Avian Acute RQs Size Class (grams) 20	100	1000
Short Grass	4.39	1.97	0.62
Tall Grass	2.01	0.90	0.29
Broadleaf plants	2.47	1.11	0.35
Fruits/pods	0.27	0.12	0.04
Arthropods	1.72	0.77	0.24
Seeds	0.06	0.03	0.01

Dietary-based RQs (Dietary-based EEC/LC50 or	RQs Acute	Chronic
Short Grass	4.99	#DIV/0!
Tall Grass	2.29	#DIV/0!
Broadleaf plants	2.81	#DIV/0!
Fruits/pods/seeds	0.31	#DIV/0!
Arthropods	1.96	#DIV/0!

Note: To provide risk management with the maximum possible information, it is recommended that both the dose-based and concentration-based RQs be calculated when data are available

Diphacinone 1 Upper bound Kenaga Residues

Mammalian Results

Mammalian Class	Body Weight	Ingestion (Fdry) (g bwt/day)	Ingestion (Fwet) (g/day)	% body wgt consumed	FI (kg-diet/day)
Herbivores/ insectivores	15	3	14	95	1.43E-02
	35	5	23	66	2.31E-02
	1000	31	153	15	1.53E-01
Grainvores	15	3	3	21	3.18E-03
	35	5	5	15	5.13E-03
	1000	31	34	3	3.40E-02

Mammalian Class	Body Weight	Adjusted LD50	Adjusted NOAEL
Herbivores/ insectivores	15	4.18	0.00
	35	3.38	0.00
	1000	1.46	0.00
Granivores	15	4.18	0.00
	35	3.38	0.00
	1000	1.46	0.00

Dose-Based EECs (mg/kg-bw)	Mammalian Classes and Body weight (grams) 15	35	1000
Short Grass	4312.74	2980.68	691.08
Tall Grass	1976.67	1366.15	316.75
Broadleaf plants	2426.92	1676.63	388.73
Fruits/pods	269.55	186.29	43.19
Arthropods	1689.16	1167.43	270.67
Seeds	59.90	41.40	9.60

Dose-based RQs (Dose-based EEC/LD50 or	Small mammal 15 grams Acute	Chronic	Medium mammal 35 grams Acute	Chronic	Large mammal 1000 grams Acute	Chronic
Short Grass	1032.77	#DIV/0!	882.19	#DIV/0!	472.89	#DIV/0!
Tall Grass	473.35	#DIV/0!	404.34	#DIV/0!	216.74	#DIV/0!
Broadleaf plants	580.94	#DIV/0!	496.23	#DIV/0!	266.00	#DIV/0!
Fruits/pods	64.55	#DIV/0!	55.14	#DIV/0!	29.56	#DIV/0!
Arthropods	404.50	#DIV/0!	345.52	#DIV/0!	185.21	#DIV/0!
Seeds	14.34	#DIV/0!	12.25	#DIV/0!	6.57	#DIV/0!

Dietary-based RQs (Dietary-based EEC/LC50 or NOAEC)	Mammal RQs Acute	Chronic
Short Grass	2174.72	#DIV/0!
Tall Grass	996.75	#DIV/0!
Broadleaf plants	1223.28	#DIV/0!
Fruits/pods/seeds	135.92	#DIV/0!
Arthropods	851.77	#DIV/0!

Note: To provide risk management with the maximum possible information, it is recommended that both the dose-based and concentration-based RQs be calculated when data are available

Appendix D. California Department of Pesticide Regulation Figures

Table 1. DPR Analysis of AR exposure rates based on DFW loss reports.

Parameter	2014	2015	2016	2017	2018
Total Reported Animals Tested	18	42	56	24	12
No. of Reported Mammals Tested	16	28	45	14	6
No. of Reported Birds Tested	2	14	10	10	6
No. of Reported Non-Bird/Mammals Tested	0	0	1	0	0
No. of Reported Animals with Detectable Levels of ARs	16 / 18	41 / 42	52 / 56	20 / 24	12 / 12
Maximum No. of ARs Detected	5	4	5	5	4
Minimum No. of ARs Detected	0	0	0	0	1
Mean No. of ARs Detected	2.5	2.1	2.2	2.5	2.4
No. of Reported Animals with Detectable Levels of FGARs	9 / 18	21 / 42	16 / 56	9 / 24	3 / 12
No. of Reported Animals with Detectable Levels of Chlorophacinone	1 / 18	3 / 42	3 / 56	6 / 24	0 / 12
No. of Reported Animals with Detectable Levels of Diphacinone	9 / 18	18 / 42	15 / 56	6 / 24	3 / 12
No. of Reported Animals with Detectable Levels of Warfarin	1 / 18	1 / 42	1 / 56	1 / 24	0 / 12
No. of Reported Animals with Detectable Levels of SGARs	16 / 18	35 / 42	51 / 56	19 / 24	12 / 12
No. of Reported Animals with Detectable Levels of Brodifacoum	14 / 18	32 / 42	48 / 56	19 / 24	11 / 12
No. of Reported Animals with Detectable Levels of Bromodiolone	14 / 18	18 / 42	32 / 56	13 / 24	7 / 12
No. of Reported Animals with Detectable Levels of Difenacoum	1 / 18	2 / 42	0 / 56	3 / 24	1 / 12
No. of Reported Animals with Detectable Levels of Difethialone	5 / 18	15 / 42	23 / 56	12 / 24	7 / 12

Notes:

This table includes all data provided to DPR by DFW from 2014 to 2018.

ARs: Anticoagulant Rodenticides

FGARs: First Generation Anticoagulant Rodenticides

SGARs: Second Generation Anticoagulant Rodenticides

Figure 1 – DPR's preliminary analysis of SGAR non-target wildlife exposure rates based on loss reports submitted by DFW.

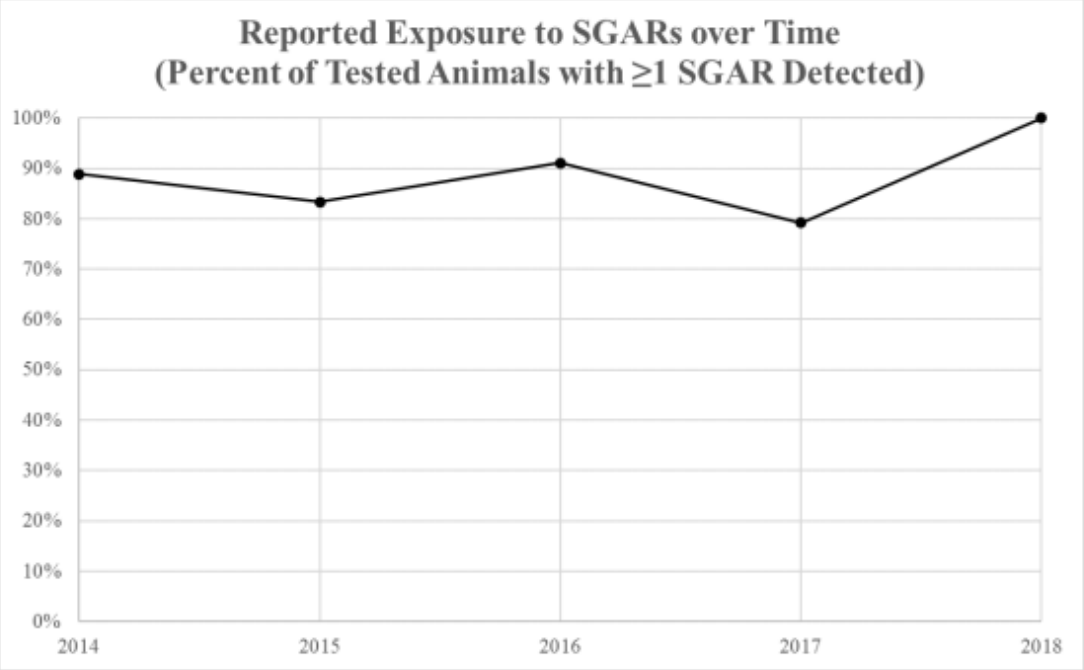


Figure 2 – Exposure rates of individual SGAR active ingredients from 2014-2018 (chart created by DPR scientists from non-target wildlife loss reports submitted by DFW).

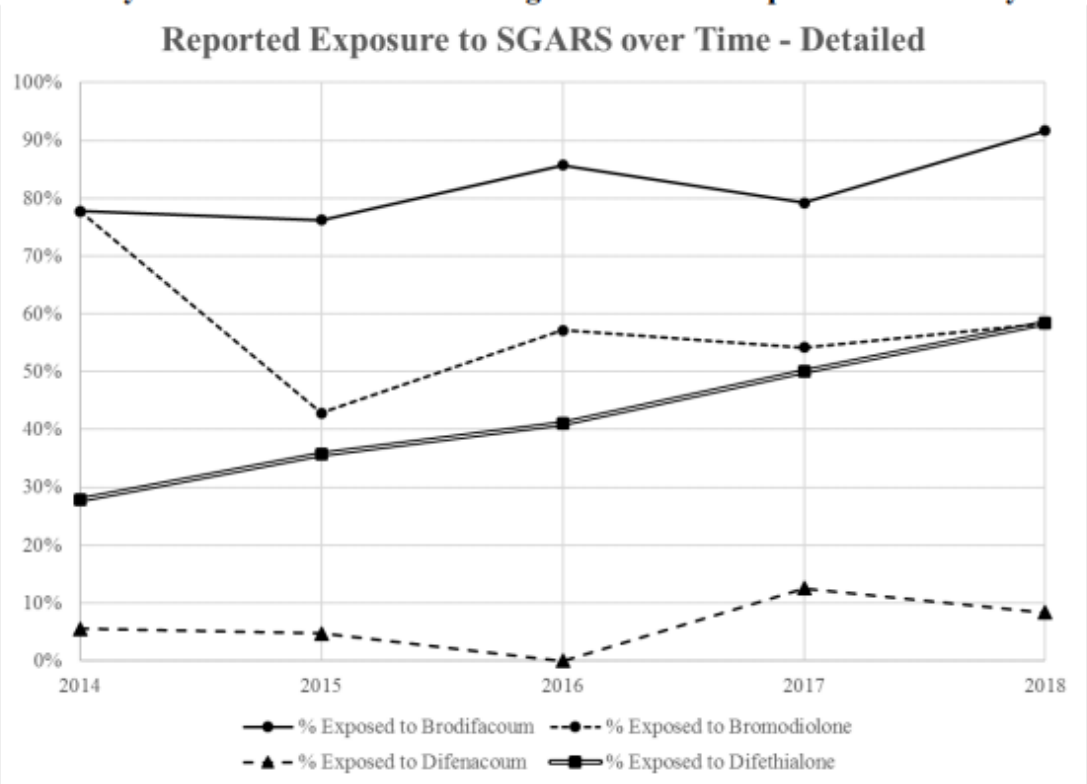


Figure 3 – DPR's preliminary analysis of FGAR non-target wildlife exposure rates based on loss reports submitted by DFW.

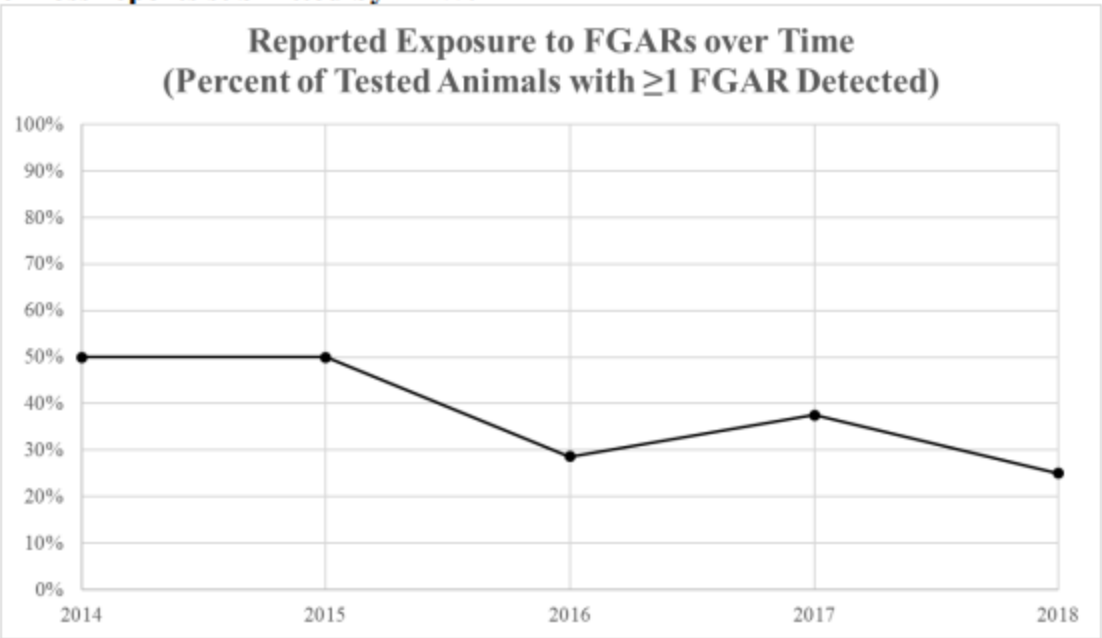


Figure 4 – Exposure rates of individual FGAR active ingredients from 2014-2018 (chart created by DPR scientists from non-target wildlife loss reports submitted by DFW).