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Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: a Comparative Approach

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Prepared by:

William Erickson, Biologist
Environmental Risk Branch 2

Douglas Urban, Senior Biologist
Environmental Risk Branch 3

Executive Summary

This document presents the Agency's assessment of potential risks to birds and nontarget mammals from 9 rodenticides, including 3 second-generation anticoagulants (brodifacoum, difethialone, bromadiolone), 3 first-generation anticoagulants (diphacinone, chlorophacinone, warfarin), and 3 non-anticoagulant compounds (zinc phosphide, bromethalin, cholecalciferol). These rodenticides are predominantly used to control commensal rats and mice in and around buildings, transport vehicles, and in sewers. Some, mainly zinc phosphide, chlorophacinone, and diphacinone, also have products registered for other outdoor uses against other rodent and small mammalian pests. A major concern in using rodenticides is that they are not selective to the target species; birds and nontarget mammals that feed on grain-based baits (pellets, meal, treated grains, wax blocks) or meat-based, vegetable, or fruit baits are potentially at risk. The available information from laboratory and pen studies, field studies, control programs, reported incidents, and toxicokinetics also indicates that a variety of avian and mammalian predators and scavengers are potentially at risk from consuming animals poisoned with some of these rodenticides.

The assessment focuses on the potential primary and secondary risks to birds and nontarget mammals posed by applications of these 9 rodenticides (11 baits) to control rats and mice in and around buildings (commensal use) and in field and other outdoor settings to control various rodent and other small mammalian pests. Risk is a function of exposure and hazard (toxicity), and data are available to estimate toxicity based on laboratory acute and secondary-hazard tests. However, typical use information used to estimate nontarget organism exposure, such as amount of active ingredient or formulated product applied per unit area, is not available for commensal uses. Thus, exposure estimates are largely based on the amount of active ingredient available per kilogram of the formulated bait (mg ai/kg bait). An assumption is made in most OPP/EFED risk assessments that birds and nontarget mammals are likely to be exposed to the pesticide via consumption of contaminated foods. This assumption is well established for rodenticides, for which ingestion of the formulated bait is the route of exposure.

Refining the exposure assessment to establish a quantitative measure of likelihood of exposure and effects would require a much more extensive data set than registrants have submitted for their rodenticides and for the nontarget species potentially at risk. The Agency provided the preliminary risk assessment to rodenticide registrants in October, 2001 and posted it in the EDocket on EPA's website for public comments from January 29 to May 30, 2003. No additional data or relevant information to refine the exposure assessment has been provided by the registrants or other stakeholders. Nevertheless, the existence of substantial incident data along with liver-residue analysis confirms that birds and nontarget mammals are being exposed and adversely affected by applications of rodenticide baits. The fact that numerous species of birds and mammals, including predators and scavengers, have been found exposed to these baits indicates that both primary and secondary exposures are occurring.

The risk conclusions are based both on the lines of evidence of the available data and comparative analysis modeling. Each rodenticide is ranked or categorized and compared to the other rodenticides according to the following criteria: (1) overall potential risk; (2) potential

primary risk to birds; (3) potential primary risk to nontarget mammals; (4) potential secondary risk to avian predators and scavengers; and (5) potential secondary risk to mammalian predators and scavengers. Conclusions are presented below.

- Brodifacoum and difethialone stand out as the two rodenticides posing the greatest potential overall risk to birds and nontarget mammals, followed by bromadiolone and diphacinone. Zinc phosphide also ranked high for overall risk based on the comparative analysis modeling, primarily because of high potential primary risks.

- Brodifacoum, difethialone, and zinc phosphide pose the greatest potential primary risks to birds that eat bait. A single zinc phosphide or brodifacoum bait pellet provides more than an LD50 dose for a small bird. In contrast, a small bird would need to eat more than twice its body weight in bait pellets to ingest a comparable dose of a first-generation anticoagulant in a single feeding.

- Rodenticide baits are formulated to be lethal to small mammals, and they are not selective to the target species. All baits pose a high potential primary risk to nontarget mammals that eat bait. However, the first-generation anticoagulants likely pose less risk to mammals that only occasionally feed on 1 or just a few bait pellets, because they are more rapidly metabolized and generally must be eaten for several days to provide a lethal dose.

- Brodifacoum and difethialone pose the greatest potential risks to avian predators and scavengers that feed on target or nontarget animals poisoned with bait. The available data indicate that the first-generation anticoagulants are less hazardous than the more highly toxic and persistent second-generation anticoagulants.

- Mammalian predators and scavengers are at risk from feeding on animals poisoned with anticoagulant baits. Although the non-anticoagulant rodenticides appear to be much less hazardous to secondary consumers, confirmatory data are still needed to make this assumption for bromethalin and cholecalciferol baits.

- The available toxicokinetic data indicate that the second-generation anticoagulants are considerably more persistent in animal tissues than are the first-generation anticoagulants, and bioaccumulation may increase whole-body residues with repeat feedings.

- More than 300 documented wildlife incidents attest to exposure of birds and nontarget mammals, including endangered species, to some rodenticides, especially brodifacoum (244 incidents). Brodifacoum residue has been detected in liver tissue of 27 of 32 endangered kit foxes screened for rodenticide residues from 1999 to 2003. Birds in which rodenticides are most frequently detected include owls, hawks, eagles, and crows; mammals include wild canids and felids, tree squirrels, raccoons, deer, and others.

- The U. S. Fish and Wildlife Service issued a Biological Opinion in 1993 that includes reasonable and prudent alternatives and measures for protection of 29 mammalian and 11 avian threatened or endangered species potentially at risk from exposure to 8 of these rodenticides. These issues will be addressed by OPP's Endangered Species Protection Program.

- Adverse effects of possible sublethal exposure are unknown, and avian and mammalian reproduction studies are needed to establish a no-observable-adverse-effects concentration (i.e., "toxicity threshold") for each rodenticide.

A number of factors contribute uncertainty to the assessment. Those that appear to contribute the most uncertainty are: (1) missing data, including acute, chronic, and secondary toxicity as well as 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 nontarget 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 nontarget mammals frequenting baited areas and their 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 sublethal effects on reproduction and nontarget 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 sublethal exposures to bait or poisoned rodents utilized as food by predators and scavengers; and (8) lack of incident reporting.

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Potential Risks of Nine Rodenticides to
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Presented here is the Agency's assessment of rodenticide risks to birds and nontarget mammals. The 9 rodenticides include those addressed in the Reregistration Eligibility Decisions (REDs) for the Rodenticide Cluster (brodifacoum, bromadiolone, chlorophacinone, diphacinone, bromethalin; EPA 1998a), Zinc Phosphide (EPA 1998b), and Warfarin and its Sodium Salt (EPA 1991a). Difethialone and cholecalciferol, which are not subject to the current reregistration process but are alternative compounds for rat and mouse control, also are included. All 9 rodenticides are available to the public "over the counter" as grain-based food baits for control of commensal rats and mice, predominantly the Norway rat (*Rattus norvegicus*), roof rat (*R. rattus*), and house mouse (*Mus musculus*), in and around buildings, transport vehicles, and inside sewers. Some products, mostly "restricted-use" (i.e., available only to Certified Applicators) products containing zinc phosphide, chlorophacinone, or diphacinone, also are available for control of various rodent and other small mammal pests in field and other outdoor settings.

The purpose of this assessment is to evaluate potential primary and secondary risks of each rodenticide and to compare and rank them among compounds. The Agency's concern about risks to birds and nontarget mammals is based on several factors, including (1) the high acute toxicity of these rodenticide baits, which are designed to be lethal to small mammals; (2) risk estimates, based on available exposure and toxicity data, that exceed Agency levels of concern (LOCs); (3) mortality of birds and nontarget mammals exposed to rodenticide baits or poisoned prey in laboratory, pen, and field settings; (4) retention time of residues in body tissues of primary consumers, and (5) numerous reported incidents that indicate exposure of numerous nontarget species, including avian and mammalian predators and scavengers. Rodenticide baits are formulated to be lethal to rodents and a few other small mammals, and they are not selective to target species. Many factors influence which nontarget animals might be exposed to baits, but many birds and mammals are attracted to seeds and grains and are likely to consume grain-based baits. A few commensal baits also contain flavorizers such as fish, molasses/peanut butter, or apple, and some field baits are formulated with foods other than grains (ground meat, canned or dry meat-based pet foods, fruits, vegetables) that might appeal to carnivores and omnivores. Rodenticide baits also pose potential secondary risks, because predators and scavengers are likely to be attracted to dead or dying rats, mice, and poisoned nontarget animals.

Risk is a function of exposure and hazard (toxicity). Data are available to estimate toxicity based on laboratory acute-toxicity and secondary-hazard tests. Use information, such as amount of active ingredient or formulated product applied per unit area per application, is typically used to estimate nontarget organism exposure but is not available for most rodenticide uses. Therefore, exposure estimates are largely based on the amount of active ingredient available per kilogram of grain-bait formulation (mg ai/kg bait, or ppm ai). See the "*Exposure*" section under

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"*Use and Exposure Considerations*" for additional discussion of the differences in estimating expected environmental concentrations (EECs) for rodenticide food baits versus other types of pesticide applications (e.g., foliar sprays).

Risk conclusions are presented in tabular and graphical form based on two analyses of the available data. One analysis is a ranking of potential risks of each rodenticide based on a comparative analysis model. That methodology is explained in more detail in the "*Comparative analysis model*" section of the assessment and in Appendix C. The other analysis uses a lines-of-evidence approach in which the available quantitative and qualitative information is evaluated and each rodenticide assigned a rating of high, moderate, or low for primary risk to birds, primary risk to mammals, secondary risk to birds (avian predators and scavengers), and secondary risk to mammals (mammalian predators and scavengers). For primary risks, the amount of bait and number of bait pellets that need to be eaten to provide an LD50 dose (i.e., dose expected to be lethal to 50% of the individuals in a population) are calculated for 3 size classes (25 g, 100 g, 1000 g) of birds and mammals. Dietary risk quotients that compare the amount of toxicant (ppm ai) in a bait to the dietary toxicity (LC50) of the rodenticide also are used as a comparative index of primary risk. For secondary risks, these methods cannot be used, because LD50 and LC50 data are not available for predatory species of birds and mammals. Consequently, assessments of secondary risk are made based on mortality and other adverse effects reported in laboratory and field studies and operational control programs, incident reports, toxicokinetic data, and residues reported in primary consumers. This approach is in accord with EPA's risk-assessment guidelines (EPA 1998c), which assert that professional judgement or other qualitative evaluation techniques are appropriate for ranking risks into categories such as low, medium, and high when exposure and effects data are limited or are not easily expressed in quantitative terms. A lines-of-evidence approach for improving field-study interpretation also has been advocated by the Avian Effects Dialogue Group (Rymph 1994).

The information used in this assessment was obtained from studies submitted to the Agency in support of registration/reregistration, from published literature and personal communications, and from the Agency's Ecological Incident Information System (EIIS). For some rodenticides, few data are available other than acute oral (LD50) and dietary toxicity (LC50) values for the Agency's required test species: northern bobwhite (*Colinus virginianus*), mallard (*Anas platyrhynchos*), and laboratory rat (*R. norvegicus*). The quality and quantity of data available on metabolism and retention times in rodents and secondary toxicity to nontarget birds and mammals vary among the rodenticides, but the available data are sufficient to identify the most persistent and hazardous compounds.

Modes of action

The anticoagulant rodenticides are vitamin-K antagonists that disrupt normal blood-clotting mechanisms and induce capillary damage (Pelfrene 1991). Death results from hemorrhage, and exposed animals may exhibit increasing weakness prior to death. Behavior also may be affected (Cox and Smith 1992). The anticoagulants are typically grouped into "first-generation" (warfarin, chlorophacinone, diphacinone) and "second-generation" (brodifacoum, bromadiolone,

difethialone) compounds. Second-generation anticoagulants tend to be more acutely toxic than are the first-generation anticoagulants, and they are retained much longer in body tissues of primary consumers. They generally provide a lethal dose after a single feeding, although death is usually delayed 5 to 10 days and animals continue feeding. In contrast, the first-generation compounds, because they are less acutely toxic and more rapidly metabolized and/or excreted, generally must be ingested for several days to provide a dose lethal to most individuals. Diphacinone and chlorophacinone may kill some animals in a single feeding, but multiple feedings are generally needed for sufficient population control (Timm 1994). The structural relationships of these rodenticides and some of their physical/chemical properties are presented in Attachment A.

The non-anticoagulant rodenticides belong to 3 chemical classes that differ from one another and the anticoagulants in their mode of action. They can provide a lethal dose from a single feeding but are much less likely than the anticoagulants to be retained in toxicologically significant amounts in body tissues of primary consumers. Bromethalin, a diphenylamine, is a neurotoxicant that causes respiratory arrest from inadequate nerve impulse transmission after fluid build-up and demyelination inside the central nervous system (Spaulding and Spannring 1988, Hyngstrom et al. 1994). Further feeding is inhibited after ingestion of a lethal dose, and death typically occurs within 2 days. Zinc phosphide is an inorganic compound whose toxicity results from liberation of phosphine gas from reaction of the active ingredient with water and acid in the stomach (Hyngstrom et al. 1994). Death can occur within a few hours of ingestion. Cholecalciferol is a sterol (vitamin D_3). Its ingestion results in hypercalcemia from mobilization of calcium from bone matrix into blood plasma (Pelfrene 1991). Death can occur 3 to 4 days after a single feeding.

Terms and definitions

Dietary toxicity test: To support registration of a pesticide, the Agency's Office of Pesticides Program (OPP), Environmental Fate and Effects Division (EFED), requires 2 avian dietary (LC50) studies: one using northern bobwhite chicks as test animals and the other using mallard ducklings (40 CFR §158.490 Wildlife and Aquatic Organisms Data Requirements, Guideline Reference No. 71-2). The dietary test consists of a 5-day exposure period during which toxicant is added to the birds' diet at 5 concentrations using 10 test animals (5 males, 5 females) per concentration. The exposure period is followed by a 3-day observation period; however, because death is delayed for several days after exposure to an anticoagulant, the post-treatment observation period has been extended 15 days or more for those compounds. The test material is the technical grade of the active ingredient.

Dietary toxicity testing is not usually conducted for mammals, although the Agency may require a wild-mammal toxicity test (40 CFR §158.490 Wildlife and Aquatic Organisms Data Requirements, Guideline Reference No. 71-3) if deemed necessary. Because rodenticides are formulated to be lethal to mammals and the Agency requires efficacy testing for all rodenticide end-use products (40 CFR §158.640 Product Performance Data Requirements, Guideline Reference No. 96-10 and 96-12), EFED has not required a wild-mammal toxicity test for any of

the rodenticides. However, EFED has found reports for laboratory-rat dietary tests for 5 rodenticides tested by the Agency's former Toxicology Unit, Chemical and Biological Investigations Branch. During 1980 and 1981, McCann et al (1981) developed a short-term dietary LC50 test for small mammals. They exposed 5-male and 5-female immature albino Norway rats (Wistar strain) per test concentration to dry diet offered *ad libitum* and treated with one of 17 chemicals pesticides, mostly organophosphate and carbamate pesticides. The tests consisted of a 5-day acclimation period, a 5-day exposure period, and a post-treatment observation period lasting at least 9 days. Following submission of the paper for publication, testing continued and included 5 rodenticides: brodifacoum, bromadialone, chlorphacinone, diphacinone, and warfarin. Results of these tests were not published but the test reports are available, and multiple studies exist for each of those 5 rodenticides.

LC50: Median lethal concentration. A statistically estimated dietary concentration expected to be lethal to 50% of the test animals. The LC50 is expressed in ppm. The 95% confidence intervals are reported when available.

Acute oral toxicity test: For individual pesticides, EFED requires one acute oral (LD50) test for birds, using either the northern bobwhite or the mallard as the test species (40 CFR §158.490 Wildlife and Aquatic Organisms Data Requirements, Guideline Reference No. 71-1). Data are available for both species for some rodenticides. The toxicant is orally administered via capsule or gavage in a single dose to adult animals. The test required by the Agency includes 5 concentrations, with 10 test animals (5 males, 5 females) per concentration. Unless otherwise noted, the test material is the technical grade of the active ingredient. OPP's Health Effects Division (HED) also requires acute oral testing with the laboratory rat (40 CFR §158.340 Toxicology Data Requirements, Guideline Reference No. 81-1) and sometimes has data for other mammals (e.g., laboratory mouse, dog). EFED uses these data in the mammalian risk assessment.

LD50: Median lethal dose. A statistically estimated oral dose expected to be lethal to 50% of the test animals. The LD50 is expressed in mg of active ingredient per kg of body weight of animal. The 95% confidence intervals are reported when available.

> *Note:* Some LD50 values for birds and mammals were obtained from the literature. These are considered supplemental data, because the test concentrations, number of animals tested, and confidence intervals often are not reported or may not meet Agency test guideline requirements. Calculations of risk quotients and estimates of ingestion of active ingredient from bait consumption utilize the toxicity data reviewed and accepted by the Agency.

Primary Risk: Risk to target or nontarget organisms that consume bait.

Secondary Risk: Risk to predatory or scavenging birds or mammals that feed on target or nontarget animals that ate bait.

Dietary Risk Quotient (RQ): An index of exposure to dietary toxicity (LC50), where exposure is expressed as the amount of rodenticide in food (ppm ai in bait for primary exposure or in target species for secondary exposure). Risk presumptions are based on whether or not RQs exceed OPP's Levels of Concern. RQs do not quantify risk, but they are useful for comparing risks among alternative compounds (ECOFRAM 1999).

Level of Concern (LOC): A presumption of risk is made if an RQ equals or exceeds the Agency's LOCs: 0.5 for acute risk to non-endangered species and 0.1 for acute risk to endangered species. Additionally, an RQ that equals or exceeds 0.2 triggers consideration of "restricted-use" classification to mitigate acute risk.

*A note on scientific names***:** The scientific name of a species is provided after the first mention of its common name in the text. A complete list of common and scientific names of the birds and mammals referred to in the document is included in Attachment B.

Comparative analysis model

A comparative analysis model also is used to rank and compare potential primary and secondary risks. The underlying methodology is a simple multi-attribute rating technique, or SMART (Goodwin and Wright 1998). SMART is adapted for comparing potential risks among rodenticides based on a number of measure-of-effect values for primary and secondary risk to birds and mammals. Each type of risk is quantitatively evaluated by the following measures of effect:

Primary risk to birds:	dietary RQ (mean value if more than one dietary RQ available); inverse of the number of bait pellets needed for a 100-g bird to ingest an LD50 dose in a single feeding
Primary risk to mammals:	inverse of the number of bait pellets needed for a 100-g mammal to ingest an LD50 dose in a single feeding
Secondary risk to birds:	mean % mortality from secondary toxicity studies; retention time (days) of active ingredient in the blood; retention time (days) of active ingredient in the liver
Secondary risk to mammals:	mean % mortality from secondary toxicity studies; retention time (days) of active ingredient in the blood; retention time (days) of active ingredient in the liver

Retention time is not a direct measure of effect for secondary risk to birds and mammals, but it is an important contributing factor. The combination of mean % mortality from secondary laboratory toxicity studies, which characterizes the secondary toxicity from short-term exposures, and available data on retention time in both blood and liver, which indicates how long

toxic levels can persist in target animal tissues, can characterize the secondary risk to birds and mammals.

When faced with a number of alternatives and a number of types of risk with measures of effect, SMART prescribes the following: (1) each alternative rodenticide is rated on each measure of effect; (2) each measure of effect is assigned a measure of importance to the risk assessor; and (3) a summary score for each alternative rodenticide is calculated as a weighted average of the ratings, where the weights represent the relative importance of the measure of effect for each type of risk. The higher the resultant summary score, the higher the potential risk for that rodenticide.

The following basic equation is used to calculate the summary values for the risk comparison:

$$\text{Summary Value}_{(\text{scale from 0 to 10})} = 3 \; f(\text{ME}_i)(\text{ME}_{max})^{-1} \, _{,,} \, f(\text{Weight}) \, (3 \, \text{Weights})^{-1} \, _{,,} \, (10)$$

where "ME_i" is the measure of effect value for a rodenticide and "ME_{max}" is the maximum ME for all rodenticides; "Weight" is the importance value, from 10 to 0, placed on each measure of effect, with high = 10 to 6.67, medium = 6.68 to 3.33, and low = 3.34 to 0; "3 Weights" is the sum of all the weights for all the measures of effect. All measures of effect, except two, are assigned a "high" (10 out of 10) measure of importance for the rodenticide analysis. The half-life in blood and liver are each given a weight of "low" (2.5 out of 10) for analyzing secondary risks to birds and mammals, so that the overall importance of the persistence data (2.5 x 4=10) equals but does not exceed that of the mortality data.

A sensitivity analysis also is performed to evaluate how changes in each measure-of-effect value could affect the overall summary risk results. Each measure-of-effect value is separately decreased and increased by 50% (154 variations). To further examine the robustness of the rankings, selected high and low summary risk values are subsequently changed by up to $\pm 99\%$. Further details of the SMART analysis, including the input values for measures of effects, are presented in Attachment C.

The methodology used in the comparative analysis model is similar to that used in the Agency's "Comparative Analysis of Acute Risk From Granular Pesticides" (EPA 1992) and "A Comparative Analysis of Ecological Risks from Pesticides and Their Use: Background, Methodology, Case Study" (EPA 1998d); both were reviewed by a FIFRA Scientific Review Panel. Concerning the latter analysis, the Panel noted the many scientific uncertainties in the method, yet agreed that it was a useful screening tool that provides an estimate of relative risk. The Panel made a number of helpful suggestions to improve the utility of the method, most of which are included here. In this analysis, a risk quotient (RQ), calculated as the ratio of toxicant potentially ingested to the inherent toxicity of the rodenticide, is used to compare potential primary risks to birds and nontarget mammals. RQs are compared among rodenticide baits based on the amount of bait and number of bait pellets that birds or nontarget mammals of various sizes would need to eat to ingest an acute oral (LD50) dose. Dietary data (LC50) also are available, and RQs based on bait concentration and avian dietary toxicity are compared

among the rodenticides. As noted by the Ecological Committee on FIFRA Risk Assessment Methods (ECOFRAM 1999), RQs do not quantify risk but are useful for comparisons among alternative compounds. EPA's "Guidelines for Ecological Risk Assessment" (EPA/630/R-95/002F, 1998c) also notes that quotients provide an efficient, inexpensive means of identifying high- or low-risk situations that can allow risk management decisions to be made without the need for further information.

Use and Exposure Considerations

This assessment focuses on the potential primary and secondary risks to birds and nontarget mammals posed by applications of these 9 rodenticides to control rats and mice in and around buildings (commensal uses) and elsewhere outdoors (field uses) to control rodents and certain other mammalian pests. As previously noted, rodenticide products for field use (except those for underground baiting of pocket gophers and moles) are currently registered as "restricted-use" or restricted-use classification is being imposed during reregistration. This classification provides increased protection of birds and nontarget mammals, because baits may only be applied by a Certified Applicator or someone directly supervised by a Certified Applicator. These applicators are trained to closely follow label use directions and restrictions that may help limit exposure, and thus risk, to nontarget organisms. However, even with this increased protection, there remains a potential risk to nontarget organisms from these uses since the rodenticides are lethal to birds and mammals, are not selective, and their grain-based bait formulations may be highly attractive to many nontarget organisms.

Product labels for commensal uses specify that applicators should comply with the following *DIRECTIONS FOR USE*:

> "Apply bait in locations out of reach of children, pets, domestic animals and nontarget wildlife, or in tamper-resistant bait stations. These stations must be resistant to destruction by dogs and by children under 6 years of age, and must be used in a manner that prevents such children from reaching into bait compartments and obtaining bait. If bait can be shaken from stations when they are lifted, units must be secured or otherwise immobilized. Even stronger bait stations are needed in areas open to hoofed livestock, raccoons, bears, or other potentially destructive animals, or in areas prone to vandalism."

To what extent applicators comply with these use directions or even use bait stations is unclear. As noted in Pesticide Regulation (PR) Notice 94-7 (EPA 1994), "Nonprofessional users (i.e., the "general public") often apply baits in open containers or in ready-to-use, non-protective, packaging. Bait stations typically are not offered for sale at the outlets where nonprofessional users buy rodenticides. Attempts to market ready-to-use (bait-filled) protective rodenticide bait stations to the general public have not been reported as commercially successful ventures." Tamper-resistant or stronger bait stations exclude mammals larger than adults of the target species, because the entrance holes to the bait compartment are designed to be no larger than necessary. However, mammals smaller than the target species can enter bait stations and feed on bait and are at risk. Because target species leave bait stations after feeding, bait stations likely

have little if any impact on secondary exposure of predators and scavengers that feed on dead or dying rodents.

The commensal use in and around buildings is common to all 9 rodenticides. However, difethialone and bromadiolone can be applied only inside of buildings and similar manmade structures in non-urban areas. Indoor applications likely reduce primary exposure of nontarget organisms. Nevertheless, rats or mice that eat bait, especially an anticoagulant bait, do not die for several days after ingesting a lethal dose. Because these target species may move outdoors before dying, some predators and scavengers might still be exposed as a result of indoor application.

Field uses involve a variety of bait applications, including broadcasting, spot-baiting, or application of bait in some type of bait station. Depending on the use, broadcasting is done by hand, ground-based mechanical spreader, or by air. Some, but not all, broadcast applications limit the number of treatments that can be made and specify an interval between applications. Some uses also allow spot baiting, in which bait is placed by hand in small pile or scattered across smaller areas (e.g., bare ground around burrow openings) at a treatment site. Bait stations should be covered or enclosed. For some uses an uninterrupted supply of bait is maintained for 1 to 4 weeks, whereas for others no time interval is specified. Bait stations are usually placed on the ground in areas frequented by the target species, such as by burrow openings, runways, or feeding areas. Floating bait stations are used for some target species (e.g., muskrats). In some situations, customized bait stations have been developed to exclude nontarget species that are smaller than individuals of the target species. Elevated and "T" bait stations have been developed to reduce exposure of some nontarget species, such as deer mice (Erickson et al. 1990) and kangaroo rats (California Department of Pesticide Regulations
http://www.cdpr.ca.gov/docs/es/espdfs/baitsta1.pdf
http://www.cdpr.ca.gov/docs/es/espdfs/baitsta2.pdf).
More research is warranted to devise means of selectively applying baits to protect nontarget species while adequately maintaining efficacy against target species.

For control of pocket gophers and moles in lawns, golf courses, and other noncrop areas, bait is applied in subsurface runways or deeper underground tunnels and is not exposed on the ground surface. Hand baiting is done using a mechanical probe or similar device to locate an underground runway. Bait is inserted through the probe hole, and the hole is then sealed with sod or a stone. In some situations a mechanical burrow-builder is used by a Certified Applicator to construct artificial pocket-gopher burrows into which bait is mechanically inserted at 4- to 5-foot intervals.

Exposure

Exposure is an integral component of ecological risk. Many factors influence which nontarget animals might be exposed to rodenticide baits. They include the species found in and around treatment areas, species' food habits and foraging behavior, home range, propensity to feed in and near human buildings, bait availability (e.g., quantity, how applied, where applied, when applied), and other such factors. However, there is no doubt that many birds and nontarget mammals are attracted to and will consume grain-based foods. Additionally, many nontarget predators and scavengers feed on rats, mice or other target species. They are not likely to avoid feeding on rats, mice, voles, ground squirrels, or other animals that have eaten bait.

EFED's exposure assessment for the rodenticides differs from that for most other pesticides. For foliar-applied pesticides, EECs on potential food items (grasses, seeds, insects) of birds and mammals are extrapolated from field-residue data compiled by Hoerger and Kenaga (1972) as modified by Fletcher et al. (1994). The maximum EEC on avian and mammalian food items is 240 ppm on short grass, 135 ppm on broadleaf plants and insects, and 15 ppm on seeds for every 1.0 lb ai applied per acre. EECs for granular formulations or soil-applied sprays are typically based on the number of LD50s applied per square foot. For each specific crop or use site, EECs depend on the label-specified application rate (lb ai/acre), number of applications, interval between applications, and the application method. However, 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 the EEC. This information is used to estimate the amount of bait and number of bait pellets that birds and mammals of various sizes need to consume in a single feeding to obtain a dose expected to be lethal to 50% of the individuals in the population (i.e., LD50 dose). Estimates of food-ingestion rates (g dry matter per day) were determined from established allometric equations presented in EPA's Wildlife Exposure Factors Handbook (EPA 1993). The concentrations of active ingredient in the bait pellets are also used to estimate initial dietary exposure (mg ai per kg in bait) used to calculate avian and mammalian dietary risk quotients.

These estimates of acute primary exposure of nontarget organisms are not appropriate for estimates of secondary exposure. Secondary exposure estimates are considerably more complex and require consideration of residues in tissues of target organisms that are commonly consumed by predators and scavengers, as well as knowledge of what residue level will result in mortality or adverse chronic effects. Moreover, it is important to know how long the residue persists in body tissues. A number of laboratory tests using avian and mammalian predators or scavengers are available to assess mortality from secondary exposure resulting from consumption of prey animals that had been exposed to rodenticides. Design and methodology vary among studies, adding unknown variability to the results and analysis. Pending development of standard methods and testing requirements for such studies, these tests provide the best data available. The mean percent (%) mortality for these bird and mammal laboratory tests are used to estimate both secondary exposure and hazard. Because retention time in tissues consumed by scavengers and predators is an important factor in estimating secondary exposure and potential risk, available retention times (half-life in days) of rodenticide in liver and blood are also factored into secondary exposure and risk estimates. A discussion of residue levels in tissues of target species

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is included in the assessment. Uncertainties remain in establishing levels indicative of mortality or other adverse effects in nontarget organisms.

In most pesticide assessments the assumption is made that nontarget birds and mammals are likely to be exposed to the pesticide without attempting to establish a quantitative measure of this likelihood. This assumption is used in this assessment for these 9 rodenticides and 11 bait formulations. The existence of substantial incident data along with liver residues corroborates the assumption that nontarget birds and mammals are exposed and adversely affected by the use these rodenticide baits. The fact that numerous species have been found exposed to these rodenticide formulations, including predators and scavengers, indicates that both primary and secondary exposure occurs.

Target species, use sites, and rodenticide usage

Control of commensal rats and mice is the predominant use of most of the rodenticides. Most products for rat and mouse control are formulated as grain-based pellets or, for sewer use, as paraffinized food blocks. Several rodenticides also are registered for field and other outdoor uses (Table 1). Zinc phosphide is used to control ground squirrels (*Spermophilus* spp.), prairie dogs (*Cynomys* spp.), pocket gophers (Geomyidae), and moles (Talpidae) in addition to commensal rats and mice. Most are pellets or grain baits, but meat (ground meat, canned dog or cat food, dry meat-based pet food), sunflower seed, and fruit or vegetable (carrots, sweet potatoes, dandelions, alfalfa, beet tops, cabbage, potatoes, grapes, mulberry, apricots, figs, nuts, apples, pears) baits also are used against some target species. Nine states also have individual state registrations (FIFRA §24c Special Local Need [SLN]) for using zinc phosphide to control a variety of localized rodent (e.g., voles, tree squirrels, kangaroo and other rats, deer mice, muskrats, nutria) and jackrabbit pests. Brodifacoum and bromethalin are or have been used under emergency exemptions (FIFRA §18) to control introduced rats on U. S. islands in the Pacific Ocean. Twenty-three states have SLNs for chlorophacinone and/or diphacinone, mostly to control meadow voles (*M. pennsylvanicus*) and/or pine voles (*M. pinetorum*) in orchards or ground squirrels in rangeland or other uncultivated areas. Other limited uses include control of mongooses (*Herpestes auropunctatus*) in Hawaii, voles in small-grain crops in Washington, and a variety of other rodent pests and jack rabbits (*Lepus* spp.) in California. New Mexico uses cholecalciferol to control rock squirrels (*Spermophilus variegatus*).

Table 1. Commensal and Field Uses of Rodenticides in the United States (adapted from EPA 1998a,b)

Rodenticide	Date ai registered	Commensal uses	Field and other outdoor uses	mg ai/kg bait (ppm)
Second-generation anticoagulants				
Brodifacoum	1979	Rat and mouse control in and around buildings, transport vehicles, and inside sewers	Restricted-use applications for rat control on some oceanic islands (FIFRA §24c Special Local Needs [SLN] or FIFRA §18 emergency exemption)	50 25 (Anacapa Island, CA)
Difethialone	1995	Rat and mouse control in and around buildings in urban areas; limited to indoor use in non-urban areas	None	25
Bromadiolone	1980	Rat and mouse control in and around buildings, transport vehicles, and inside sewers in urban areas; limited to indoor use in non-urban areas	None	50
First-generation anticoagulants				
Chlorophacinone	1971	Rat and mouse control in and around buildings and inside sewers	Control of pocket gophers and moles in underground burrows; SLNs for control of pine and/or meadow voles in orchards (17 states), ground squirrels in rangeland and around burrows (8 states), jack rabbits (CA, OR), and a variety of other field rodents (e.g., deer mice, woodrats, muskrats) in CA	50 100 (some field uses) other[a]

Rodenticide	Date ai registered	Commensal uses	Field and other outdoor uses	mg ai/kg bait (ppm)
Diphacinone	1960	Rat and mouse control in and around buildings and inside sewers	Control of pocket gophers in underground burrows; SLNs for control of pine and/or meadow voles in orchards (16 states), ground squirrels in rangeland and around burrows (6 states), a variety of other field rodents (e.g., deer mice, woodrats, muskrats) and jack rabbits in CA, various field rodents in several other states, rat control on oceanic islands (HI, AK), and mongoose control (HI)	50 100 (some field uses) other[a,b]
Warfarin	1950	Rat and mouse control in and around buildings	Deer mouse and white-footed mouse control in and around buildings and in bait stations in other areas such as parks and woodlots	250 other[b]
Others (non-anticoagulants)				
Bromethalin	1984	Rat and mouse control in and around buildings, transport vehicles, and inside sewers	Restricted-use application for rat control on an oceanic island (emergency exemption)	100
Zinc phosphide	1940s	Rat and mouse control in and around buildings[a]	For control of a wide variety of field rodents (e.g., ground squirrels, prairie dogs, voles, rats, kangaroo rats, deer mice, moles, pocket gophers) in various sties, including rangeland, uncultivated areas, orchards, turf, forage, sugarcane, and other sites; 9 states also have SLNs for use against various rodents at local use sites	20,000 10,000 (CA only)
Cholecalciferol	1984	Rat and mouse control in and around buildings and inside transport vehicles	SLNs for control of rock squirrels (NM); also roof rats on an oceanic island (CA)	750

[a] chlorophacinone (0.2% ai), diphacinone (0.2% ai), and zinc phosphide (10% ai) tracking powders are registered for indoor use and inside burrows along building foundations; all are restricted-use products
[b] sodium salts of diphacinone and warfarin are registered for use in water baits for indoor use only

Adequate information quantifying usage of rodenticide baits is lacking. EPA obtains data on the amount of each product produced annually, and the Rodenticide Registrants Task Force (RRTF) provided some limited information on the pounds of active ingredient produced or imported in 1996 and 1997 for 4 of the 9 rodenticides (Kaukeinen et al. 2000). However, these data provide no information on when, where, or how the products are used and thus provide little relevant information for assessing exposure and risk. The RRTF data are difficult to interpret, because they lump containers and placement units, even though containers differ, often considerably, from placement units. A placement for commensal rodents is defined on product labels as 3 to 16 oz of bait for rats and 0.25 to 0.5 oz of bait for mice. In contrast, containers can hold anywhere from several to many individual rat or mouse placements. The problem with lumping these units together is illustrated in Table 2. Both brodifacoum and bromadiolone, for example, are formulated as 0.005% ai food baits solely for commensal rat and mouse control. The data for 1996 indicate that 395 lb ai of brodifacoum was formulated into more than 40 million "container/placement units" (i.e., 3 oz bait per container/placement unit), whereas 233 lb ai of bromadiolone was formulated into few more than 275,000 container/placement units (i.e., 271 oz bait per container/placement unit). Such differences also occur for 1997 and for chlorophacinone and diphacinone. Refining the exposure assessment would necessitate much better information for each rodenticide, including the amount of bait applied annually and seasonally; geographically by state or region; in field settings versus in and around buildings; in urban versus suburban and rural locales; indoor versus outdoor placements; applications for rats versus those for mice; use by the general public versus that by Certified Applicators; proportion of bait placements made in tamper-resistant bait stations; and, for chlorophacinone and diphacinone, use of 0.005% versus 0.01% ai baits.

Table 2. Amount of Bait and Number of "Container/Placement Units" For Four Anticoagulant Rodenticides in 1996 and 1997 (adapted from Kaukeinen et al. 2000). Information was not provided for difethialone, warfarin, or the non-anticoagulants.

Anticoagulant[a]	Year	lb ai[b]	oz bait[c]	no. containers/ placement units[b]	oz bait per container/ placement unit
Brodifacoum	1996	395	126,400,000	40,895,724	3
	1997	441	141,120,000	44,144,456	3
Bromadiolone	1996	233	74,560,000	275,376	271
	1997	164	52,480,000	294,706	178
Diphacinone	1996	486	155,520,000	1,551,161	100
	1997	608	194,560,000	2,860,419	68
Chlorophacinone	1996	1608	514,560,000	21,552	23,875
	1997	2677	856,640,000	18,360	46,658

[a] brodifacoum and bromadiolone are registered only for control of commensal rats and mice; diphacinone and chlorophacinone are registered for commensal rats and mice and are also used for control of field rodents in rangelands, orchards, and other settings
[b] data from Kaukeinen et al. 2000
[c] based on 0.005% ai food baits

Primary-hazards Data

Birds

Acute-oral and dietary toxicity: The available acute-oral and dietary toxicity data for birds are presented in Tables 3, 4, and 5. LC50 values for the northern bobwhite and mallard, required test species for EPA/OPP avian guideline studies, are used in calculating dietary RQs. The bobwhite or mallard LD50 also is used to calculate the amount of bait and number of rat-bait pellets that birds of various sizes need to eat to ingest a dose lethal to 50% of the individuals in the population. Some toxicity data also are available for other species for some rodenticides. Most of those values (e.g., Godfrey 1986) were determined using fewer test concentrations and fewer test animals per concentration than are required for EPA guideline studies. EFED considers these values as supplemental data that provide additional characterization of avian toxicity.

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Table 3. Acute Oral and Dietary Toxicity of Second-generation Anticoagulants to Birds

Rodenticide/ Species	LD50, mg/kg (95% CI)	LC50, ppm (95% CI)	Reference
Brodifacoum			
Northern bobwhite		0.8 (0.1-4.7)	EPA 1998a
Mallard	0.26 (0-0.8)	2.0 (0.8-4.8)	EPA 1998a
Laughing gull		0.7	ICI 1979a
Laughing gull		1.6 (0.8-3.3)	ICI 1979b
Canada goose	<0.75[a]		Godfrey 1986
Black-backed gull	<0.75[a]		Godfrey 1986
Purple gallinule	0.95		Godfrey 1986
California quail	3.3		Godfrey 1986
Mallard	4.6		Godfrey 1986
Black-billed gull	<5[a]		Godfrey 1986
Ring-necked pheasant	10		Godfrey 1986
Australasian harrier	10		Godfrey 1986
Blackbird	>3[b]		Godfrey 1986
Hedge sparrow	>3[b]		Godfrey 1986
House sparrow	>6[b]		Godfrey 1986
Difethialone			
Northern bobwhite	0.26 (0.17-0.40)	0.56 (0.16-1.91)	EFED[c]
Mallard		1.4 (0.7-5.1)	EFED[c]
Bromadiolone			
Mallard		158 (7-762)	EPA 1998a
Mallard		440 (229-847)	EPA 1998a
Northern bobwhite	138 (81-235)	37.6 (9-85)	EPA 1998a
Northern bobwhite	170 (115-261)		EPA 1998a

[a] the lowest concentration tested
[b] the highest concentration tested
[c] OPP/EFED Toxicity Database

Table 4. Acute Oral and Dietary Toxicity of First-generation Anticoagulants to Birds

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	LC50, ppm (95% CI)	Reference
Chlorophacinone			
Mallard		172 (75-498)	EPA 1998a
Northern bobwhite	258 (167-356)	56 (22-105)	EPA 1998a
Ring-necked pheasant	>100		Clark 1994
Red-winged blackbird	430		Clark 1994
Diphacinone			
Mallard	3158 (1605-6211)	906 (187-35,107)	EPA 1998a
Northern bobwhite	400 < LD50 <2000	>5000	EPA 1998a
Warfarin			
Mallard	620	890 (480-1649)	EFED[a]
Northern bobwhite	>2150	625 (300-1303)	EFED[a]
Chicken (domestic)	942		Bai and Krishnakumari 1986

[a] OPP/EFED Toxicity Database

Table 5. Acute Oral and Dietary Toxicity of non-Anticoagulant Rodenticides to Birds

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	LC50, ppm (95% CI)	Reference
Bromethalin			
Northern bobwhite	4.6 (3.6-5.8)	210 (150-280)	EPA 1998a
Northern bobwhite	11.0 (9.3-13.1)		EPA 1998a
Mallard		620 (460-820)	EPA 1998a
Chicken (domestic)	8.3		HED[a]
Zinc phosphide			
Northern bobwhite	12.9 (12.0-13.9)	469 (356-546)	EPA 1998b
Mallard	35.7 (11.8-108)	1285 (1026-1620)	EFED[b]
Mallard	67.4 (56.3-80.9)	2885 (1970-4329)	EPA 1998b
Mallard	13		CDFG 1962[c]
White-fronted goose	7.5		CDFG 1962[c]
Snow goose	8.8		CDFG 1962[c]
Ring-necked pheasant	8.8		CDFG 1962[c]
Canada goose	12.0		CDFG 1962[c]
California quail	13.5		CDFG 1962[c]
Gray partridge	26.7		Janda and Bosseova 1970
Ring-necked pheasant	26.7		Janda and Bosseova 1970
Red-winged blackbird	23.7		Clark 1994
Mourning dove	34.3		CDFG 1962[c]
Horned lark	47.2		EFED[b]
Golden eagle	>20		EFED[b]
Cholecalciferol			
Northern bobwhite		528[d]	EFED[b]
Mallard	>600[d]	1190[d]	EFED[b]

[a] OPP/HED Toxicity Database
[b] OPP/EFED Toxicity Database
[c] cited in Johnson and Fagerstone 1994
[d] values for cholecalciferol have been adjusted, based on the purity of test material (30% ai); reported values for the 30% ai test material are LD50 >2000 mg/kg; northern bobwhite LC50 = 1744 (1233-2516); and mallard LC50 = 3926 (2631-9890)

Feeding studies: Several studies are available that provide additional information for characterizing hazards of rodenticide baits fed to birds. Some of these provide useful comparative information among different rodenticides tested under the same test protocol. For example, Lund (1981) fed 0.005% ai brodifacoum, 0.005% ai bromadiolone, and 0.025% ai warfarin baits to adult leghorn chickens (*Gallus gallus*). Two anticoagulants (coumatetralyl and difenacoum) not registered in the U. S. also were tested. Four hens per anticoagulant were individually presented with a choice of bait or untreated chicken food for up to 15 days; survivors were observed for an additional 2 weeks. All 4 hens fed brodifacoum bait died within 6 to 12 days (Table 6). Bromadiolone bait resulted in the deaths of 2 of 4 hens. No deaths or signs of toxicity occurred in 3 hens that ate warfarin bait (1 other hen refused to eat bait).

Christopher et al. (1984) also examined the hazards of several anticoagulant baits to 3-week-old leghorn chickens. Brodifacoum bait (0.005% ai) was given to 4 groups (6 chicks per group) on alternate days for 1, 2, 3, or 4 feedings. Bromadiolone bait (0.005% ai) was presented to 3 groups (6 chicks per group) on alternate days for 1, 2, or 3 feedings. Warfarin bait (0.025% ai) was fed to 2 groups (6 chicks per group) for either 3 or 21 consecutive days. Results are comparable to those reported by Lund (1981). Twelve (50%) of the 24 birds fed brodifacoum bait died (Table 7), whereas all birds survived after feeding on bromadiolone bait (18 birds) or warfarin bait (12 birds).

Two other studies provide additional information help on the hazard of brodifacoum bait to birds. Ross et al. (1979a,b) exposed 10 northern bobwhites and 10 ring-necked pheasants (*Phasianus colchicus*) to 0.005% brodifacoum pellets for 14 days. Six bobwhite and 6 pheasants died after feeding ad lib. on a choice of pellets or untreated food. ICI Americas, Inc. (1981) also reported deaths of several pheasants exposed to 50 ppm brodifacoum pellets broadcast in a pen study.

Two laboratory studies provide supplemental data on the primary hazard of warfarin to birds. Crabtree and Robison (1952) maintained chukar (*Alectoris chukar*) on a diet of warfarin bait for 30 consecutive days with no deaths. Jones and Townsend (1978; cited in Townsend et al.1981) reported no mortality of Japanese quail (*Coturnix coturnix*) fed 8 mg ai/kg/day of warfarin for 14 days.

Johnson and Fagerstone (1994) reviewed primary hazard information for zinc phosphide. They indicate that some birds are repelled by zinc phosphide and others may regurgitate bait. Spotted doves (*Streptopelia chinensis*), for example, reportedly regurgitated treated seeds about 1 hour after ingestion (Hilton et al. 1972, Pank et al. 1972). However, some laughing doves (*Streptopelia senegalensis*) died about 2 hours after eating treated bait, even though they had regurgitated bait about 20 minutes after ingestion (Siegfried 1968). In another study, 14 of 15 red-winged blackbirds (*Agelaius phoeniceus*) died after feeding for 48 hours on a 1:1 mixture of treated (2% ai) and untreated cracked corn (Schafer et al. 1970).

Table 6. Adverse Effects of Five Anticoagulant Baits Fed to Adult Leghorn Chickens for up to 15 Days (adapted from Lund 1981)

Anticoagulant	Avg. intake per bird[a]		Mortality	Adverse effects
	bait (g)	ai (mg/kg)		
Brodifacoum (0.005% ai)	362 (252-443)	10.5 (7.1-15.0)	4/4	death from day 6
Bromadiolone (0.005% ai)	496 (329-684)	12 (5.9-16.9)	2/4	loss of appetite; hemorrhage from day 6
Warfarin (0.025% ai)	922 (584-1232)	149 (132-171)	0/3	none
Coumatetralyl[b] (0.03% ai)	594 (313-820)	107 (79-137)	2/4	loss of appetite from day 8; hemorrhage
Difenacoum[b] (0.005% ai)	611 (458-835)	19 (13.5-28.3)	2/4	loss of appetite; hemorrhage from day 5

[a] range is given in parenthesis
[b] coumatetralyl and difenacoum are not registered in the U. S.

Table 7. Adverse Effects of Three Anticoagulant Baits Fed to 3-week-old Leghorn Chickens for 1 to 21 Days (adapted from Christopher et al. 1984)

Anticoagulant	No. feedings[a]	Avg. bait intake (g)	mg ai/kg	Mortality	Adverse effects
Brodifacoum (0.005% ai)	1	15.5	11.0	1/6	1 death on day 4;1 bird sick on day 12 but recovered
	2	30.0	21.0	1/6	1 death on day 7;1 bird sick on day 6 but recovered
	3	42.8	28.9	5/6	mortality from days 7-16; 1 bird sick on day 5 (sporadic bleeding) had not recovered by end of test (day 21)
	4	43.8	20.9	5/6	mortality from days 5-15; 1 bird sick on day 4 (sporadic bleeding) had not recovered by end of test (day 21)
Bromadiolone (0.005% ai)	1	13.2	12.1	0/6	none
	2	29.5	22.1	0/6	1 bird sick on day 17 but recovered
	3	13.2	36.9	0/6	1 bird sick on day 16 did not recover by end of test (day 21)
Warfarin (0.025% ai)	3	49.4	183.7	0/6	none
	21	305.3	1092.2	0/6	bleeding in 1 bird on days 12-16 but survived

[a] brodifacoum and bromadiolone baits were offered ad lib. on alternate days; warfarin bait was fed ad lib. for either 3 or 21 consecutive days

Other studies indicate that zinc phosphide bait poses a hazard to some birds, although some species may be less susceptible than others. Janda and Bosseova (1970) reported deaths of gray partridges that consumed as few as 6 to 9 treated (2.5% ai) wheat kernels, and ring-necked pheasants died after consuming as few as 18 to 25 kernels. The California Department of Fish and Game (CDFA 1962) reports that about 260 to 310 treated zinc phosphide grains (1% ai) provides an LD50 dose for geese, and a 5-lb goose is capable of ingesting as many as 6400 kernels in one feeding (Keith and O'Neill unpubl.; cited in Johnson and Fagerstone 1994). Ramey et al. (1994) exposed ring-necked pheasants and California quail (*Callipepla californica*) to 2% zinc phosphide bait in 0.2-ha alfalfa enclosures. Based on necropsy results, 16 (62%) of 26 pheasants died from consuming bait. None of the 26 California quail died. Glahn and Lamper (1983) exposed 12 Canada geese (*Branta canadensis*) and 12 white-fronted geese (*Anser albifrons*) to 1% zinc phosphide bait applied in hay cover crops in California. The geese, held in portable enclosures that were moved daily, were allowed to feed for 4 days. Four (33%) Canada geese died. All white-fronted geese survived, which the authors attributed to their developing an aversion to bait after ingesting sublethal doses during the first 2 days of exposure.

Avian reproduction/sublethal effects: No guideline data are currently available for any of the rodenticides. OPP will be requiring avian reproduction tests with the mallard and northern bobwhite to fulfill this guideline requirement (40 CFR §158.490 Wildlife and Aquatic Organisms Data Requirements, Guideline Reference No. 71-4). EFED notes that there is a published abstract reporting the deaths of 2 turkey vulture (*Cathartes aura*) offspring that were fed brodifacoum-poisoned mice by their parents (Borst et al. 2000). The possibility exists that young animals may be more susceptible to rodenticide poisoning than are adults (see also the section on "*Mammalian reproduction/sublethal effects*"). EFED will assess the potential for adverse reproductive and chronic effects when the guideline studies become available.

Mammals

Acute-oral and dietary toxicity: The available acute-oral and dietary toxicity data for mammals are presented in Tables 8, 9, and 10. Laboratory-rat or mouse LD50 values are used to calculate the amount of formulated bait and number of bait pellets that nontarget mammals of various sizes need to eat to ingest a dose lethal to 50% of the individuals in the population. Data for other species provide additional characterization of mammalian toxicity and indicate that rodenticides are not selective for the target species. Some dietary data also are available for the laboratory rat for 5 of the anticoagulants, and these data are used to calculate dietary RQs. Additionally, as previously noted, all registered rodenticide products have been tested under Agency guideline requirements and proven efficacious in killing target species.

Warfarin toxicity values deserve special mention. LD50 values for the laboratory rat vary markedly among warfarin studies in the EPA/EFED toxicity database, ranging from 2.5 to 680 mg/kg. Jackson and Ashton (1992) cite values ranging from 14 to 186 mg/kg and Hone and Mulligan (1982; cited in Buckle 1994) values from 1.5 to 323 mg/kg. According to Meehan (1984; cited in Buckle 1994), the most reliable estimates now place the LD50 for the Norway rat as somewhere between 10 and 20 mg/kg. Discrepancies might exist due to difference in strain

and gender of the rats and in the carrier used to administer the dose. Poché and Mach (2001) also suggest that the degradation rate of warfarin in the gastrointestinal tract (GIT) of rats probably depends on the variation of bacterial species present and their abundance.

Table 8. Acute Oral Toxicity of Second-generation Anticoagulants to Mammals

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	LC50, ppm (95% CI)	Reference
Brodifacoum			
Laboratory rat		0.53 (0.45-0.68) 0.55 (0.45-0.68) 0.55 (0.45-0.68) 0.57 (0.53-0.61) 0.85 (0.67-1.06)	EPA unpublished data[a]
Laboratory rat	0.41♀(0.35-0.50) 0.56♂ (0.47-0.66)		EPA 1998a
Rat	0.39		HED[b]
Mouse	0.4		HED[b]
Vole	0.2 (0.11-0.32)	1.4 (0.77-2.0)	HED[b]
Richardson's ground squirrel	0.13 (0.06-0.19)		Baril and Pallister 1981[c]
Possum	0.17		Godfrey 1985
Pine vole	0.36 (0.22-0.59)		Byers 1978
Meadow vole	0.72 (0.53-0.98)		Byers 1978
Dog	0.25-1.0		HED[b]
Rabbit	0.29		HED[b]
Pig	<2.0		HED[b]
Guinea pig	2.7		HED[b]
Mink	9.2 (0-19.5)		Ringer and Aulerich 1978
Cat	~25		HED[b]
Sheep	>25		HED[b]

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	LC50, ppm (95% CI)	Reference
Difethialone			
Laboratory rat	0.55 (0.53-0.57)		HED[b]
Rat	0.4-0.8		HED[b]
Laboratory mouse	1.29 (0.73-1.85)		HED[b]
Roof rat	0.38		Lorgue et al.[d]
House mouse	0.47		Lorgue et al.[d]
Norway rat (wild)	0.29-0.51		Lorgue et al.[d]
Hare	0.75		Lorgue et al.[d]
Pig	2-3		Lorgue et al.[d]
Dog	4		Harling et al. 1986[f]
Dog	11.8 (6.6-21.2)		HED[b]
Cat	>16		Lorgue 1986[e]
Bromadiolone			
Laboratory rat		0.92 (0.54-1.13) 1.49 (1.21-2.06) 1.79 (1.57-2.06) 1.99 (1.62-2.27)	EPA unpublished data[a]
Laboratory rat	0.56-0.84[f]		EPA 1998a
Laboratory mouse	1.75 (0.2-3.3)		HED[b]
Pine vole	3.9 (2.3-6.8)		Byers 1978
Rabbit	1		HED[b]
Dog	8.1		Poché 1988
Cat	>25		HED[b]

[a] the 5 dietary tests for brodifacoum and 4 dietary tests for bromadiolone were conducted at EPA's former Toxicology Unit, Beltsville, MD; methodology follows that described in McCann et al. 1981
[b] OPP/HED Toxicity Database
[c] cited in Matschke et al. 1983
[d] cited in Lechevin and Poché 1988
[e] cited in LiphaTech 1997
[f] an LD50 could not be statistically determined from the data but was estimated to be between these two test concentrations

Table 9. Acute Oral Toxicity of First-generation Anticoagulants to Mammals

Rodenticide/ Species	LD50, mg/kg (95% CI)	LC50, ppm (95% CI)	Reference
Chlorophacinone			
Laboratory rat		1.14 (1.02-1.36) 1.14 (0.98-1.35) 1.26 (1.11-1.47) 1.26 (0.97-1.64)	EPA unpublished data[a]
Laboratory rat	6.2 3.1%(1.5-6.7) 11.0& (6.5-18.5)		HED[b]
Laboratory rat	0.95 (5-day dose @ 0.19/day)		Jackson and Ashton 1992
Norway rat (wild)	0.80 (5-day dose @ 0.16/day)		Jackson and Ashton 1992
House mouse	1.0 6		Hone and Mulligan 1982[c]
Laboratory mouse	5.95 (5-day dose @ 1.19/day) 1.90% 17.40&		Jackson and Ashton 1992
Deer mouse	0.49		Clark 1994
Deer mouse	1.0-3.75[d]		Schafer and Bowles 1985
Norway rat	5.0		Clark 1994
Pine vole	14.2 (11.4-17.6)		Byers 1978
Roof rat	15.0		Clark 1994
Dog	50-100		Labe and Lorgue 1977
Diphacinone			
Laboratory rat		2.08 (1.57-2.76) 2.55 (1.79-3.19)	EPA unpublished data[a]
Laboratory rat	2.5%(1.3-3.4) 2.1& (1.5-2.9)		HED[b]
Laboratory rat	7.0 (5.2-9.5)		HED[b]
Laboratory rat	1.05 (5-day dose @ 0.21/day)		Jackson and Ashton 1992

Rodenticide/ Species	LD50, mg/kg (95% CI)	LC50, ppm (95% CI)	Reference
Norway rat (wild)	1.75 (5-day dose @ 0.35/day)		Jackson and Ashton 1992
Laboratory rat	1.9		Gaines 1969
House mouse	141-340		Hone and Mulligan 1982[c]
Laboratory mouse	7.05 (5-day dose @ 1.41/day) 2.10% 14.15&		Jackson and Ashton 1992
Meadow vole	14.0 (8.8-22.1)		Byers 1978
Pine vole	57.0 (34.4-94.3)		Byers 1978
Mongoose	0.2		EPA 1998a
Coyote	0.6		EPA 1998a
Dog	0.88		Kosmin and Barlow 1976[e]
Dog	3.0-7.5		Mount and Feldman 1983[e]
Dog	5-15		Lisella et al. 1971[e]
Cat	14.7		Clark 1994
Cat	5-15		Lisella et al. 1971[e]
Rabbit	35		Clark 1994

Warfarin

Laboratory rat		4.41 (3.43-5.64) 5.43 (4.23-7.00) 5.91 (4.66-7.51) 6.03 (4.45-8.20)	EPA unpublished data[a]
Laboratory rat	2.5-5.0		WARF Institute 1977[f]
Laboratory rat	2.5-20		Til et al. 1974[f]
Laboratory rat	3		Gaines 1969
Laboratory rat	35.7% 41.9&		EPA 1982
Laboratory rat	323%[g] 58&[g]		Hagan and Radomski 1953[f]

Rodenticide/ Species	LD50, mg/kg (95% CI)	LC50, ppm (95% CI)	Reference
Laboratory rat	450-680% <10&		WARF Institute 1977[f]
Laboratory rat	100%[g] 8.7&[g]		Back et al. 1978[f]
Laboratory rat	1.65 (5-day dose @ 0.33/day)		Jackson and Ashton 1992
Norway rat (wild)	2.20 (5-day dose @ 0.44/day)		Jackson and Ashton 1992
Laboratory mouse	374[g]		Hagan and Radomski 1953[f]
Laboratory mouse	11.00 (5-day dose @ 2.20/day) 4.35% 40.00&		Jackson and Ashton 1992
Rabbit	800[g]		Hagan and Radomski 1953[f]
Cat	2.5-20		HED[a]
Dog	20-50		USFWS[h]
Dog	200-300[g]		Hagan and Radomski 1953[f]

[a] the 5 dietary tests for brodifacoum and 4 dietary tests for bromadiolone were conducted at EPA's former Toxicology Unit, Beltsville, MD; methodology follows that described in McCann et al. 1981
[b] OPP/HED Toxicity Database
[c] cited in Hyngstrom et al. 1994
[d] an approximate lethal dose (ALD); the ALD is estimated from an acute oral test that uses too few concentrations and test animals to statistically derive an LD50
[e] cited in LiphaTech 1997
[f] cited in EPA 1981
[g] values are for sodium warfarin
[h] cited in Papworth 1958

Table 10. Acute Oral Toxicity of non-Anticoagulant Rodenticides to Mammals

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	Reference
Bromethalin		
Laboratory rat	10.7% 9.1&	HED[a]
Roof rat	6.6	Jackson et al. 1982
Mouse	5.3% 8.1&	HED[a]
Mouse	35.9% 28.9&	HED[a]
Rabbit	2.4% 2.0&	HED[a]
Dog	4.8	HED[a]
Cat	18	HED[a]
Zinc phosphide		
Norway rat (wild)	21 (13-34)	EPA 1998b
Rat	30 (20-45)	HED[a]
Rat	40	HED[a]
Roof rat	2.9-40	EPA 1998b
Polynesian rat	23	EPA 1998b
Deer mouse	40.5	Clark 1994
Deer mouse	42[b]	Schafer and Bowles 1985
Meadow vole	18	EPA 1998b
Nutria	5.5	EPA 1998b
Pocket gopher	6.8	EPA 1998b
Banner-tailed kangaroo rat	8	Clark 1994
Black-tailed prairie dog	18	EPA 1998b
Muskrat	29.9	Evans et al. 1966[c]
California ground squirrel	33.1	EPA 1998b
Black-tailed jack rabbit	8.2	EPA 1998b
Dog	40[b]	Matschke and LaVoie 1976[c]
Cat	40[b,c]	Matschke and LaVoie 1976[c]

Rodenticide/ Species	LD50, mg ai/kg (95% CI)	Reference
Kit fox	93 (62-140)	Schitoskey 1975
Cholecalciferol		
Laboratory mouse	26[d]	HED[a]
Laboratory rat	42 (33-53)[e]	HED[a]
Dog	88[e]	Marshall 1984

[a] OPP/HED Toxicity Database

[b] an approximate lethal dose (ALD); the ALD is estimated from an acute oral test that uses too few concentrations and test animals to statistically derive an LD50

[c] cited in Johnson and Fagerstone 1994

[d] the value is adjusted, based on the purity of the test material (62.5%)

[e] the purity of the test material was not reported

Other toxicity information: ICI Americas, Inc. (1978b) provided some pertinent information on the approximate number of LD50 doses captive wild Norway rats consumed in their food (50 ppm brodifacoum bait) at various times until death, which averaged 6.5 days. The rats (sample size not specified) were either offered bait only or a choice of bait and untreated food. The rats in the no-choice group consumed an average of approximately 20 LD50 doses after 1 day of feeding and 80 LD50 doses by death (Figure 1). Rats offered a choice of bait or untreated food still consumed enough bait to have ingested an average of 40 LD50 doses at death.

Figure 1. Average number of LD50 doses consumed by captive wild Norway rats offered 50 ppm brodifacoum bait in no-choice (bait only) or choice (bait and untreated food) feeding tests (after ICI Americas, Inc. 1978b)
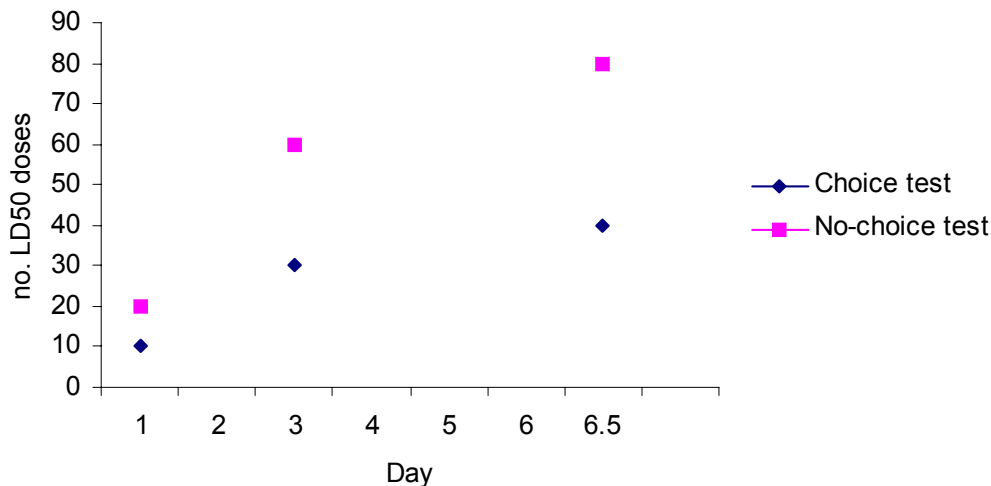
Some information is available to characterize the primary hazard of rodenticide bait to dogs and other nontarget species. Mackintosh et al. (1988) reported that some dogs have died after consuming as few as 8 brodifacoum (Talon) pellets. Lechevin and Poché (1988) indicate that 400 g of 0025% ai difethialone bait is the maximum amount tolerated by 10-kg dogs. In a study in which 2 dogs were exposed to a 0.025% ai warfarin bait, 1 died after feeding for 7 days on 12 g of bait daily and the other after feeding on 4.8 g of bait daily for 12 days (Prier and Derse 1962). Marsh (1985) calculated that an LD50 dose to a 10-lb dog could be provided with 23 g of brodifacoum bait, 85 g of diphacinone bait, 369 g of warfarin bait, and 1000 g of bromadiolone bait. Gunther et al. (1988) fed cholecalciferol bait to 4 dogs as a follow-up to an investigation of 2 dogs that died after consuming cholecalciferol bait. Two dogs were given a single meal containing approximately 540 g of bait (20 mg ai/kg) and 2 were given half that amount. All 4 dogs became lethargic, weak, and anorectic within 48 hours and all died 65 to 77 hours after treatment. These findings suggest that cholecalciferol bait may present more of a hazard to dogs than the LD50 of 88 mg ai/kg would suggest.

Dubock and Kaukeinen (1978) reported the following nontarget-hazards data for brodifacoum: "The deer mouse *Peromyscus maniculatus* completely succumbed (20/20 mortality) in a 1-day no-choice feeding test with 50 ppm brodifacoum (Marsh, unpublished)." and "100% mortality has been obtained against the ground squirrel *Spermophilus beecheyi* when offered 50 ppm brodifacoum bait no choice for 1, 2 or 3 days (Marsh, unpublished)."

Mammalian reproduction/sublethal effects: EFED typically utilizes the rat two-generation reproduction test to assess reproductive risks to mammals. This study (40 CFR §158.340 Toxicology Data Requirements, Guidelines Reference No. 83-4) is required by HED to support registration of pesticides with food uses or where use of the product is likely to result in human exposure over a significant portion of the human lifespan. This study is not currently available for any of the 9 rodenticides. HED also requires other subchronic/chronic studies, but most (e.g., dermal, inhalation, oncogenicity, neurotoxicity) provide measurement endpoints not relevant to assessing risk to nontarget mammals other than humans.

Some evidence exists that sublethal doses can have adverse effects. The Warfarin RED (EPA 1991a) notes that warfarin is a teratogen, and product labels are required to warn that "Exposure to warfarin during pregnancy should be avoided. Warfarin may cause harm to the fetus, including possible birth defects." The Rodenticide Cluster RED (EPA 1998a) reports developmental toxicity (e.g., vaginal bleeding, hypotonicity) in rats and rabbits exposed to bromadiolone at about two orders of magnitude less than the LD50 dose. In brodifacoum studies, internal hemorrhage and significantly prolonged prothrombin time of rabbits was reported for those dosed during gestation at about two orders of magnitude less than the LD50 dose. More recently, Munday and Thompson (2003) detected brodifacoum in two dog pups that died a few hours after birth. Of 13 pups from a single litter, eight were born dead or died within 48 hours of birth. Three puppies that died shortly after birth were necropsied. Two exhibited hemorrhage in the thoracic and peritoneal cavities, intestinal serosa, and meninges, and brodifacoum was detected in the liver of both puppies. The mother did not have any clinical signs of coagulopathy before or subsequent to whelping, and the authors suggest that fetuses may be more susceptible to brodifacoum than are adults.

Secondary-hazards Data

Birds

The available laboratory studies indicate that major differences occur among the rodenticides in their secondary hazard to birds, with brodifacoum displaying the greatest hazard and chlorophacinone and the non-anticoagulants the least. Thirty-one studies are cited in which raptors or avian scavengers were exposed to rodenticide in whole or ground carcasses, usually those of rats or mice, or in fortified meat. Second-generation anticoagulants were tested in 15 studies, first-generation-anticoagulants in 13 studies, and non-anticoagulants in 6 studies (note: some studies included more than one rodenticide group). Most prey animals were fed treated bait, although some were orally dosed. Most studies involved only 1 rodenticide but often more than 1 raptor or scavenger species was tested. Mortality is a measurement endpoint in all studies.

Some studies also report signs of toxicosis (e.g., bleeding, prolonged blood-coagulation time, abnormal behavior, regurgitation) in surviving test animals, and that information is included if reported. Although exposure scenarios, test species, and the number of test animals vary among the studies, collectively they provide sufficient information to characterize secondary hazards from short-term exposure. The studies are summarized and tabulated below. Two studies merit additional attention, because they test different rodenticides against the same test species under the same test conditions, and are discussed in more detail in the section "*Comparative anticoagulant studies*".

Second-generation anticoagulants: Some data are available for brodifacoum and bromadiolone but none for difethialone. Brodifacoum was tested in 11 studies involving 8 species. Of 149 individuals exposed to brodifacoum-poisoned prey, 63 (42%) individuals died (Table 11). Mortality occurred in 11 of 20 barn owls (*Tyto alba*), 6 of 6 red-tailed hawks (*Buteo jamaicensis*) and red-shouldered hawks (*Buteo lineatus*), 13 of 65 American kestrels (*Falco sparverius*), 1 of 4 Eurasian harriers (*Circus pygargus*), and 32 of 50 laughing gulls (*Larus atricilla*). No deaths occurred in 4 golden eagles (*Aquila chrysactos*) tested by Marsh and Howard (1978), but 3 bled externally. Some studies did not report whether signs of toxicosis were observed in surviving birds or not. In those studies that examined survivors for signs of toxicosis, such as external bleeding, internal hemorrhaging, and/or prolonged blood-coagulation time, about one-third of the survivors visually examined or necropsied exhibited symptoms of toxicity.

In contrast to brodifacoum, secondary exposure to bromadiolone caused the deaths of only 9 (8%) of 118 individuals in 5 studies (Table 12) that tested great-horned owls (*Bubo virginianus*), barn owls, red-tailed hawks, and Eurasian buzzards (*Buteo buteo*). Survivors also exhibited fewer signs of intoxication than did survivors in brodifacoum studies. Grolleau et al. (1989) reported bleeding in some of the 27 Eurasian buzzards that survived feeding on bromadiolone-poisoned voles for 3 days but reported no signs of intoxication in 59 survivors exposed for only 1 or 2 days. No signs of intoxication are reported by Poché (1988) or Mendenhall and Pank (1980) in 12 raptors (barn owls and red-tailed hawks) that survived feeding on bromadiolone-treated rodents for 3 to 10 days. Wyllie (1995) reported increased blood coagulation time in 6 barn owls fed bromadiolone-poisoned mice for 6 days, but coagulation times returned to normal within 10 days; all owls survived, and no evidence of hemorrhaging was seen.

Table 11. Secondary Hazards of Brodifacoum to Birds in Laboratory Studies

Predator/ scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of brodifacoum toxicity[a]	Reference
Barn owl	rats fed choice of 0.002% bait[b] and untreated food for 5 days	1-2	1	1	0	0	Mendenhall and Pank 1980
			3	2	2	no survivors	
			6	1	1	no survivors	
			8	2	2	no survivors	
Barn owl	mice fed 0.002% bait[b] for 1 day	3	1	6	4	nr	Newton et al. 1990 and Wyllie 1995
		2	3	2[c]	0	nr	
		2	6	2[c]	0	2 (eb/ct)	
Barn owl	mice fed 0.005% bait for 1-2 days	enough to provide 50-220 µg ai per day	15	4	1	3 (eb/ih)	Gray et al. 1994
Barn owl	rats fed 0.005% bait	4 total	5-7	4	1	0	Lee 1994[d]
Red-tailed hawk	rats fed 0.005% bait for 3 days	limited[e]	4	4	4	no survivors	Marsh and Howard 1978
Red-shouldered hawk	mice fed 0.005% bait for 3 days	limited[e]	4	2	2	no survivors	Marsh and Howard 1978
Golden eagle	rats fed 0.005% bait for 3 days	limited[e]	4	4	0	3 (eb)	Marsh and Howard 1978
American kestrel	voles fed 0.005% bait for 3 days	1	2	10	0		Savarie and LaVoie 1979
		1	6	10	4	(ct)	
American kestrel	ground vole tissue at 5 concentrations: 0.3 ppm	ad lib.	5	8	0	nr	LaVoie 1990
	0.8 ppm		5	8	1	nr	
	1.6 ppm		5	8	0	nr	
	3.2 ppm		5	8	0	nr	
	6.0 ppm		5	8	4	nr	

Predator/ scavenger (p/s)	Prey offered to p/s		No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of brodifacoum toxicity[a]	Reference
Eurasian buzzard	mice fed 0.005% bait		5	6	5	4	1 (bl)	Lutz 1987[d]
Australasian harrier	rabbit dosed at 6.5 mg ai/kg		1	1	4	1	nr	Godfrey 1985
Laughing gull	ground, spiked rat tissue at 5 concentrations:	0.72 ppm	ad lib.	5	5	3	0	ICI Americas, Inc. 1979a
		1.62 ppm		5	5	5	no survivors	
		3.41 ppm		5	5	5	no survivors	
		7.26 ppm		5	5	5	no survivors	
		14.0 ppm		5	5	5	no survivors	
Laughing gull	ground, spiked rat tissue at 5 concentrations:	0.13 ppm	ad lib.	5	5	0	0	ICI Americas, Inc. 1979b
		0.34 ppm		5	5	1	0	
		0.84 ppm		5	5	0	1 (eb)	
		2.10 ppm		5	5	4	0	
		5.26 ppm		5	5	4	0	

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported

[a] registered baits are 0.005% ai

[c] the 2 owls that survived the initial 1-day exposure were subsequently re-exposed for 3 days and again for 6 days; the owls were allowed to recover for 75 to 79 days between exposure periods

[d] cited in Joermann 1998

[e] the amount of food offered to the raptors was "limited" to prevent overindulgence on any given day

Table 12. Secondary Hazards of Bromadiolone to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of bromadiolone toxicity[a]	Reference
Barn owl	rats fed choice of 0.005% bait or untreated food for 5 days	1-2	1	1	0	0	Mendenhall and Pank 1980
			3	2	0	0	
			6	1	0	0	
			10	2	1	0	
Barn owl	mice fed commercial bait (% ai not reported) and allowed to die	2-3	6	6	0	(ct)[c]	Wyllie 1995
Barn owl	rats fed 0.005% bait	4	5-7	4	1	nr	Lee 1994[d]
Eurasian buzzard	voles fed 0.01% bait[b]	1	1	40	0	0	Grolleau et al. 1989[d]
			1+1[e]	10	1	0	
			2	10	0	0	
			3	30	2	some (bl)	
Eurasian buzzard	mice fed 0.005% bait	?	10	4	3	1 (ct)	Lutz 1986[d]

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported

[b] rat and mouse baits registered in the U. S. are 0.005% ai

[c] coagulation time returned to normal within 10 days; no signs of hemorrhage in any individuals

[d] cited in Joermann 1998

[e] a second 1-day exposure period occurred 10 days after the first exposure

Only a few studies provide information on the residue level in the prey species offered to the secondary consumer. In those studies, the experimenter often manipulated residue levels to provide a known concentration or range of concentrations (e.g., ICI Americas, Inc. 1979a,b; LaVoie 1990; Gray et al. 1994). Additional information on whole-body residues in target species exposed to second-generation anticoagulants is provided in Table 13. Note that animals collected in the field were exposed to bait for an undetermined number of days. Some laboratory studies used bait concentrations different from that in baits registered in the U. S. and some exposed the primary consumer for only 1 day (e.g., Newton et al. 1990, Poché 1988).

Two residue studies indicate that the amount of whole-body residue in the target species is related to the amount of active ingredient in the bait. Kaukeinen (1982) provides mean tissue residue levels in voles exposed to brodifacoum bait in the laboratory. Separate groups of males and females were exposed for 4 days to 50 ppm bait or 10 ppm bait. Residues are 5.21 ppm and 2.17 ppm for males and females, respectively, exposed to 50 ppm bait but only 0.53 ppm and 0.40 ppm, respectively, for those exposed to 10 ppm bait. In field trials for vole control in orchards, Merson et al. (1984) collected voles 1 to 7 days after bait application. Two collections of voles exposed to 0.005% ai bait had mean whole-body residues of 2.07 ppm and 4.07 ppm, whereas those exposed to 0.001% ai bait had a mean residue level of 0.35 ppm.

Table 13. Second-generation Anticoagulant Residue Levels in Primary Consumers

Rodenticide	mg ai/kg bait	Target species	Site	Sample size	Days exposed	Whole-carcass residue (ppm)	Reference
Brodifacoum	50	rat	field	50	unknown	most <7; some up to 11-13	Kaukeinen 1993
Brodifacoum	50	rat	field	6	unknown	2.7 (0.1-6.6)	ICI 1979c
Brodifacoum	50	rat	field	4 % 3 & 3 juv.	unknown	7.08 (3.92-9.17) 5.61 (1.39-12.19) 8.63 (1.77-25.97)	Howald 1997
Brodifacoum	50	vole	field	74	1-7	4.07 ± 0.20 (SE)	Merson et al. 1984
Brodifacoum	50	vole	field	62	1-7	2.07 ± 0.17 (SE)	Merson et al. 1984
Brodifacoum	50	vole	laboratory	15 % 15 &	4 4	5.21 ± 2.06 (sd) 2.17 ± 1.17 (sd)	Kaukeinen 1982
Brodifacoum	25[a]	deer mouse	field	10	4-9	2.71 (0.68-4.25)	Howald et al. 2001
Brodifacoum	20[a]	mouse	laboratory	?	3	2.21	Anonymous 1981[b]
Brodifacoum	20[a]	mouse	laboratory	10	1	0.44	Newton et al. 1990
Brodifacoum	10[a]	vole	laboratory	15 % 15 &	4 4	0.53 ± 0.24 (sd) 0.40 ± 0.20 (sd)	Kaukeinen 1982
Brodifacoum	10[a]	vole	field	43	1-7	0.35 ± 0.03 (SE)	Merson et al. 1984
Difethialone	25	rat	laboratory	20	3	2.0 ± 0.51 (sd)	Goldade et al. 2001
Bromadiolone	50	rat	laboratory	6	1	2.08	Poché 1988
Bromadiolone	50	mouse	laboratory	10	1	2.29	Poché 1988
Bromadiolone	50	rat	field	16	unknown	1.92	Poché 1988
Bromadiolone	50	mouse	field	6	unknown	1.17	Poché 1988

Rodenticide	mg ai/kg bait	Target species	Site	Sample size	Days exposed	Whole-carcass residue (ppm)	Reference
Bromadiolone	50	ground squirrel	field	16	unknown	0.49	Poché 1988
Bromadiolone	100[a]	vole	laboratory	?	1	6.5-6.75	Grolleau et al. 1989
Bromadiolone	100[a]	vole	laboratory	?	3	8.7-10.9	Grolleau et al. 1989
Bromadiolone	100[a]	vole	laboratory	?	3	5.8	Grolleau et al. 1989
Bromadiolone	150[a]	vole	field	44	$\leq$3	0.91 (0.05-2.97)	Delley and Joseph 1985[c]
Bromadiolone	150[a]	vole	laboratory	12	$\leq$3	0.11 (0.04-0.19)	Delley and Joseph 1985[c]

[a] brodifacoum and bromadiolone baits registered in the U. S. are 0.005% ai
[b] cited in Joermann 1998
[c] cited in Saucy et al. (2001)

First-generation anticoagulants: Mortality in studies with the 3 first-generation anticoagulants ranged from 0 to 9%. No mortality occurred in 8 chlorophacinone studies with 112 individuals from 9 species (Table 14). Birds tested included 28 carrion crows (*Corvus corone*), 20 Eurasian buzzards, 20 American kestrels, 20 black-billed magpies, 10 red-tailed hawks, 6 white storks (*Ciconia ciconia*), 4 tawny owls (*Strix aluco*), 2 barn owls, and 2 great horned owls. Some survivors showed signs of intoxication, mostly prolonged blood-coagulation time. About 9% mortality was recorded in 3 diphacinone studies with 34 individuals (Table 15). Test species were barn owls, great horned owls, saw-whet owls (*Aegolius acadicus*), golden eagles, and American crows (*Corvus brachyrhynchos*). Thirteen (42%) of the survivors displayed some signs of toxicity. In 4 warfarin studies, 2 (9%) of 23 individuals died (Table 16); no adverse signs were reported in the survivors. Whole-body residues in target species exposed to chlorophacinone, diphacinone, and warfarin are presented in Table 17.

Table 14. Secondary Hazards of Chlorophacinone to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of chlorophacinone toxicity[a]	Reference
Barn owl	rats fed choice of 0.005% bait or untreated bait for 5 days	1-2	10	2	0	0	Mendenhall and Pank 1980
Black-billed magpie	rats fed 0.005% bait for 5 days	ad lib.	5	20	0	0	Baroch 1997
American kestrel	voles fed 0.01% bait until dead	1	21	10	0	10 (eb/ih)	Radvanyi et al. 1988
		1 every 3 days	61	10	0	10 (eb/ih)	
Red-tailed hawk	voles fed 10 g 0.005% bait daily for up to 9 days	2	6	5	0	0	Askham and Poché 1992
Great horned owl	voles fed 10 g 0.005% bait daily for up to 9 days	2	6	1	0	0	Askham and Poché 1992
Red-tailed hawk	voles fed 0.005% bait for up to 9 days	2	6	5	0	0	Askham 1988
Great horned owl	voles fed 0.005% bait for up to 9 days	2	6	1	0	0	Askham 1988
Tawny owl	mice fed 0.0075% bait[b]	ad lib.	10	4	0	(ct)	Riedel et al. 1991[c]
Eurasian buzzard	mice fed 0.0075% bait[b]	ad lib.	7	4	0	(ct)	Riedel et al. 1991[c]
			10	6	0	(ct)	
			5+5+5[d]	3	0	(ct)	
			40	3	0	(ct)	
Eurasian buzzard	mice fed 0.0075% bait[b]	4	7	4	0	0	Anonymous 1978[c]
Carrion crow	mice fed 0.0075% bait[b]	ad lib.	10	4	0	(ct)	Riedel et al. 1991[c]
Carrion crow	mice fed 0.0075% bait[b]	3-4	3	12	0	0	Sterner 1978[c]
			5	12	0	0	

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of chlorophacinone toxicity[a]	Reference
White stork	mice fed 0.0075% bait[b]	ad lib. (treated /untreated)	3 14	3 3	0 0	1 or 2 (ct) 1 or 2 (ct)	Sterner 1981[c]

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] baits registered in the U.S. are either 0.005% or 0.01% ai
[c] cited in Joermann 1998
[d] the 3 5-day treatment periods are separated by 3 days when the birds were fed untreated mice

Table 15. Secondary Hazards of Diphacinone to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of diphacinone toxicity[a]	Reference
Great horned owl	mice fed choice of 0.01% bait or untreated food for 10 days	2	5	3	2	1 (ct)	Mendenhall and Pank 1980
Saw-whet owl	mice fed choice of 0.01% bait or untreated food for 10 days	2	5	1	1	no survivors	Mendenhall and Pank 1980
Barn owl	rats fed choice of 0.005% bait or untreated food for 5 days	ad lib.	10	2	0	0	Mendenhall and Pank 1980
American crow	rats fed 0.005% bait until death	1 1-2[b]	1 6	10 11	0 0	0 5 (eb/ct)	Massey et al. 1997
Golden eagle	meat laced at 2.7 ppm ai	454 g	5 10	4 3	0 0	4 (eb/ct) 3 (eb/ct)[c]	Savarie et al. 1979

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] offered 1 rat per crow for 5 days and 2 rats per crow on day 6
[c] general weakness of all eagles was observed after 5 days

Table 16. Secondary Hazards of Warfarin to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of warfarin toxicity[a]	Reference
Tawny owl	mice fed bait for 3 days	1 every other day	90	4	0	0	Townsend et al. 1981
			28	2[c]	0	0	
Black-billed magpie	rats fed 0.05% bait[b] for 4-7 days	ad lib.	5	14	0	0	March 1997
Barn owl	rats fed 0.005% bait[b]	4 total	5-7	4	2	nr	Lee 1994[d]
Eurasian buzzard	rat/mouse	ad lib.	18	1	0	nr	Telle 1955[d]

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] rat and mouse baits registered in the U.S. are 0.025% ai
[c] the 2 owls had previously been exposed for 90 days; untreated mice were offered for 3 weeks preceding the second test
[d] cited in Joermann 1998

Table 17. First-generation Anticoagulant Residue Levels in Primary Consumers

Rodenticide	mg ai/kg bait	Target species	Site	Sample size	Days exposed	Whole-carcass residue (ppm)	Reference
Chlorophacinone	100	ground squirrel	field	10	unknown	1.27 $\pm$ 0.56 (sd)	Baroch 1996b
Chlorophacinone	75[b]	mouse	laboratory	?	3	6.0	Riedel et al. 1991[a]
Chlorophacinone	50	ground squirrel	field	10	unknown	0.57 $\pm$ 0.27 (sd)	Baroch 1996a
Chlorophacinone	50	ground squirrel	field	10	unknown	0.52 + 0.31(sd)	Baroch 1996b
Chlorophacinone	50	rat	laboratory	5	5	0.47 (0.21-0.93)	Baroch 1997
Chlorophacinone	50	rat	laboratory	4	5	0.45 (0.18-0.81)	Ahmed et al. 1996
Chlorophacinone	50	vole	laboratory	10	$\leq$9	3.2	Askham and Poché 1992
Chlorophacinone	50 or 100[c]	ground squirrel	field	62	unknown	0.264	Primus et al. 2001
Chlorophacinone	50 or 100[c]	vole	field	3	unknown	1.58 (0.26-4.1)	Primus et al. 2001
Chlorophacinone	50	mouse	laboratory	?	3	5.8	Anonymous 1981[a]
Chlorophacinone	50 or 100[c]	pocket gopher	field	8	unknown	0.518	Primus et al. 2001
Chlorophacinone	50 and 100[d]	ground squirrel	field	53	unknown	0.93	Goodall et al. 2002
Diphacinone	50	ground squirrel	field	10	unknown	1.4 (0.6-3.4)	Baroch 1994a
Diphacinone	50	ground squirrel	field	7	unknown	0.9 (0.48-1.89)	Baroch 1994b
Diphacinone	100	ground squirrel	field	10	unknown	1.4 (0.6-2.6)	Baroch 1994a
Diphacinone	50 and 100[d]	ground squirrel	field	76	unknown	0.98	Goodall et al. 2002
Warfarin	200[e]	mouse	laboratory	17	3	2.95 $\pm$ 0.26 (SE)	Townsend et al. 1984
Warfarin	67[e]	rabbit	laboratory	nr	35	104	Aulerich et al. 1987
Warfarin	50[e]	mouse	laboratory	62	3	1.63 $\pm$ 0.1 (SE)	Townsend et al. 1981

Rodenticide	mg ai/kg bait	Target species	Site	Sample size	Days exposed	Whole-carcass residue (ppm)	Reference
Warfarin	50[e]	mouse	laboratory	18	3	1.58 ± 0.1 (SE)	Townsend et al. 1984
Warfarin	25[e]	rabbit	laboratory	nr	35	82	Aulerich et al. 1987
Warfarin	10[e]	mouse	laboratory	15	3	0.42 ± 0.04 (SE)	Townsend et al. 1984

[a] cited in Joermann 1998
[b] chlorophacinone baits registered in the U. S. are either 0.005% or 0.01% ai
[c] carcasses were collected in the field in CA, where both 50 ppm and 100 ppm chlorophacinone baits are registered
[d] the study did not allow distinguishing among ground squirrels exposed to 50 ppm and 100 ppm baits
[e] warfarin baits registered in the U. S. are 0.025% ai

Comparative anticoagulant studies: Some of the most meaningful studies for comparing hazards are those in which more than one rodenticide was tested by the same researchers under the same test conditions and with the same test species. Any adverse effects observed can more readily be attributed to differences among the rodenticides than to differences potentially confounded from utilizing different exposure scenarios or test species. The 2 studies summarized below indicate that brodifacoum has greater secondary toxicity to birds than do other anticoagulants tested, including bromadiolone, difenacoum and flocoumafen (both second-generation anticoagulants not registered in the U. S.), diphacinone, chlorophacinone, and fumarin (a first-generation compound no longer registered in the U.S.).

Mendenhall and Pank (1980) compared secondary hazards of 3 second-generation and 3 first-generation anticoagulants to barn owls. Six owls per rodenticide were exposed for either 1, 3, 6, or 10 days to rats fed with either brodifacoum (20 ppm bait), bromadiolone (50 ppm bait), or difenacoum (50 ppm). The exposed rats had been offered free choice of bait (5 to 13 g daily) or laboratory chow for 10 days; thus, none were forced to eat bait. An additional 2 owls per rodenticide were exposed for 10 days to rats fed with either diphacinone (50 ppm), chlorophacinone (50 ppm), or fumarin (250 ppm). Six of the 18 owls exposed to second-generation anticoagulants died, whereas none of the 6 owls offered first-generation anticoagulant-poisoned rats exhibited any signs of intoxication. Brodifacoum-fed rats accounted for 5 of the 6 owl deaths, even though the concentration of active ingredient in the bait fed to the rats is less than the 50 ppm in baits registered for rat and mouse control. The other mortality occurred in 1 of 2 owls exposed to bromadiolone-fed rats for 10 days. The amount of anticoagulant residue in the rats offered to the owls was not determined.

Wyllie (1995) and Newton et al. (1990) reported on toxic effects to barn owls fed mice exposed to brodifacoum (6 owls), bromadiolone (6 owls), or 2 other anticoagulants (difenacoum, flocoumafen). The mice had been fed bait (no choice) for a single day and allowed to die, which took 2 to 11 days. Dead mice were then offered to the owls in 3 phases, each phase separated by a recovery period lasting at least 75 days. In phase I, each owl was offered 3 mice for 1 day only. Surviving owls were offered 6 mice each during a 3-day period in phase II and 12 mice each during a 6-day period in phase III. Mortality, evidence of external bleeding, and delays in blood-coagulation times were monitored. Four of the 6 owls fed brodifacoum-exposed mice died within 6 to 17 days of phase I. Both survivors also survived feeding on poisoned mice in phases II and III, but both exhibited bleeding from the mouth, feet, and newly-grown feathers for up to 30 days, and blood-coagulation times did not reach normal until 16 to 78 days after treatment. In contrast, none of the owls exposed to bromadiolone-poisoned mice died or exhibited signs of hemorrhaging, and blood coagulation times returned to normal 4 to 6 days after treatment.

Others (non-anticoagulants): The few studies available for the non-anticoagulant rodenticides indicate few adverse secondary effects. Five studies are available for zinc phosphide (Table 18). Test birds included 2 great horned owls, 3 spotted eagle owls (*Bubo africanus*), 3 kestrels (*Falco tinnunculus*), 3 bald eagles (*Haliaeetus leucocephalus*), 3 black vultures (*Coragyps atratus*), 3 carrion crows, a magpie, and a jay. None of the 19 birds died, but signs of intoxication were noted in several individuals. Roosting-behavior irregularities were noted in 2 owls exposed to poisoned voles for 3 days (Bell and Dimmick 1975), and 3 bald eagles fed poisoned nutria (*Myocastor coypus*) for 4 to 5 weeks regurgitated some prey (Evans et al. 1966; cited in Johnson and Fagerstone 1994). In the only study available for cholecalciferol (Table 19), no adverse effects were observed in 2 turkey vultures and 1 red-tailed hawk exposed to rats fed for 1-day with 0.075% ai bait (Marsh and Koehler 1991). Each bird was offered 1 large or 2 small rats daily for 10 days. No hazard data are available for bromethalin.

Some whole-body residue data are available for zinc phosphide but none was found for cholecalciferol or bromethalin. Sterner et al. (1998) reported a mean whole-body residue of 0.42 ($\pm$ 0.68) mg ai per vole for 6 voles each offered 5 oat-groat particles treated with 2% zinc phosphide. Mean particle weight was 23 mg, resulting in individual voles being offered only about 0.12 g of bait. In an earlier study (Sterner and Maudlin 1995), whole-body residues averaged 1.73 mg ai per vole (range = 0.31 to 4.95 mg ai) in voles offered bait ad libitum. Almost all zinc phosphide detected in carcasses apparently was in undigested bait in the GIT. Matscke and Andrews (1990) recovered only 8.9% of the amount of 2% ai bait ingested by voles, and 99.9% of that was in the GIT, especially the stomach. Only 0.1% of that recovered was detected in the kidneys, gall bladder, liver, and spleen combined, and none was detected in the lungs, heart, or in muscle. Tkadlec and Rychnovsky (1990) also reported that 99% of the zinc phosphide residue they detected in voles was in the GIT.

Table 18. Secondary Hazards of Zinc Phosphide to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey of red daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of zinc phosphide toxicity	Reference
Great horned owl	voles fed bait (86.94 mg ai/kg)	ad lib.	3	2	0	2[a]	Bell and Dimmick 1975
Spotted eagle owl	gerbils fed 3-4 treated kernels (2% ai)	1	5 10 40	1 1 1	0 0 0	0 0 0	Siegfried 1968[b]
Kestrel	voles fed 5% bait[c]	1	3	3	0	0	Tkadlec and Rychnovsky 1990
Bald eagle	nutria fed 275 g bait (% ai not reported)	13-28 total per bird	28-35	3	0	3[d]	Evans et al. 1966[e]
Black vulture	nutria fed bait (% ai not reported)	not reported	10-11	3	0	0	Evans et al. 1966[e]
Carrion crow	mice fed 2.5% bait[c]	2-4	7	3	0	0	Anonymous 1980[b]
Magpie	mice fed 2.5% bait[c]	2-4	7	1	0	0	Anonymous 1980[b]
Jay	mice fed 2.5% bait[c]	2-4	7	1	0	0	Anonymous 1980[b]

[a] irregular roosting behavior was reported
[b] cited in Joermann 1998
[c] baits registered in the U. S. are 2% ai
[d] regurgitated prey
[e] cited in Johnson and Fagerstone 1994

Table 19. Secondary Hazards of Cholecalciferol to Birds in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of cholecalciferol toxicity[a]	Reference
Turkey vulture	rats fed 0.075% ai bait for 1 day	1 large or 2 small	10	2	0	0	Marsh and Koehler 1991
Red-tailed hawk	rats fed 0.075% ai bait for 1 day	1 large or 2 small	10	1	0	0	Marsh and Koehler 1991

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Mammals

Laboratory tests indicate that the second-generation anticoagulants, as well as chlorophacinone and diphacinone, present a hazard to mammalian predators and scavengers. Thirty-three studies were found in which mammalian predators or scavengers were exposed to rodenticide in whole or ground carcasses, usually rats or mice, or in spiked meat. Second-generation anticoagulants were tested in 8 studies, first-generation-anticoagulants in 15 studies, and non-anticoagulants, mainly zinc phosphide, in 13 studies. Collectively, these studies provide sufficient information to characterize short-term secondary hazards for most of the rodenticides. Three studies in which different rodenticides were tested against the same test species under the same test conditions are discussed in more detail in the section *"Comparative anticoagulant studies"*.

Second-generation anticoagulants: Mortality of 8 (42%) of 19 individuals (foxes, mustelids, domestic dogs) occurred in 4 brodifacoum studies (Table 20). Test subjects included 5 red foxes (*Vulpes vulpes*) and gray foxes (*Urocyon cinereoargenteus*), 4 mongooses (*Herpestes auropunctatus*), 4 weasels (*Mustela* sp.), and 6 domestic dogs. Signs of toxicity are reported for most survivors. In 4 bromadiolone studies (Table 21), 6 (23%) of 26 test animals died, including coyotes (*Canis latrans*), mongooses, and an ermine (*Mustela erminea*). Bleeding was observed in all 10 ermine that survived being fed 1 bromadiolone treated vole per day for 3 to 5 days, but not in 5 coyotes or 4 stone martens fed treated ground squirrels or mice for periods ranging from 1 to 5 days. No comparable secondary-hazard studies are available for difethialone. Goldade et al. (2001) estimated a chronic LD50 for European ferrets (*Mustela putorius furo*) fed difethialone-fortified dog food at various concentrations. The chronic LD50 of 760 mg ai/kg was estimated from cumulative daily food intake, difethialone concentration, and individual bird body weights, but only 2 ferrets were exposed to each test concentration and the duration of exposure was not specified.

First-generation anticoagulants: Laboratory studies indicate that chlorophacinone and diphacinone present a hazard to mammalian predators and scavengers. In 8 chlorophacinone studies, 32 (58%) of 55 individuals died, including 7 of 8 mongooses, 3 of 7 coyotes, 1 of 4 red foxes, 18 of 35 ferrets, and 3 of 4 weasels (Table 22). In 3 diphacinone studies, 19 (58%) of 33 test animals died after feeding on rodents fed diphacinone, liver tissue from owls fed diphacinone, or fortified meat. Species affected included mink (*Mustela vison*), mongooses, ermine, deer mice, rats, and dogs (Table 23). Warfarin appears to be less hazardous than other anticoagulants. In 7 studies, only 9 (9%) of 100 individuals died after eating warfarin-treated rodents (Table 24). Dead animals included 3 mink, 3 least weasels (*Mustela nivalis*), and 3 dogs.

Table 20. Secondary Hazards of Brodifacoum to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of brodifacoum toxicity[a]	Reference
Red fox and Gray fox	rats dosed at 15 mg ai/kg[b]	400 g	1	2	0	2 (eb/ih)	ICI Americas, Inc. 1978a
			3	1	1	no survivors	
			4	2	1	1 (eb/ih)	
Mongoose	rats fed 0.002% bait[c] for 5 days	1	1	1	0	nr	Pank and Hirata 1976
			3	1	1	no survivors	
			6	1	0	nr	
			10	1	0	nr	
Weasel	mice fed 0.002% bait[c]	ad lib.	16-52	4	4	no survivors	Anonymous 1981[d]
Dog (domestic)	rats dosed at 15 mg ai/kg[b]	650 g	1-4	6	1	4 (eb/ih)	ICI Americas, Inc. 1978b

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] the rats were dosed to simulate feeding on 0.005% bait
[c] registered baits are 0.005% ai
[d] cited in Joermann (1998)

Table 21. Secondary Hazards of Bromadiolone to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of bromadiolone toxicity[a]	Reference
Mongoose	rats fed 0.005% bait for 5 days	1	1	1	0	nr	Pank and Hirata 1976
			3	1	1		
			5	1	1		
			6	1	1		
Coyote	ground squirrels fed 15 g of 0.01% bait[b] for 3 days	1	5	7	2	0[c]	Marsh and Howard 1986
Ermine	voles fed 0.01% bait[b]	1	3	8	0	8 (bl)	Grolleau et al. 1989[d]
			5	3	1	2 (bl)	
Stone marten	mice fed 0.005% bait	8	1	2	0	0	Lund and Rasmussen 1986[d]
			4	2	0	0	

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] rat and mouse baits registered in the U. S. are 0.005% ai
[c] 2 coyotes stopped feeding for 8 and 16 days, which was attributed to bromadiolone intoxication; both resumed feeding and survived
[d] cited in Joermann 1998

Table 22. Secondary Hazards of Chlorophacinone to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of chlorophacinone toxicity[a]	Reference
Mongoose	rats fed 0.005% bait for 5 days	1	1	1	0	nr	Pank and Hirata 1976
			3	1	1	no survivors	
			5	2	2	no survivors	
			6	1	1	no survivors	
			7	1	1	no survivors	
			9	1	1	no survivors	
			10	1	1	no survivors	
Coyote	ground squirrels fed 15 g of 0.01% bait for 6 days[b]	1	5	7	3	0	Marsh and Howard 1986
Red fox	mice fed 0.0075% bait[c]	20 total	4	1	1[d]	no survivors	Bachhuber and Beck 1988[e]
European ferret	rats fed 0.005% bait for 5 days	ad lib.	5	20	11	nr	Ahmed et al. 1996
European ferret	prairie dogs fed 25 g of 0.0025% bait daily for 6 days[c]	4 (1 every other day)	8	6	5	nr	Fisher and Timm 1987
European ferret	voles/mice fed 0.0075% bait[c]	5 total	4	2	1[f]	(ct)	Bachhuber and Beck 1988[e]
European ferret	muskrats fed 0.005% bait	ad lib.	4	2	0	1 (bl)	Jobsen 1978[e]
			8	1	1	no survivors	
European ferret	voles fed 0.0075% bait[c]	ad lib.	3	4	0	(ct)	Anonymous 1983[e]
Weasel	mice fed 0.005% bait	ad lib.	90	4	3	0	Anonymous 1981[e]

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] ground squirrels were fed no-choice for 3 days followed by 3 days in which they had a choice of bait or untreated laboratory chow
[c] baits registered in the U.S. are either 0.005% or 0.01% ai
[d] individual was sacrificed but considered 'dead' based on coagulation index
[e] cited in Joermann 1998
[f] individual recovered from moribund state after administration of antidote, but assumed 'dead' without antidote treatment

Table 23. Secondary Hazards of Diphacinone to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of diphacinone toxicity[a]	Reference
Mink	nutria fed 0.01% carrot bait for up to 10 days	ad lib.	5-18	3	3	no survivors	Evans and Ward 1967
Mongoose	rats fed 0.005% bait for 5 days	1	1	1	0	nr	Pank and Hirata 1976
			3	1	1	no survivors	
			5	2	2	no survivors	
			6	1	1	no survivors	
			7	1	1	no survivors	
			8	1	1	no survivors	
			10	1	1	no survivors	
Ermine	deer mice fed 0.01% bait for 10 days	2	5	2	1	nr	Pank and Hirata 1976
Striped skunk	deer mice fed 0.01% bait for 10 days	2	5	5	0	nr	Pank and Hirata 1976
Deer mouse	liver from diphacinone-poisoned owls	1 g daily	7	4	1	3 (ct)	Pank and Hirata 1976
Rat	meat containing 0.5 ppm ai	ad lib.	6	8	4	nr	Savarie et al. 1979
Dog (domestic)	nutria fed 0.01% carrot bait for up to 10 days	ad lib.	6-10	3	3	no survivors	Evans and Ward 1967

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported

Table 24. Secondary Hazards of Warfarin to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of warfarin toxicity[a]	Reference
Mink	nutria fed 0.025% bait for at least 7 days	ad lib.	8-15	3	3	no survivors	Evans and Ward 1967
Mink	rabbits fed 25 or 67 ppm ai bait[b] for 5 weeks	ad lib.	28	50	0	0	Aulerich et al. 1987
Least weasel	mice fed 0.001% bait, 0.005% bait, or 0.02% bait for 3 days	ad lib.	90 / 29-90 / 12-57	2 / 2 / 2	0 / 1 / 2	2 (ct) / 1 (ct) / no survivors	Townsend et al. 1984
European ferret	prairie dogs fed 0.05% bait[b] for 15 days	1	7	10	0	0	Carlet and Mach 1997
European ferret	prairie dogs fed 0.05% bait[b] for 5 days	ad lib.	5	10	0	0	Mach 1998
Raccoon	rats fed 0.025% bait for 5 days	1 / 3	5 / 5	8 / 10[c]	0 / 0	0 / 0	EPA 1982
Dog (domestic)	nutria fed 0.025% bait for at least 7 days	ad lib.	8-16	3	1	2 (eb/ct)	Evans and Ward 1967
Dog (domestic)	mice fed 0.025% bait, 0.05% bait; mice dosed with 2.5 mg ai; 10 mg ai; 40 mg ai	4-10 / 10 / 1 / 1 / 1	56 / 56 / 56 / 25 / 17	4 / 1 / 1 / 1 / 1	0 / 0 / 0 / 1 / 1	0 / 0 / 0 / no survivors / no survivors	Prier and Derse 1962

[a] eb = external bleeding; ih = internal hematoma; bl = bleeding (unspecified); ct = increased blood coagulation time; nr = not reported
[b] registered baits are 0.025% ai
[c] the 10 test animals included the 8 individuals from the first trial plus 2 additional untested individuals

Comparative anticoagulant studies: Marsh and Howard (1986) conducted a pen study to determine if ground squirrels fed either bromadiolone or chlorophacinone pose a secondary hazard to coyotes. The ground squirrels were fed either 0.01% ai bromadiolone bait or 0.01% ai chlorophacinone bait for 5 consecutive days. Each coyote (7 per rodenticide) was offered 1 dead ground squirrel per day for 5 days and observed for 30 days posttreatment. Three coyotes died after feeding on the dead ground squirrels previously fed chlorophacinone. All 7 coyotes fed dead ground squirrels previously fed bromadialone survived, although 2 consumed very little of their normal food rations for 8 to 16 days after treatment.

Pank and Hirata (1976) fed poisoned rats to mongooses to examine possible secondary hazards of anticoagulant rodenticides. The rats were fed for 5 days with baits that included 0.002% ai brodifacoum, 0.005% ai bromadiolone, 0.005% ai chlorophacinone, and 0.005% ai diphacinone. One rat per day was offered to mongooses for periods ranging from 1 to 10 days. Exposure to rats fed either chlorophacinone or diphacinone resulted in deaths of 7 of 8 mongooses exposed for 3 to 10 days. Three of four mongooses fed rats that were previously fed bromadiolone were killed, however only 1 mongoose death (of 4 tested) was attributed to brodifacoum. It is noteworthy that although baits registered for rat and mouse control are 50 ppm bromadiolone, the bait used to feed the rats in this study was only 20 ppm.

Evans and Ward (1967) demonstrated that feeding on nutria for several days or more can pose a hazard to minks and dogs when these nutria have been previously been fed diphacinone and warfarin. In this study the rodenticide exposed nutria, with skin, head, tail, feet, and intestines removed, were fed to 3 commercial mink and 3 mongrel dogs. All mink and dogs died within 5 to 17 days of the secondary exposure to diphacinone. The 3 mink exposed to warfarin died within 8 to 15 days. Two of the 3 dogs survived exposure to warfarin for 16 days, although both had bloody feces and one became lethargic.

Others (non-anticoagulants): Fewer secondary-hazard testing has been done with the non-anticoagulant rodenticides, but the available data indicate considerably less hazards than for the anticoagulants. Only 3 (4%) of 77 test animals (foxes, dogs, ferrets, weasels, domestic cats, mink, mongooses) died after feeding on rodents poisoned with zinc phosphide in 10 studies (Table 25). Some regurgitation of prey was reported in animals that died and in some survivors that consumed GI tracts of zinc phosphide-poisoned rodents (Evans 1965, Schitoskey 1975, Hill and Carpenter 1982, Tkadlec and Rychnovsky 1990). Some animals learned to avoid eating the GI tract. In 2 cholecalciferol studies, 18 dogs and 12 feral house cats consumed either poisoned ground rats or brushtail possums (*Trichosurus vulpecula*) for up to 5 days with no deaths, although some reversible signs of toxicosis were reported in the dogs (Table 26). In one study with bromethalin, 4 dogs survived with no observed adverse effects after feeding for 14 days on rats that were poisoned for 1 day (Table 27).

Table 25. Secondary Hazards of Zinc Phosphide to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of zinc phosphide toxicity	Reference
Red fox and Gray fox	voles fed bait (86.94 mg ai/kg)	ad lib.	3	4	0	2[a]	Bell and Dimmick 1975
Kit fox	kangaroo rats dosed at 480 mg/rat	1 1	1 3	1 2	0 0	1[b] 2[b]	Schitoskey 1975
Dog (domestic)	poisoned nutria carcasses or organs	varied or not reported	varied from 1 to 150 days	8	1	2[b]	Evans 1965
Least weasel	voles fed 5% bait[c]	1	3	2	0	0	Tkadlec and Rychnovsky 1990
Cat (domestic)	voles fed 5% bait[c]	7-11	1-2	2	1	1[b]	Tkadlec and Rychnovsky 1990
Cat (domestic)	poisoned nutria carcasses or liver	ad lib.	1-10	3	1	2[b]	Evans 1965
Mink	prairie dogs fed 2% ai bait	200 g	30	5	0	0	Tietjen 1976
Mink	poisoned nutria	ad lib.	10 20	3 2	0 0	0 0	Evans 1965
Mongoose	rats fed bait (% ai not reported)	10 total	5-10	4	0	0	Pank 1972
Mongoose	rats fed 1% ai bait[c]	5-7 total	35	2	0	0	Doty 1945[d]
Siberian ferret	rats fed 2% bait or orally dosed at 40, 80, or 160 mg/rat	1 rat every other day	10	16	0	13[e]	Hill and Carpenter 1982
European ferret	organs or carcass from prairie dogs fed 2% bait	ad lib.	3	20	0	0	Matschke and Andrews 1990

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of zinc phosphide toxicity	Reference
European ferret	mice	3-4	1	3	0	0	Ueckermann 1982[f]

[a] feeding-behavior irregularities were reported
[b] some prey regurgitated if stomach contents consumed; no other ill effects were observed
[c] baits registered in the U. S. are 2% ai
[d] cited in Johnson and Fagerstone 1994 and Evans 1965
[e] some altered blood chemistry (hemoglobin, globulin, cholesterol, triglycerides) and prey regurgitation was reported
[f] personal communication to G. Joermann (Joermann 1998)

Table 26. Secondary Hazards of Cholecalciferol to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of cholecalciferol toxicity	Reference
Cat (domestic)	brushtail possums dosed with 20 mg ai/kg	ad lib.	5	12	0	0	Eason et al. 1996
Dog (domestic)	brushtail possums poisoned with an LD95 dose in cereal bait	1	1	4	0	0	Eason et al. 2000
			2	2	0	0	
			5	12	0	12[a]	

[a] partial anorexia and varying degrees of lethargy from day 4 to 14 after dosing; all recovered

Table 27. Secondary Hazards of Bromethalin to Mammals in Laboratory Studies

Predator/scavenger (p/s)	Prey offered to p/s	No. prey offered daily per p/s	No. days p/s exposed	No. p/s exposed	No. p/s dead	No. survivors with signs of bromethalin toxicity	Reference
Dog (domestic)	ground meat from rats fed 0.005% ai bait for 1 day	600 g	14	4	0	0	van Lier 1981

Potential Primary Risks

Birds

The amount of bait and number of rat-bait pellets (0.2 g each) that birds of various sizes need to eat in a single feeding to obtain a dose expected to be lethal to 50% of the individuals in the population (i.e., LD50 dose) are estimated from the acute oral toxicity for the northern bobwhite or mallard. Estimates of food-ingestion rates (g dry matter per day) are determined from allometric equations in Nagy (1987; cited in EPA 1993): 6.1 g for a 25-g passerine, 9.6 g for a 100-g non-passerine, and 53.9 g for a 1000-g non-passerine. A 25-g passerine can potentially ingest an LD50 dose by consuming 0.02 g zinc phosphide bait (<1 pellet), 0.13 g brodifacoum bait (<1 pellet), 0.26 g difethialone bait (<2 pellets), or 1.2 g (6 pellets) of bromethalin bait (Table 28). Larger non-passerines need to consume more pellets to obtain an LD50 dose but could potentially do so. In contrast, 25- to 1000-g birds would need to eat 100 or more pellets to ingest an LD50 dose of bromadiolone, chlorophacinone, diphacinone, warfarin, or cholecalciferol.

Most of the rodenticide baits, but especially brodifacoum, difethialone, and zinc phosphide, exceed the Agency's LOC for avian dietary risk (Table 29). The Agency presumes potential acute risk when the dietary RQ equals or exceeds 0.5 for non-endangered species and 0.1 for endangered species. Brodifacoum, difethialone, and zinc phosphide exceed the LOC for non-endangered species by 86- to 126-fold for the northern bobwhite and 14- to 50-fold for the mallard. The exceedances are even higher for endangered species.

Table 28. Comparative Risk to Birds From a Single Feeding of Rodenticide, Based on the Amount of Bait Needed to Ingest an LD50 Dose (i.e., a dose lethal to 50% of the individuals in a population)

Rodenticide	mg ai/kg in bait	LD50[a] (mg ai/kg)	25-g passerine bait (g)	25-g passerine % of daily food intake[b]	25-g passerine no. bait pellets[c]	100-g non-passerine bait (g)	100-g non-passerine % of daily food intake	100-g non-passerine no. bait pellets	1000-g non-passerine bait (g)	1000-g non-passerine % of daily food intake	1000-g non-passerine no. bait pellets
Second-generation anticoagulants											
Brodifacoum	50	0.26	0.13	2.1	0.6	0.52	5.4	2.6	5.2	9.6	26
Difethialone	25	0.26	0.26	4.3	1.3	1.04	10.8	5.2	10.4	19.3	52
Bromadiolone	50	138	69	>100	345	276	>100	1380	2760	>100	>1000
First-generation anticoagulants											
Chlorophacinone	50	258	129	>100	645	516	>100	2580	5160	>100	>1000
Chlorophacinone	100	258	64.5	>100	322	258	>100	1290	2580	>100	>1000
Diphacinone	50	>400	200	>100	1000	800	>100	4000	8000	>100	>1000
Diphacinone	100	>400	100	>100	500	400	>100	2000	4000	>100	>1000
Warfarin	250	620	62	>100	310	248	>100	1240	2480	>100	>1000
Others (non-anticoagulants)											
Bromethalin	100	4.6	1.2	18.8	6	4.6	47.9	23	46	85.3	230
Zinc phosphide	20,000	12.9	0.02	0.3	<0.1	0.07	0.7	0.3	0.7	1.2	3.2
Cholecalciferol	750	>600	20	>100	100	80	>100	400	800	>100	4000

[a] the LD50 values used in the calculations are from northern bobwhite or mallard acute-oral toxicity studies required by the Agency to support pesticide registration (see Tables 3, 4, and 5); ">" values are assumed to be "=" values for the calculations

[b] food ingestion rates (g dry matter per day) are based on the allometric equations of Nagy 1987 (cited in EPA 1993): 6.1 g for a 25-g passerine, 9.6 g for a 100-g non-passerine, and 53.9 g for a 1000-g non-passerine

[c] assuming a bait pellet weighs 0.2 g (information provided by Syngenta Crop Protection, Inc., Greensboro, NC)

Table 29. Avian Dietary Risk Quotients. RQs ≥0.5 (for non-endangered species) or ≥ 0.1 (for endangered species) Exceed the Agency's Level of Concern for Acute Risk to Birds.

Rodenticide	mg ai/kg in bait	Test species	LC50[a] (ppm)	Dietary RQ[b]
Second-generation anticoagulants				
Brodifacoum	50	northern bobwhite	0.8	63
		mallard	2.0	25
Difethialone	25	northern bobwhite	0.5	50
		mallard	1.4	18
Bromadiolone	50	northern bobwhite	37.6	1.4
		mallard	158	0.3
First-generation anticoagulants				
Chlorophacinone	50	northern bobwhite	56	0.9
		mallard	172	0.3
Chlorophacinone	100	northern bobwhite	56	1.8
		mallard	172	0.6
Diphacinone	50	northern bobwhite	>5000	n/a
		mallard	906	<0.1
Diphacinone	100	northern bobwhite	>5000	n/a
		mallard	906	0.1
Warfarin	250	northern bobwhite	625	0.4
		mallard	890	0.3
Others (non-anticoagulants)				
Bromethalin	100	northern bobwhite	210	0.5
		mallard	620	0.2
Zinc phosphide	20,000	northern bobwhite	469	43
		mallard	2885	7
Cholecalciferol	750	northern bobwhite	528	1.4
		mallard	1190	0.6

[a] LC50 values used to calculate the dietary RQs are from dietary toxicity studies required by the Agency to support pesticide registration (see Tables 3, 4, and 5)
[b] RQ = ppm ai in bait/LC50; RQs are not calculated when the LC_{50} value categorizes the active ingredient as practically nontoxic (i.e., LC50 >5000 ppm) to the test species

Based on the comparative analysis model, zinc phosphide, brodifacoum, and difethialone stand out as the rodenticides posing the greatest potential primary risk to birds. This result is based on two measures of effect: mean dietary RQ (ppm bait/LC50) and the number of bait pellets needed for a 100-g bird to ingest an LD50 dose in a single feeding. In order to correctly calculate the weighted averages, the inverse of the number of bait pellets needed for a 100-g bird to ingest an LD50 dose in a single feeding was calculated and used in the comparative analysis model. The sum of the weighted average values for all the rodenticides is tabulated in the 'Summary values' column in Table 30 and also is depicted in Figure 2. Brodifacoum has higher summary risk values than difethialone for both measures of effect. The mean dietary RQ appears to be the most significant measure of effect leading to the conclusion that brodifacoum poses greater potential risk to birds than either difethialone or zinc phosphide and that difethialone poses greater potential risk to birds than does zinc phosphide.

Table 30. Comparative Analysis Model Results for Primary Risk to Birds

Rodenticide	mg ai/kg bait	Measure-of-effect values		Summary values
		Mean dietary RQ[a]	Inverse of the LD50 dose for a 100-g bird (no. bait pellets)[b]	
Brodifacoum	50	44.00	0.38	5.58
Bromadiolone	50	0.85	0.00	0.10
Bromethalin	100	0.35	0.04	0.10
Chlorophacinone	100	1.20	0.00	0.14
Chlorophacinone	50	0.60	0.00	0.07
Cholecalciferol	750	1.00	0.00	0.12
Difethialone	25	34.00	0.19	4.15
Diphacinone	100	0.10	0.00	0.01
Diphacinone	50	0.10	0.00	0.01
Warfarin	250	0.35	0.00	0.04
Zinc Phosphide	20,000	24.75	3.33	7.81

[a] from Table 29
[b] from Table 28

Figure 2. Comparative Analysis Model Summary Values For Primary Risk to Birds

Graph 1. Greatest Primary Risk to Birds
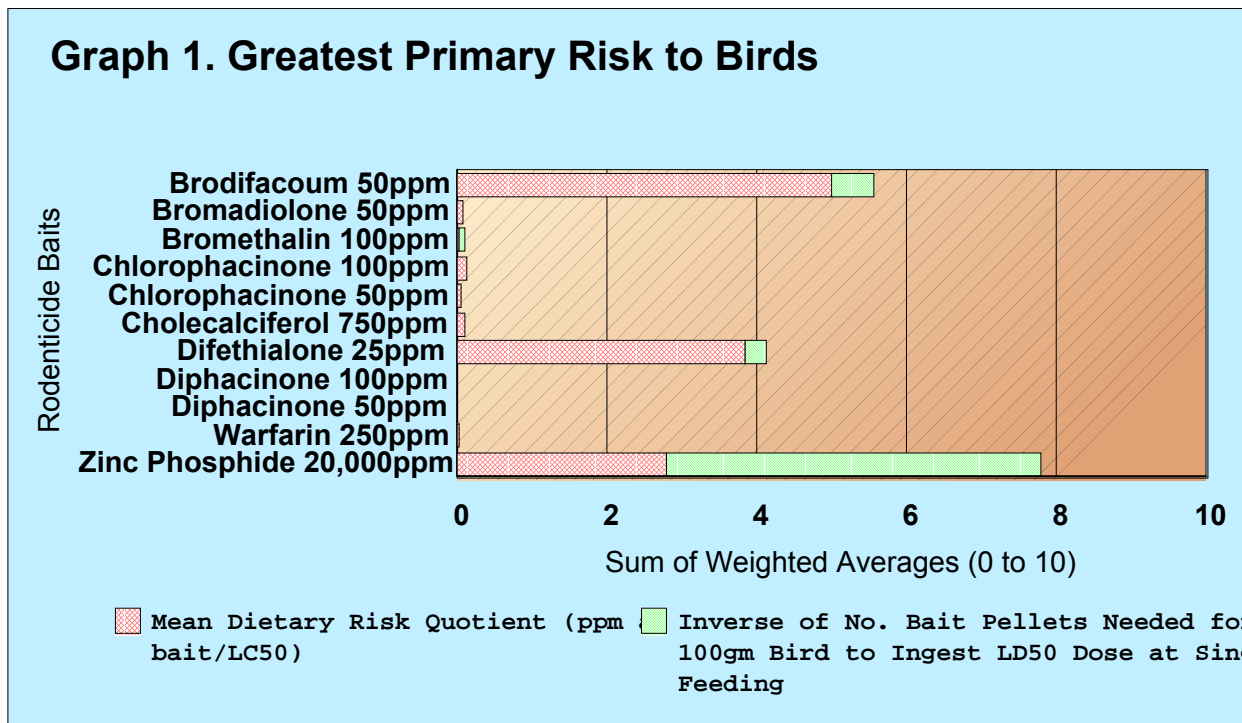
Primary risk to birds also is analyzed by an alternative approach, using an $HD_5(50\%)$ reference value to calculate the amount of bait needed to provide an LD50 dose to a 100-g bird instead of the LD50 values for bobwhite quail or mallard ducks. The $HD_5(50\%)$ is the 5% tail of the avian LD50 toxicity distribution calculated with 50% probability of overestimation (Mineau et al.2001). The authors believe that the *"approach of using reference values based on species specific extrapolation factors represents the most unbiased attempt to date to compare the toxicity of pesticides for which many data points are available with those about which we know very little."* Utilizing the $HD_5(50\%)$ reference value, rather than the LD50, does not change the rankings (see Attachment C for more details, including reference values for the rodenticides and a graphical comparison of the summary measures of effect for each of the 2 approaches).

Findings from experimental studies conducted in field or other outdoor settings, along with information obtained during operational programs, provide useful data linking exposure to adverse effects in birds. Zinc phosphide, chlorophacinone, and diphacinone are registered for field and other outdoor uses, and brodifacoum has been used to control introduced rats on some U. S. oceanic islands. Such uses often allow broadcast or other unprotected applications (e.g., spot-baiting) that exposes bait to birds that might be attracted to grain pellets or treated grains (e.g., corn, wheat, oats).

Howald et al. (1999) reported nontarget effects to birds during a brodifacoum rat-control program on Langara Island, Canada. Thirteen common ravens (*Corvus corax*) were found dead 12 to 47

days after baiting began, and all had brodifacoum residue (0.985 to 2.522 ppm) in their liver. Remains of 7 other ravens also were found but not analyzed. At least 8 bait stations were raided by ravens, which either reached into the stations and pulled out bait blocks or tipped the stations to roll out the bait, even though the stations were secured. Some of the ravens also fed on poisoned rats. Brodifacoum also was detected in a pooled sample of 3 northwestern crows (*C. caurinus*) collected 12 days after the start of baiting.

Brodifacoum also was detected in song sparrows (*Melospiza melodia*) collected by shotgun on Langara Island (Howald 1997). Residue levels of 0.643 and 0.567 ppm were detected in 2 of 4 pooled liver samples (2 to 3 individuals per sample) and 0.058 ppm in 1 pooled sample (4 individuals) analyzed for whole-body residue. It is not known how the sparrows were exposed or whether any died. They may have consumed bait crumbs found scattered around bait stations and along rat runways but also might have eaten invertebrates that fed on bait. Howald (1997) also found that snails (*Vespericola* sp., *Haplotrema* sp.) and banana slugs (*Ariolimax* sp.) commonly fed on brodifacoum bait and may pose a risk to birds and nontarget mammals that consume them.

Godfrey (1985) cited an incident at an aviary where several birds (avocets, pittas, plovers, finches, thrushes, warblers, crakes, honey creepers) died after being exposed to brodifacoum. Brodifacoum concentrations of 0.081 to 1.69 ppm were reported in tissues of dead birds. Because bait was applied in bait stations, it was assumed that the birds were exposed by feeding on pavement ants and cockroaches that had eaten bait.

Brodifacoum baits (20 ppm or 50 ppm) are used for field control of rats and brushtail possums in New Zealand, and much useful information on nontarget risks has been reported. However, because of increased concerns about nontarget mortality and movement of brodifacoum through the food chain, its use is being reviewed and curtailed in many areas in New Zealand (Eason and Murphy 2001). The following studies provide further information on primary risks to birds, based on mortality reported during field studies or operational control programs.

Eason and Spurr (1995) reviewed the impacts of brodifacoum baiting on nontarget birds during baiting programs in New Zealand, where bait is applied in bait stations (50 ppm cereal-based wax blocks) or aerially broadcast (20 ppm pellets) in a single application. They report mortality of a wide range of bird species, including 33 indigenous species or subspecies and 8 introduced species or subspecies, and presume most resulted from primary exposure. Populations of indigenous rails (weka, *Gallirallus australis*; pukeko, *Porphyrio porphyrio*) monitored during rodenticide baiting operations were severely reduced: "For example, the entire population of western weka on Tawhitinui island were exterminated by consumption of Talon® 50WB intended for ship rats, which they obtained by reaching into bait stations, by eating baits dropped by rats, and by eating dead or dying rats (Taylor 1984)." On another island, 80 to 90% of the Stewart Island weka population was killed by baits applied for Norway rats. Aerial application of 0.002% bait on two other islands reduced a weka population by about 98% and a pukeka population by >90%. Numbers of quail, blackbirds, sparrows, and myna were markedly reduced on another island. Some other species suffered no apparent adverse effects.

Dowding et al. (1999) found numerous dead birds after an aerial baiting operation to eradicate rats and mice and reduce rabbit numbers on Motuihe Island, New Zealand. Brodifacoum bait (20 ppm) was applied twice, with 9 days between applications. Nontarget species were monitored, including pukeka (3 groups of 98 birds), a flock of 52 paradise shelduck (*Tadorna variegata*), 8 New Zealand dotterels (*Charadrius obscurus*), and 14 variable oystercatchers (*Haematopus unicolor*). There was no evidence that dotterels or oystercatchers were adversely affected, but mortality of pukeko and shelduck was 49% and 60%, respectively. Birds of 10 species were found dead. The liver from each of 29 dead birds of 10 species was analyzed. All livers contained brodifacoum residue, with mean levels per species ranging from 0.56 to 1.43 ppm. Chaffinch (*Fringilla coelebs*), North Island robin (*Persica australis longipes*), North Island weka, and North Island saddleback (*Philesturnus carunculatus rufusater*) also were found dead after a brodifacoum baiting on Mokoia Island, New Zealand (Stephenson et al.1999).

Eason and Spurr (1995) report that invertebrates have been observed eating brodifacoum bait, and residues were detected in beetles collected in bait stations in New Zealand. Invertebrates have different blood-clotting mechanisms than vertebrates and may not be affected by anticoagulants, but insectivorous animals feeding on the contaminated invertebrates might be at risk. Robertson et al. (1999) monitored brown kiwis (*Apteryx mantelli*) potentially at risk from brodifacoum applications in bait stations placed for possum control. Although there was no evidence that adult kiwi died as a result of the applications, including 55 that were radio-tagged, brodifacoum was detected at levels of 0.01 to 0.18 ppm in 3 of 4 chicks found dead from unknown causes. The authors speculated that the chicks may have obtained bait or may have eaten invertebrates that ingested bait. The death of an endangered Seychelles magpie-robin (*Copsychus sechellarum*) on Fregate Island, Seychelles, was likely due to its feeding on insects that had taken brodifacoum baits from bait stations (Thorsen et al. 2000). Loss of bait, attributed mostly to consumption by millipedes, crabs, and skinks, averaged 17% per night.

Hegdal (1985) conducted a study in Washington to examine risks to game birds from a 0.005% ai diphacinone bait applied for vole control in orchards. Most orchards were treated twice, with 20 to 30 days between treatments, at an average rate of 12.9 kg/ha (11.5 lb/acre). Telemetry was used to monitor the fate of 52 ring-necked pheasants, 18 California quail, and 30 chukar potentially exposed to the bait. About half of the quail and all chukar were pen-raised and had been released into the orchards. Dead game birds and other animals found were necropsied and any available tissue collected for residue analysis. Eight of 30 pheasants, 9 of 15 quail, and 1 of 10 chukar collected by the researchers or shot by hunters contained diphacinone residue in the liver. Bait made up as much as 90% of crop contents of some birds. No residue was detected in 4 passerines collected 31 to 73 days after treatment. The author concluded that risk to game birds in orchards appeared to be low but emphasized that substantial quantities of bait were eaten and longer-term behavioral and physiological effects, such as susceptibility to predation, need to be considered along with direct mortality in order to evaluate potential hazards from exposure.

Some information on potential nontarget risks was gained during field studies conducted to assess the efficacy of 0.01% ai and 0.005% ai diphacinone and chlorophacinone baits against California ground squirrels inhabiting rangeland (Baroch 1994 a,b; 1996a,b). For each of these rodenticides,

trials included separate spot-baiting applications with 0.01% ai and 0.005% ai grain baits and a trial in which 0.005% ai grain bait was only available in bait stations. Searches for nontarget carcasses were made on and around treated plots after baiting. One dead dove and 2 dead roadrunners (*Geococcyx californicus*) were found on treatment plots, but there was no evidence that these birds had eaten any bait.

Hegdal and Gatz (1977) evaluated risks to nontarget wildlife from zinc phosphide bait (2% ai) broadcast by ground or air at rates of 5 to 10 lb per acre for vole control in Michigan orchards. Carcass searches were made across 672 of 950 treated acres in the 2 weeks after treatment. Bird carcasses recovered included 1 blue jay (*Cyanocitta cristata*) and 1 of 5 radio-equipped pheasants. Northern bobwhite were observed, and some were seen feeding on bait, but no carcasses were found.

Ramey et al. (1998) examined risk to radio-collared ring-necked pheasants from zinc phosphide baiting in alfalfa fields in California. Pheasants were rarely found in fields when bait was applied after the alfalfa was cut. The pheasants preferred other habitats at this time, and none died as a result of the baiting. Results were somewhat confounded by the use of some pen-reared pheasants, most of which were quickly taken by predators.

Johnson and Fagerstone (1994) reviewed a number of field studies conducted to evaluate primary effects of zinc phosphide on nontarget wildlife for the following uses: prairie dogs, ground squirrels, and jackrabbits on rangeland; California ground squirrels and rats on ditch banks; voles and rats in orchards; and rats in sugarcane. They also note that some information on nontarget hazards has also been gathered for use against voles in alfalfa and muskrats and nutria in wetlands. They concluded: "Although field studies to determine effects of zinc phosphide on nontarget wildlife have generally found no significant effects, under certain circumstances operational zinc phosphide applications have resulted in mortality of nontarget wildlife."

Quy et al. (1995) observed small song birds, especially chaffinches, that had difficulty flying and appeared to be ill during a rat-control operation with calciferol bait in the United Kingdom. A number of dead birds were found; all had abnormally high calcium deposits in their kidneys, suggesting calciferol toxicosis.

Nontarget mammals

The amount of bait and number of rat-bait pellets that nontarget mammals of various sizes need to eat in a single feeding to obtain an LD50 dose (i.e., the dose expected to be lethal to 50% of the individuals in the population) is estimated from the acute oral toxicity for the laboratory rat. Estimates of food-ingestion rates (g dry matter per day) are determined from allometric equations in Nagy (1987; cited in EPA 1993): 3.8 g for a 25-g rodent, 8.3 g for a 100-g rodent, and 68.7 g for a 1000-g mammal. A 25-g rodent can potentially ingest an LD50 dose by consuming less than 1 g (~5 pellets) of most baits, and a single pellet of zinc phosphide or brodifacoum can provide this dose (Table 31). Larger mammals also are potentially at risk if they eat baits of most of these rodenticides. For warfarin, there is some uncertainty that a single feeding would be lethal to most individuals, because warfarin is reported to require multiple feedings over a period of a few days to be efficacious (Papworth 1958, Jackson and Ashton 1992, Timm 1994).

Dietary RQs are calculated for brodifacoum, bromadiolone, and the 3 first-generation anticoagulants (Table 32). RQs cannot be determined for difethialone and the 3 non-anticoagulants, because dietary data are not available. The RQs exceed the LOC 48- to 188-fold for non-endangered mammals and 240- to 943-fold for endangered mammals. This indicates a significant risk to nontarget mammals that feed on any of these baits.

Based on the comparative analysis model, zinc phosphide is ranked as the rodenticide posing the greatest potential primary risk to nontarget mammals, with brodifacoum ranked a distant second, and warfarin and bromadiolone an even more distant third and fourth. The results are based on a single measure of effect: the number of bait pellets needed for a 100-g mammal to ingest an LD50 dose in a single feeding. In order to correctly calculate the weighted averages, the inverse of the number of bait pellets needed for a 100-g mammal to ingest an LD50 dose in a single feeding was calculated and used in the comparative analysis model. The sum of the weighted average values for all the rodenticides is tabulated in the 'Summary values' column in Table 33 and presented graphically in Figure 3.

Table 31. Comparative Risk to Mammals From a Single Feeding of Rodenticide, Based on the Amount of Bait Needed to Ingest an LD50 Dose (i.e., a dose lethal to 50% of the individuals in a population)

Rodenticide	mg ai/kg in bait	LD50[a] (mg ai/kg)	25-g rodent			100-g rodent			1000-g mammal		
			bait (g)	% of daily food intake[b]	no. bait pellets[c]	bait (g)	% of daily food intake	no. bait pellets	bait (g)	% of daily food intake	no. bait pellets
Second-generation anticoagulants											
Brodifacoum	50	0.4	0.2	5.2	1	0.8	9.6	4	8	11.6	40
Difethialone	25	0.55	0.56	14.7	2.8	2.2	26.5	11	22	32	110
Bromadiolone	50	0.7	0.35	9.2	1.8	1.4	16.2	7	14	20.4	70
First-generation anticoagulants											
Chlorophacinone	50	6.2	3.1	81.6	15.5	12.4	>100	62	124	>100	620
Chlorophacinone	100	6.2	1.6	42	8	6.2	74.7	31	62	90.2	310
Diphacinone	50	2.3	1.2	31.6	6	4.6	55.4	23	46	67	230
Diphacinone	100	2.3	0.6	15.8	3	2.3	27.7	11.5	23	33.5	115
Warfarin	250	3	0.3	7.9	1.5	1.2	14.5	6	12	17.5	60
Others (non-anticoagulants)											
Bromethalin	100	9.9	2.5	65.8	12.5	9.9	119	49.5	99	>100	495
Zinc phosphide	20,000	21	0.03	0.7	0.13	0.1	1.2	0.5	1	1.5	5
Cholecalciferol	750	42	1.4	36.8	7	5.6	67.5	28	56	81.5	280

[a] the LD50 values used in the calculations are from laboratory rat or mouse acute-oral toxicity studies required by the Agency to support pesticide registration (see Tables 6, 7, and 8); the tabulated value is provided as an average if the LD50 differed between male and female

[b] food ingestion rates (g dry matter per day) are based on the allometric equations of Nagy 1987 (cited in EPA 1993): 3.8 g for a 25-g rodent, 8.3 g for a 100-g rodent, and 68.7 g for a 1000-g mammal

[c] assuming a bait pellet weighs 0.2 g (information provided by Syngenta Crop Protection, Inc., Greensboro, NC)

Table 32. Mammalian Dietary Risk Quotients. RQs ≥0.1 (endangered species) or ≥0.5 (non-endangered species) Exceed the Agency's Level of Concern for Acute Risk to Mammals.

Rodenticide	mg ai/kg in bait	Test species	LC50[a] (ppm)	Dietary RQ[b]
Second-generation anticoagulants				
Brodifacoum	50	laboratory rat	0.53	94.3
Bromadiolone	50	laboratory rat	0.92	54.3
First-generation anticoagulants				
Chlorophacinone	50	laboratory rat	1.14	43.8
Chlorophacinone	100	laboratory rat	1.14	87.7
Diphacinone	50	laboratory rat	2.08	24.0
Diphacinone	100	laboratory rat	2.08	48.1
Warfarin	250	laboratory rat	4.41	56.7

[a] LC50 values used to calculate the dietary RQs are from dietary toxicity studies conducted by the Agency's former Toxicology Section (see Tables 6 and 7); mammalian dietary data are not available for difethialone, bromethalin, zinc phosphide, and cholecalciferol
[b] RQ = ppm ai in bait/LC50

Table 33. Comparative Analysis Model Results for Primary Risk to Nontarget Mammals

Rodenticide	mg ai/kg bait	Inverse of the LD50 dose for a 100-g rodent (no. bait pellets)[a]	Summary value
Brodifacoum	50	0.25	1.25
Bromadiolone	50	0.14	0.71
Bromethalin	100	0.02	0.10
Chlorophacinone	100	0.03	0.16
Chlorophacinone	50	0.02	0.08
Cholecalciferol	750	0.04	0.18
Difethialone	25	0.09	0.45
Diphacinone	100	0.09	0.43
Diphacinone	50	0.04	0.22
Warfarin	250	0.17	0.83
Zinc Phosphide	20,000	2.00	10.00

[a] from Table 31

Figure 3. Comparative Analysis Model Summary Values For Primary Risk to Nontarget Mammals

Graph 2. Greatest Primary Risk to Mammals
Sum of Weighted Averages of Measure of Effect

Rodenticide Baits (y-axis):
- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

X-axis: Sum of Weighted Averages (0 to 10) — scale: 0, 2, 4, 6, 8, 10

Legend: ▨ Inverse of No. Bait Pellets Needed for 100gm Mammal to Ingest LD50 Dose at Feeding

The little information available on primary risk to mammals in the field has mostly come from animals found dead or moribund on treatment plots during efficacy trials and from an operational control program on a Canadian island. Howald (1997) reported that dusky shrews (*Sorex monticolus*) entered bait stations and fed on brodifacoum bait during a rat-control program on a Canadian island. By day 20 of baiting, shrews had eaten bait in 80% of the 42 rat bait stations. The shrew population declined sharply but rebounded to about half the prebaiting level after baiting stopped in 1994; however, shrew numbers declined further when baiting resumed in 1995. The long-term impact of baiting on the shrew population is unclear. No difference in population size was found pre- and post-baiting on a larger, adjacent island.

Some information on nontarget risks was gained during studies conducted to assess the efficacy of 0.01% ai and 0.005% ai chlorophacinone and diphacinone baits against California ground squirrels inhabiting rangeland. Baroch (1996a,b) applied chlorophacinone bait by spot-baiting or in bait stations, and treatment plots were searched periodically for target and nontarget carcasses . Thirty-six nontarget deer mice, San Joaquin pocket mice (*Perognathus inornatus*), and woodrats were found dead; based on the presence of blue dye incorporated into the bait and/or signs of internal or external hemorrhaging, mortality of 31 (86%) mice was attributed to the baiting. Four dead desert cottontails (*Sylvilagus auduboni*) and 2 dead Botta's pocket gophers (*Thomomys*

bottae) also were collected, but there was no evidence that these had been exposed to bait. In another study designed to assess the efficacy of chlorophacinone and diphacinone baits, some small mammals, especially kangaroo rats (*Dipodomys* spp.), were found dead on treated plots (Salmon et al. 2002). Collectively, these studies indicate that some small nontarget mammals will be killed when these baits are applied for controlling ground squirrels.

Comparative Toxicokinetics: Absorption, Metabolism and Excretion of Anticoagulants

Considerable differences exist in absorption, metabolism and excretion of the anticoagulants, which may have important consequences for both primary and secondary risk. A compound that is rapidly metabolized or excreted from a primary consumer may result in a lesser risk than one that bioaccumulates with repeated sublethal exposure, even if repeated exposure occurs weeks or even months after initial exposure (Eason and Murphy 2000). Those compounds more rapidly cleared from the body are less likely to pose such long-term risk. The available information indicates that the second-generation anticoagulants are much more persistent in animal tissue than are the first-generation anticoagulants. Data also suggest that brodifacoum may be more persistent than either difethialone or bromadiolone. Few data exist for the non-anticoagulants but, based on lack of toxicity in secondary tests, apparently they are not retained in toxicologically significant amounts in animal tissues.

Most of the available information is from studies that examined elimination and retention following a single, sublethal oral dose of anticoagulant. In a baiting situation, however, rats or mice will not die for several days or more after ingesting a lethal dose and may continue consuming bait. A wild Norway rat may ingest as many as 80 brodifacoum LD50 doses if feeding only on bait and as many as 40 LD50 doses if offered a choice of bait or untreated food (ICI Americas, Inc. 1978b). In a situation of repeat exposure for several days or more, anticoagulant may circulate in the blood at higher levels and for a longer time than suggested by studies in which only a single, sublethal dose was administered (Belleville 1981).

Elimination of anticoagulants from the body is sometimes described as rapid (e.g., Poché 1986, Kaukeinen et al. 2000). However, such characterizations usually refer to the rapid excretion of unbound or unabsorbed material being excreted principally in feces during the first few days after administration. Alternatively, it may refer to the clearance from the blood as compared with tissue retention. Rather than concentrating on the amount of anticoagulant excreted, risk assessments should focus on the material retained in the body after single and multiple exposures. The studies summarized below indicate the differences among these compounds and their potential to bioaccumulate with repeat exposure.

Second-generation anticoagulants

Second-generation compounds are not readily metabolized, and the major route of excretion of unbound compound is through the feces. After absorption, high concentrations circulate in the blood and are rapidly established in the liver and other tissues. Half-lives in the blood of rats are 1.0 to 1.4 days for bromadiolone and 6.5 days for brodifacoum (Table 34). Elimination from liver is much slower and biphasic, with a very prolonged terminal phase. It is apparent from the studies discussed below that a proportion of any ingested dose of a second-generation anticoagulant bound in the liver, kidney, or pancreas remains in a stable form for some time and is only very slowly excreted.

Hawkins et al. (1991) administered brodifacoum and bromadiolone to rats in a single oral dose of 0.2 mg ai/kg. Elimination was biphasic, with half-lives of 63 days for brodifacoum and 17 days for bromadiolone in the initial 28 days and 282 and 318 days, respectively, in the terminal phase. These differences are not statistically significant, but mean liver concentrations of brodifacoum were significantly higher for brodifacoum throughout the study (Table 35).

Bratt and Hudson (1979) found that radiolabeled brodifacoum was rapidly and almost completely absorbed when administered to rats in a single oral dose (0.25 mg ai/kg). After 10 days, about 11 to 14% had been eliminated in urine and feces, but 74.6% of the dose was still retained in body tissues. Almost half the dose administered was detected in the carcass and skin, with lesser amounts in the liver (22.8%), pancreas (2.3%), kidney (0.8%), spleen (0.2%), and heart (0.1%). The estimated half-life of brodifacoum in rat tissues was estimated to be 150 to 200 days.

Batten and Bratt (1987) orally dosed male rats with a single dose of radiolabeled brodifacoum at doses of either 0.02. 0.15, or 0.35 mg ai/kg. The highest concentration of radioactivity in the liver was found 1 day after dosing, but 21 to 34% of the dose was still detected after 13 weeks and >11% after 104 weeks (Table 36). The elimination half-life for the 2 lowest doses was 350 days. For rats dosed at 0.35 mg ai/kg, a near-lethal dose (LD50 = 0.39 to 0.56 mg ai/kg), elimination from the liver was biphasic and consisted of a rapid phase (days 1 to 4) in which the half-life was approximately 4 days and a slower phase (days 28 to 84) in which the half-life was 128 days. Two rats dosed at that level died during the study. Signs of brodifacoum toxicosis were observed in some survivors. Some dosed rats also had gained less body-weight and displayed signs of internal hemorrhage when dissected.

Table 34. Persistence of Second-generation Anticoagulants in Blood and Liver

Anticoagulant	Species	Dose (mg ai/kg)	No. doses	Blood $t_{1/2}$[a] (days)	Liver retention[a,b] (days)	Reference
Brodifacoum	rat	0.02 or 0.15 0.35	1 1		350[c] ($t_{1/2}$) 128[d] ($t_{1/2}$)	Batten and Bratt 1990
Brodifacoum	rat	0.2	1		282 ($t_{1/2}$)	Hawkins et al. 1991
Brodifacoum	rat	0.25	1		150-200 ($t_{1/2}$)	Bratt and Hudson 1979
Brodifacoum	rat	0.06	4 (at weekly intervals)		136 ($t_{1/2}$)	Belleville 1991
Brodifacoum	rat	0.35	1		130 ($t_{1/2}$)	Parmar et al. 1987
Brodifacoum	rat			6.5	>80	Bachmann and Sullivan 1983[e]
Brodifacoum	possum	0.1	1	20-30	>252	Eason et al. 1996
Brodifacoum	rabbit			2.5		Breckenridge et al. 1985[e]
Brodifacoum	sheep	0.2 or 2.0	1		>128	Laas et al. 1985
Brodifacoum	dog			6		Woody et al. 1992[e]
Brodifacoum	dog			0.9-4.7		Robben et al. 1998[e]
Brodifacoum	human			0.7-1.5		Weitzel et al. 1990[e]
Difethialone	rat	0.5	1	2.3	126 ($t_{1/2}$) (175%, 98&)	Belleville 1986
Difethialone	rat	0.06	4 (at weekly intervals)		74 ($t_{1/2}$)	Belleville 1991
Difethialone	dog			2.2-3.2		Robben et al. 1998[e]

Anticoagulant	Species	Dose (mg ai/kg)	No. doses	Blood $t_{1/2}$[a] (days)	Liver retention[a,b] (days)	Reference
Bromadiolone	rat	0.2	1		318 ($t_{1/2}$)	Hawkins et al. 1991
Bromadiolone	rat	0.93	1	1.0-1.1	170 ($t_{1/2}$)	Parmar et al. 1987
Bromadiolone	rat	0.8	1	1.1		Kamil 1987[e]
		3.0	1	2.4		
Bromadiolone	sheep	2.0	1		256	Nelson and Hickling 1994[e]

[a] $t_{1/2}$ for plasma and liver is the elimination half-life (β-phase)
[b] liver retention is expressed as either the time period for which residues persist or as the elimination half-life
[c] the elimination half-life of 350 days is for a single oral dose of 0.02 or 0.15 mg ai/kg; elimination was not biphasic
[d] the elimination half-life of 128 days is the terminal phase for a single oral dose of 0.035 mg ai/kg; elimination was biphasic
[e] cited in Eason et al. (2001)

Table 35. Hepatic Concentrations of Brodifacoum and Bromadiolone in Rats Administered a Single Oral Dose of 0.2 mg ai/kg (adapted from Hawkins et al. 1991)

Days after dosing	Brodifacoum (ppm)	Bromadiolone (ppm)
1	1.107 ± 0.038	0.983 ± 0.049
7	1.078 ± 0.088	0.844 ± 0.051
14	1.121 ± 0.077	0.727 ± 0.098
50	0.838 ± 0.075	0.440 ± 0.042
100	0.679 ± 0.061	0.366 ± 0.026
200	0.539 ± 0.028	0.282 ± 0.041

Table 36. Percentage of a Single Dose of Brodifacoum Retained in the Liver for up to 104 Weeks (adapted from Batten and Bratt 1987)

Time after dosing	% of dose retained per group		
	0.02 mg ai/kg	0.15 mg ai/kg	0.35 mg ai/kg
Day 1	47.3	29.7	28.9
Week 4	39.2	37.1	23.5
Weeks 12-13	34.0	31.7	21.2
Week 65	16.0	15.4	-
Week 104	11.8	11.7	-

Based on those findings, the authors conclude that the existence of biphasic kinetics in the liver for brodifacoum has two important consequences. "Firstly the fast and slow phases can each be characterized by a half-life estimation. It is apparent however that the half-life quoted (approximately 4 days) using data from the fast initial phase of the elimination from the liver can give a misleading impression of the potential persistence of an anticoagulant. If lethal doses were used, tissue concentrations could only be measured prior to death and since this would occur during the rapid elimination phase the subsequent slow phase of elimination would not be apparent. This probably explains why data for bromadiolone, a structurally similar anticoagulant to brodifacoum suggest that this substance is rapidly eliminated from rats (Poché 1986). Secondly, the concentration of radioactivity in the liver at the beginning of the terminal phase is independent of the dose and therefore when expressed as a percentage of the dose decreases as the dose increases. This can give a misleading impression with regard to the size of the residue present."

Parmar et al. (1987) also reported biphasic elimination of radio-labelled brodifacoum and bromadiolone from rat liver. The initial phase occurred from days 2 to 8 after dosing, followed by a prolonged terminal phase when the elimination half-lives were 130 and 170 days for brodifacoum and bromadiolone, respectively. However, the results were presented only in an abstract with too few details provided to adequately evaluate the results reported.

Belleville (1991) orally dosed rats with 0.06 mg ai/kg brodifacoum or difethialone on 4 occasions at weekly intervals. After 6 months, 21% of the total brodifacoum dose and 7% of the total difethialone dose was retained in hepatic tissue (Table 37). Hepatic half-lives calculated for the 158 days after the final dose (days 22 to 180) were 136 days for brodifacoum and 74 days for difethialone.

Table 37. Hepatic Concentrations in Rats Dosed at 0.06 mg ai/kg on Days 0, 7, 14, and 21 (adapted from Belleville 1991)

Time after initial dose	Brodifacoum (ppm)	Difethialone (ppm)
22 days	2.01 ± 0.15	1.28 ± 0.15
49 days	1.50 ± 0.48	0.84 ± 0.15
77 days	0.98 ± 0.32	0.49 ± 0.08
4 months	0.85 ± 0.15	0.35 ± 0.07
6 months	0.87 ± 0.16	0.29 ± 0.08

Studies in species other than rats also indicate that brodifacoum can be retained in animal tissue for a very long time. Eason et al. (1996) detected brodifacoum residue 9 months after administration of a sublethal dose of 0.1 ppm in possums. Laas et al. (1985) examined retention of brodifacoum in sheep tissues and its excretion via feces after a single, sublethal oral dose of either 0.2 or 2.0 mg ai/kg to 14 sheep. Sheep were sacrificed periodically 2 to 128 days after dosing and liver, carcass, and fat tissues analyzed for residue. Brodifacoum was detected in the liver after 128 days, at concentrations of 0.64 and 1.07 mg ai/kg dry weight (equivalent to 0.22 and 0.36 mg ai/kg wet weight), respectively, for the 2 doses. Residue also was detected for up to 8 days in fat and up to 15 days in the carcass. Bromadiolone was detected for 256 days in the liver of sheep that received a sublethal dose of 2 mg ai/kg (Nelson and Hickling 1994). Breckenridge et al. (1985) reported a plasma elimination half-life of about 2.5 days for rabbits dosed with brodifacoum, and Woody et al. (1992) observed an elimination half-life for brodifacoum in serum of 6± 4 days in four dogs. The plasma half-life of brodifacoum determined in three human patients with severe bleeding disorders was found to be approximately 16–36 days (Weitzel et al. 1990).

First-generation anticoagulants

Although fewer data are available for the first-generation anticoagulants (Table 38), the available information indicates they are generally less persistent in the blood and body tissues. Belleville (1981) orally administered radio-labeled chlorophacinone to rats with either a single dose of 1 to 1.26 mg ai/rat (~4 to 6 mg ai/kg) or 3 daily doses of 1.43 mg ai/rat (~6 to 7 mg ai/kg). The compound was rapidly absorbed and metabolized; 90% was excreted within 48 h and 100% within 4 days. Elimination was almost totally via the feces; <1% was via urine and CO_2. The $t_{1/2}$ in blood was 9.8 h, with the maximum concentration attained after 4 to 8 h. The maximum blood concentration in rats that received 3 doses was 1.8 to 3.7 times higher than that from rats receiving a single dose. Concentrations in body tissues after 4 h and 48 hours were highest in liver, but chlorophacinone also was present in kidneys, lungs, heart, muscle, fat, and other parts of the carcass (Table 39).

Yu et al. (1982) studied the metabolism and disposition of diphacinone in rats and mice. In rats given a single oral dose of radiolabeled diphacinone at either 0.18 or 0.4 mg ai/kg, about 70% of the dose was eliminated in feces and 10% in urine within 8 days, whereas about 20% of the dose was retained in body tissues. Mice given a single dose of 0.6 mg ai/kg eliminated most diphacinone within 4 days, and only 7% was retained in body tissues. In both rats and mice, most radioactivity (59 to 69%) was detected in the liver and the kidneys (9 to 12%). Radioactivity also was detected in the brain, heart, spleen, lungs, blood, muscle, fat, and gonads. Several major metabolites were identified, and parent diphacinone in excreta and liver accounted for only about 20% of the dose. In another study, cattle that received a single injection of 1 mg ai/kg had almost constant residue concentrations in liver and kidney at 30, 60, and 90 days after dosing (Bullard et al. 1976). The plasma half-life in humans is reported to be 15 to 20 days (WHO 1995).

Table 38. Persistence of First-generation Anticoagulants in Blood and Liver

Anticoagulant	Species	Dose (mg ai/kg)	No. doses	Blood $t_{1/2}$[a] (days)	Liver retention[a,b] (days)	Reference
Diphacinone	cattle	1.0	1		>90	Bullard et al. 1976
Diphacinone	human			15-20		WHO 1995
Chlorophacinone	rat	4-5	1	0.4		Belleville 1981
Warfarin	rat			0.7 (%) 1.2 (&)		Pyrola 1968[c]
Warfarin	rabbit			0.2		Breckenridge et al. 1985[c]
Warfarin	possum			0.5		Eason et al. 1999
Warfarin	human	0.5-100	1	0.6-2.4		O'Reilly et al. 1963[c]
Warfarin	pig				30-40	O'Brien et al. 1987[c]

[a] $t_{1/2}$ for plasma and liver is the elimination half-life ($-phase)
[b] liver retention is expressed as either the time period for which residues persist or as the elimination half-life
[c] cited in Eason et al. (2001)

Table 39. Chlorophacinone Residue in Rats 4 and 48 hours After an Oral Dose of 1.26 mg ai per Rat (adapted from Belleville 1981)

Tissue	µg ai/g (ppm)	
	4 h after dosing	48 h after dosing
Liver	31.1	2.9
Kidney	6.6	1.2
Lung	4.5	0.4
Heart	3.1	0.2
Muscle (thigh)	2.0	0.1
Fat	1.2	0.7
Carcass	5.2	0.3

Diaz and Whitacre (1976) orally dosed rats with diphacinone (0.32 mg ai/kg/day) for 1 or 2 days. Rats dosed for 2 days were sacrificed 72 h after the second dose and those dosed for 1 day were sacrificed after 48 h. In rats dosed for 2 days, about 45% of the total dose administered was excreted (86% in feces, 14% in urine) and 25% was retained in body tissues 72 h after the last dose. The remaining 30% of the dose was not recovered. The body tissues retaining the most diphacinone at 96 h were the hide and tail, liver, intestine, blood, and the carcass (Table 40). In rats dosed for 1 day and sacrificed after 48 h, about 5% of the dose was excreted and 61% retained; the remained was not recovered.

In contrast to other anticoagulants, especially the second-generation compounds, warfarin is extensively metabolized and the major route of excretion is in the urine. Limited data exist regarding persistence of warfarin in the liver. O'Brien et al. (1987; cited in Eason et al. 2001) found comparatively rapid clearance of warfarin in pigs, with concentrations declining to very low levels after approximately 30 days. Meehan (1984) states that approximately half the warfarin consumed by a rat remains in the body after 6 hours. Thijssen (1995) cites a half-life of 7 to 10 days in animal tissue, and Ford (1993; cited in Poché and Mach 2001) reported a half-life of 42 hours in the gastro-intestinal tract. EPA (1982) noted that only 7.6% of the warfarin consumed in bait by 11 rats remained in the carcass after a 5-day feeding period. According to Machlin (1984; cited in Poché and Mach 2001), warfarin concentrates in the liver, but the adrenal glands, lungs, bone marrow, kidneys, and lymph nodes also contain measurable amounts. Breckenridge et al. (1985) reported a plasma elimination half-life of 5.6 hours in rabbits. O'Reilly et al. (1963) reported that the mean half-life varied from 24 to 58 hours for disappearance of warfarin from the plasma of human volunteers given a single oral dose of 0.5 to 100 mg ai/kg; no dose-dependent effect on half-life was apparent over this range of doses.

Table 40. Percentage of Diphacinone Retained by Rats Dosed For 1 or 2 Days With 0.32 mg ai/kg (adapted from Diaz and Whitacre 1976)

Organ	% of total dose retained[a]	
	48 h after 1 dose	72 h after 2 doses
Intestine	22.1	4.1
Liver	19.4	5.4
Hide and tail	10.9	6.5
Carcass	3.9	3.8
Blood	1.8	4.0
Muscle	0.8	0.4
Kidney	0.7	0.3
Testis	not reported	0.8
Lung	0.5	0.2
Fat	0.2	0.4
Heart	0.1	0.2
Spleen	0.1	0.1
Brain	<0.1	<0.1

[a] because only 66-70% of the total dose was recovered, percentages in tissues are likely to be higher than the values tabulated

Potential Secondary Risks

       Birds

Qualitative assessments of potential secondary risks are based on mortality and other adverse effects reported in secondary-hazards tests, information obtained from field studies and operational control programs, toxicokinetic data, residue levels reported in primary consumers, and incidents. Much of the data are presented in preceding sections of this assessment. It can be difficult to extrapolate from laboratory data to wild birds in the field, because of factors such as animal behavior and environmental conditions. However, laboratory tests are not necessarily overly conservative as argued by some registrants. As discussed in the *Final Report of the Avian Effects Dialogue Group, 1988-1993* (AEDG; Rymph 1994), even sublethal effects seen in controlled laboratory conditions might result in decreased survival or reproduction in the field where animals also are exposed to other stressors, and such effects often are overlooked in the risk assessment process. The AEDG notes that "Decreases in the survival or reproduction of birds following acute or chronic pesticide exposures that would be sublethal in the laboratory may result from alterations in physiological condition, motor function and behavior."

Additional information also is available to demonstrate that exposure to rodenticide baits can have adverse effects. Information from field studies and control program is presented below, and incident data that help characterize secondary risks are discussed in an "*Incident Data: Birds and Nontarget Mammals*" section later in the document. Data gaps exist for some of the rodenticides, but some marked differences in potential secondary risk are apparent among the compounds.

Based on the available feeding studies, brodifacoum poses the greatest potential secondary risk to birds. In 11 secondary-hazard studies that exposed 149 raptors or scavengers to brodifacoum-poisoned prey, 42% of exposed birds died. Many survivors exhibited signs of intoxication, including bleeding. Moreover, mortality via secondary exposure is not limited to laboratory tests but has also been widely reported in field studies and brodifacoum control programs (see below). Brodifacoum residue also has been detected in the liver of numerous dead owls, eagles, hawks, and corvids (see Attachment D). Potential risks of difethialone cannot be adequately characterized until secondary-hazard data are available. However, based on its similarity to brodifacoum in chemical structure (Attachment A), physical and chemical properties, acute toxicity profile for birds (Table 3) and mammals (Table 8), and retention times in animal tissue (Table 34), difethialone is presumed to pose comparable risks. Some uncertainty exists due to the lack of hazard data and also because difethialone baits are formulated with less active ingredient (25 ppm) than are brodifacoum baits (50 ppm).

The other anticoagulants also exhibit a potential for secondary risk to birds but not to the same extent as brodifacoum and possibly difethialone. Secondary hazard studies suggest that bromadiolone and diphacinone pose greater potential risks than do chlorophacinone and warfarin, which are less hazardous and less likely to bioaccumulate in body tissues.

Some information is available for zinc phosphide, but additional data are needed to characterize potential secondary risks of bromethalin and cholecalciferol. Studies indicate that zinc phosphide has a low secondary hazard, probably because it is rapidly converted to phosphine gas in the stomach and not retained in toxicologically significant quantities in body tissues of primary consumers. However, undigested bait in primary consumers may pose a hazard to raptors or scavengers that might consume the GIT.

Based on the data from secondary hazard laboratory studies and the data available on retention times in blood and liver of target species, the comparative analysis model indicates that brodifacoum and difethialone pose the greatest potential secondary risks to birds (Table 41). Brodifacoum has higher summary values than difethialone for all three measures of effect. Mean (%) mortality of secondary lab studies appears to be the most significant measure of effect leading to the conclusion that brodifacoum poses substantially greater potential secondary risk to birds than the other rodenticides (Figure 4).

**Table 41. Comparative Analysis Model Results for Secondary Risk to Birds**

Rodenticide	mg ai/kg bait	Measure-of-effect values			Summary value
		mean mortality (%)[a]	blood retention time (days)[b]	liver retention time (days)[b]	
Brodifacoum	50	42.00	7.30	217.00	8.60
Bromadiolone	50	8.00	1.40	248.00	3.03
Bromethalin	100	No Data	5.60	No Data	2.20
Chlorophacinone	100	0.00	0.40	No Data	0.03
Chlorophacinone	50	0.00	0.40	No Data	0.03
Cholecalciferol	750	0.00	25.50	No Data	2.00
Difethialone	25	33.60[c]	2.50	117.70	6.29
Diphacinone	100	9.00	17.50	90.00	3.18
Diphacinone	50	9.00	17.50	90.00	3.18
Warfarin	250	9.00	0.82	35.00	1.72
Zinc phosphide	20,000	0.00	No Data	No Data	0.00

[a] from Tables 11-12, 14-16, and 18-19
[b] from Tables 13 and 17
[c] as noted in Appendix C, difethialone is considered a special case due to its similarity to brodifacoum; while missing data, it is given a % equal to 80% of that for brodifacoum.

Figure 4. Comparative Analysis Model Summary Values For Secondary Risk to Birds

Graph 3. Greatest Secondary Risk to Birds
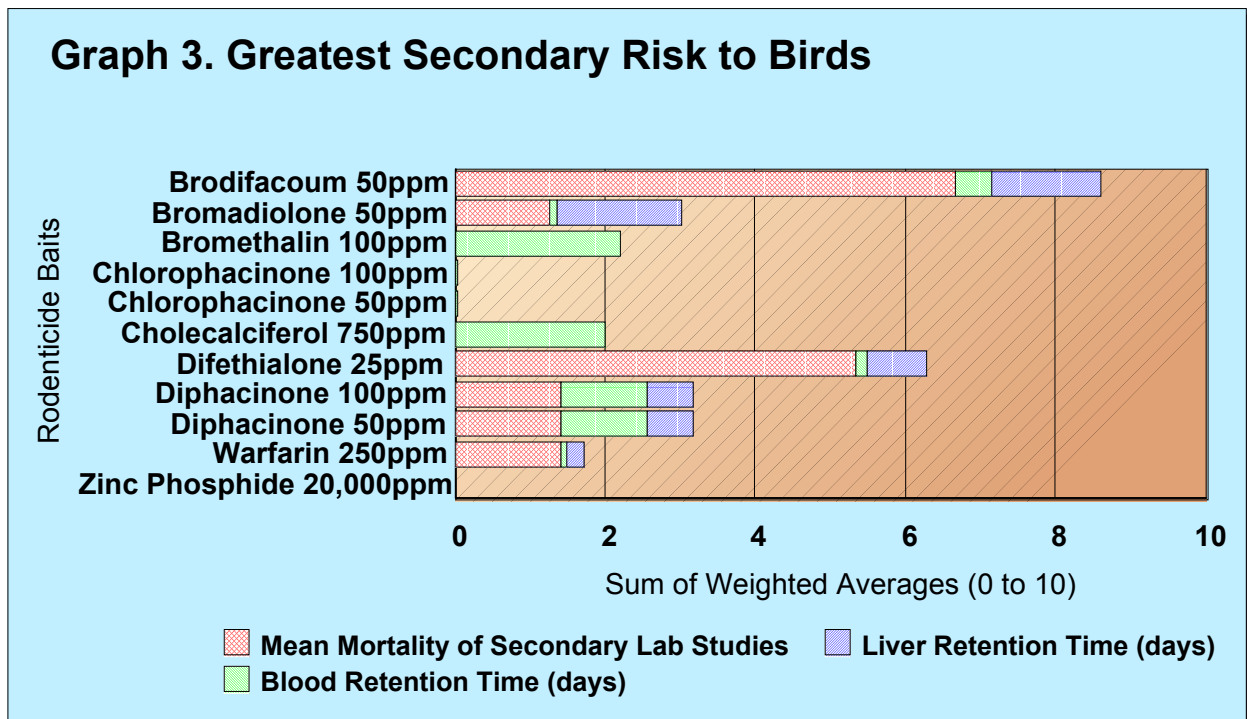
Information from field studies and control programs: Some information from field studies and control programs is available for some rodenticides, especially brodifacoum. Hegdal and Colvin (1988) examined risk to Eastern screech-owls (*Otus asio*) during experimental baiting for vole control in orchards during the fall and winter of 1981-82. The study indicates considerable risk to screech-owls and possibly other raptors that feed on voles baited with a 10 ppm brodifacoum bait (baits registered for rat and mouse control are 50 ppm). Thirty-two screech-owls were radio-tracked after the baiting. Some owls disappeared or were taken by predators, but the minimum documented mortality of screech-owls was 58% for those individuals for which more than 20% of their home range included treated orchard. Mortality was also considerable (17%) for those owls having less than 10% of their home range including treated areas. Liver-residue analysis was conducted on 16 screech-owls collected or found dead during the study. Although the limit of detection 0.3 ppm was deemed inadequate by the authors, brodifacoum residue was detected at levels ranging from 0.3 to 0.8 ppm in 9 owls., and residue was found in owls collected up to 57 days posttreatment. Death of a long-eared owl (*Asio otus*) also was presumed due to brodifacoum, based on extensive hemorrhage and detection of residue in owl pellets containing vole remains.

Hegdal and Blaskiewicz (1984) found no secondary risk to barn owls residing on New Jersey farms when brodifacoum was applied to control rats and mice from late July to September in 1980. Radio-telemetry data for 34 owls indicated they spent most feeding time hunting for meadow voles in fields and marshes and spent little time foraging for rats and mice around farms. Rats and mice comprised only 3.9% and 2% of the diet, respectively, and owl traps baited with mice and placed around farmsteads were ignored by owls. In contrast, Duckett 1984 (cited in Newton et al. 1999 and Eason and Spurr 1995) reported a major decline in a barn owl population on an oil palm plantation in Malaysia after second-generation anticoagulants were applied for rat control. The owls were feeding on rats and the owl population declined from 40 to 2 individuals.

Howald et al. (1999) examined effects of brodifacoum baiting on avian scavengers during rat control on a Canadian island. They conclude that there is a very real risk of secondary poisoning of some predators and scavengers, and the impact on ravens may have been severe. Thirteen dead ravens were found out of an island population estimated at 20 to 72 individuals. All 13 dead ravens had brodifacoum residue in the liver, with concentrations ranging from 0.98 to 2.52 ppm. Ravens were likely exposed from eating the bait as well as secondarily via prey who had previously fed on the bait. Secondary poisoning is evident from observations of ravens scavenging on rat carcasses and the presence of rat hair in the gizzard of several ravens. Assuming an LD50 of 0.56 mg ai/kg (a value offering 95% species protection for birds) and a rat total-body burden of 1.4 mg ai (based on measured residue concentrations in 10 rats), the authors calculate that a single brodifacoum-poisoned rat could provide 2 to 3 LD50 doses for a raven or crow. No mortality of bald eagles was evident during the baiting program, but exposure occurred. Twenty bald eagles were trapped and 1 other rescued during the baiting program. Brodifacoum was detected at levels of 0.037, 0.041, and 1.74 ppm in the blood plasma of 3 (15%) of 21 eagles sampled. The authors calculated that a bald eagle, because of its large size, would need to eat about 3.2 rats to obtain an LD50 dose.

Based on numerous bird kills during operational control programs with brodifacoum in New Zealand, Eason and Spurr (1995) conclude that the potential for secondary adverse effects is much greater for second-generation anticoagulants than for first-generation anticoagulants. Secondary adverse effects on Australasian harriers (*Circus approximans*), New Zealand falcons (*Falco novaeseelandiae*), rails, brown skuas (*Catharacta skua*), gulls, and owls (morepork, *Ninox novaeseelandiae*) has been reported after brodifacoum baiting (Eason and Spurr 1995, Towns et al. 1993, Ogilvie et al. 1997, Walker and Elliott 1997). Stephenson et al. (1999) studied the fate of moreporks, which feed on mice, after a single aerial application of brodifacoum to eradicate mice on Mokoia Island. Twenty-eight owls were monitored after the baiting, including 14 that were radio-tagged and tracked. Three (21%) radio-collared owls died. Seven (50%) owls not radio-collared disappeared, which the authors believe is most likely a result of secondary poisoning. Two dead owls were analyzed for residue, and brodifacoum was detected in the liver of both at concentrations of 1 and 1.1 ppm.

A survey in Great Britain indicates that exposure of barn owls to second-generation anticoagulants may be frequent and widespread. As part of a pesticide-monitoring scheme, the livers from 717 dead barn owls were analyzed for anticoagulant residue from 1983 to 1996

(Newton et al. 1990, 1999; Wyllie 1995). Although second-generation anticoagulants were detected in 26% of the owls (34 to 37% in the latter years when better analytical methods were available), most deaths resulted directly from collisions with cars and trucks or starvation. However, the authors believe that the proportion of deaths due to rodenticides may have been underestimated. Almost all carcasses had been collected from open areas, such as roadsides. As the authors note, death from anticoagulant exposure is delayed and preceded by lethargy, and most victims are likely to die in their roosts, in roof-cavities or hollow trees, where they are not likely to be found. Also, carcasses found in such locations are most often too decayed to permit tissue analysis. Newton et al. (1990) also note that ". . . there remains the possibility that sub-lethal levels of rodenticide may predispose death from other causes, or reduce the chance of recovery from accidents.", and they emphasize that ". . . more monitoring of residues and population trends is clearly desirable."

No field studies are available for difethialone or bromadiolone. Some information on nontarget exposure to bromadiolone has been reported in France and Switzerland, where bromadiolone is used for control of water voles (*Arvicola terrestris*) and coypu (nutria). From 1991 to 1994, a number of dead birds suspected to have been exposed to anticoagulant rodenticides were submitted for analysis. Bromadiolone was detected in the liver of 15 of 16 dead Eurasian buzzards, 5 of 5 kites (*Milvus migrans*), and the one harrier examined (Berny et al. 1997). Saucy et al. (2001) reported deaths of numerous birds, mostly Eurasian buzzards but also kites and carrion crows, after bromadiolone bait (150 ppm) was mechanically applied in underground burrows for water vole control in Switzerland.

The Agency is not aware of any field tests designed to assess secondary risk to raptors from first-generation anticoagulants or the non-anticoagulants. Several field tests designed to assess the efficacy of chlorophacinone and zinc phosphide included searches for nontarget carcasses as a secondary objective. None found any indications that raptors or avian scavengers were killed from feeding on target species previously exposed to the rodenticides. However, most search effort was devoted to locating nontarget carcasses on and immediately around baited plots. Because raptors may be wide-ranging and anticoagulants are slow-acting, radio-tracking individual birds is essential to evaluate their interactions with the target species and to determine their fate (Fagerstone and Hegdal 1998, Colvin et al. 1991, Colvin et al. 1988, Edwards et al. 1988).

Nontarget mammals

Based on a qualitative assessment of potential secondary risk to mammals from feeding studies, all 6 anticoagulants appear to pose a potential secondary risk to mammalian predators and scavengers, although warfarin apparently less so than the others. Secondary risks from zinc phosphide appear to be low for most species, especially those that don't consume the GIT where undigested bait may be present. Too few data are available to adequately assess potential risks of either bromethalin or cholecalciferol.

The comparative analysis model results indicate that diphacinone, chlorophacinone, and brodifacoum pose the greatest potential secondary risk to mammals (Table 42). Retention time in blood was the most significant measure of effect leading to the conclusion that diphacinone poses greater potential secondary risk than does chlorophacinone, while mean (%) mortality of secondary lab studies was the most significant measure of effect leading to the conclusion that both diphacinone and chlorophacinone poses greater potential secondary risk than does brodifacoum (Figure 5).

Table 42. Comparative Analysis Model Results for Secondary Risk to Mammals

Rodenticide	mg ai/kg bait	Measure-of-effect values			Summary value
		mean mortality (%)[a]	blood retention time (days)[b]	liver retention time (days)[b]	
Brodifacoum	50	42.00	7.30	217.00	6.76
Bromadiolone	50	23.00	1.40	248.00	4.40
Bromethalin	100	0.00	5.60	No Data	0.44
Chlorophacinone	100	55.00	0.40	No Data	7.62
Chlorophacinone	50	55.00	0.40	No Data	7.62
Cholecalciferol	750	0.00	25.50	No Data	2.00
Difethialone	25	33.60[c]	2.50	117.70	4.82
Diphacinone	100	58.00	17.50	90.00	8.42
Diphacinone	50	58.00	0.82	90.00	8.42
Warfarin	250	9.00	5.60	35.00	1.32
Zinc phosphide	20,000	4.00	No Data	No Data	0.69

[a] from Tables 20-27
[b] from Tables 13 and 17
[c] as noted in Appendix C, difethialone is considered a special case due to it's similarity to brodifacoum; while missing data, it is given a % equal to 80% of that for brodifacoum.

Figure 5. Comparative Analysis Model Summary Values For Secondary Risk to Nontarget Mammals

Graph 4. Greatest Secondary Risk to Mammals

A horizontal bar chart titled "Graph 4. Greatest Secondary Risk to Mammals." The y-axis is labeled "Rodenticide Baits" and lists the following from top to bottom:
- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

The x-axis is labeled "Sum of Weighted Averages (0 to 10)" with values 0, 2, 4, 6, 8, 10.

Legend:
- Mean Mortality of Secondary Lab Studies
- Blood Retention Time (days)
- Liver Retention Time (days)

Information from field studies and control programs: The Agency is not aware of any field studies designed to assess secondary risks to mammals, but exposure and mortality has been documented in some situations. Extensive mortality of introduced mammalian predators was reported during brodifacoum-baiting operations for rats in New Zealand forests. Mortality of stoats (ermine), ferrets, weasels, and cats was reported to be 100% after brodifacoum application (Alterio 1996, Alterio et al. 1997; cited in Stephenson et al. 1999). In one study, all 11 radio-collared stoats and the 1 radio-collared weasel died within 9 days of bait application. In another study, Murphy et al. (1998) detected brodifacoum residues in the liver of 56% of 16 feral ferrets, 78% of 40 stoats, and 71% of 14 weasels examined after baiting.

Some information on nontarget exposure of mammals to bromadiolone was obtained during vole and coypu control in France (Berny et al. 1997). Bromadiolone was detected in the liver of 22 of 31 red foxes (*Vulpes vulpes*), 4 of 28 rabbits (*Oryctolagus cuniculus*) and hares (*Lepus capensis*), 3 of 6 wild boar (*Sus scrofa*), 2 roe deer (*Capreolus capreolus*), 2 stone martens (*Martes foina*), a lynx (*Lynx lynx*), and a badger (*Meles meles*). Based on the species involved, secondary poisoning seems to have been the predominant route of exposure. Saucy et al. (2001) reported deaths of 38 wild mammals, mostly red foxes and mustelids, and 18 cats and dogs after

bromadiolone bait (150 ppm) was mechanically applied in underground burrows for water vole control in Switzerland.

Second-generation anticoagulants were detected in the liver of 31% of 29 polecats (*Mustela putorius*) analyzed from 1992 to 1994 in Britain (Shore et al. 1996, Newton et al. 1999). Most of the carcasses collected were found along roadsides. The authors believe the survey results indicate exposure of polecats to second-generation rodenticides may be common, and they suggest that studies to determine potential effects of such exposure are warranted.

Savarie et al. (1979) orally dosed 10 wild coyotes with diphacinone, with doses ranging from 0.31 to 5 mg ai/kg. Radio collars were attached to these animals, and they were released back into the wild and monitored for survival. Seven (70%) of the 10 coyotes died within 7 to 16 days, with an average time to death of 9.6 days.

Incident Data: Birds and Nontarget Mammals

Ecological Incidents Information System (EIIS)

Incident reports submitted to the Agency indicate that birds and nontarget mammals are being exposed to rodenticides, especially brodifacoum. EFED's EIIS contains information on more than 300 incidents in which one or more of the rodenticides was detected in birds or nontarget mammals (Table 43 and Attachment D). Brodifacoum was detected in more than 244 of those, including 25 of 26 involving exposure to more than one rodenticide. Bromadiolone was detected in 39 incidents, including 17 that also involved exposure to brodifacoum. Twenty-five incidents are reported for zinc phosphide, 20 for diphacinone, 13 for chlorophacinone, 4 for warfarin, 1 for difethialone, and none for bromethalin or cholecalciferol. Eleven of the incidents for the first-generation anticoagulants also included exposure to a second-generation anticoagulant, usually brodifacoum. Approximately 80 additional incidents involving raptors exposed to anticoagulant rodenticides, mostly brodifacoum (84%), have been reported by Stone et al. (2003). The New York State Department of Environmental Conservation has committed to providing those incident reports to EFED, and they will be added to the EIIS database when received.

Other anticoagulant-rodenticide incidents in the EIIS include rodents (mostly tree squirrels), opossums, and deer. Seven deer in New York state tested positive for anticoagulants, including 5 with brodifacoum and 2 with diphacinone. The deer apparently were exposed due to misuse and careless bait application.

Zinc phosphide was implicated in the deaths of some wild turkeys, waterfowl (especially geese) and a few squirrels and a rabbit. In most incidents, treated bait was present in crop or gizzard contents. Two red foxes also apparently died after eating mice who fed on zinc phosphide treated grain.

Table 43. Comparative Number of Reported Rodenticide Nontarget Incidents[a]

Rodenticide	Total[b]	Owls	Diurnal raptors	Corvids	Other birds	Wild canids	Wild felids	Other carnivores	Deer	Rodents/ Rabbits	Opossum
Second-generation anticoagulants											
Brodifacoum	244[c]	54	68	17	4	48	5	10	5	31	2
Difethialone	1	0	0	0	0	0	1	0	0	0	0
Bromadiolone	39	13	5	1	2	5	1	3	0	8	1
First-generation anticoagulants											
Chlorophacinone	13	0	1	0	2	5	1	0	0	4	0
Diphacinone	20	3	2	0	1	4	1	2	2	5	0
Warfarin	4	1	2	0	0	0	0	0	0	1	0
Others (non-anticoagulants)											
Bromethalin	0	0	0	0	0	0	0	0	0	0	0
Zinc Phosphide	25	0	0	0	22	1	0	0	0	2	0
Cholecalciferol	0	0	0	0	0	0	0	0	0	0	0

[a] based on confirmed exposure (e.g., detection of anticoagulant in the liver, zinc phosphide in crop contents); see Attachment B for additional details
[b] 26 incidents involved exposure to more than 1 registered anticoagulant
[c] Syngenta reported two incidents in 6(a)(2) aggregate reports; the species and number of individuals involved were not reported for these incidents

Most of the incidents in the EIIS occurred in New York and California, where state agencies have taken the time, effort, and expense of screening the liver of dead animals suspected to have been killed by rodenticides. Few other states appear to do so, although Wisconsin has reported several raptor incidents. A proper evaluation of rodenticide exposure requires necropsy of a dead animal by a wildlife pathologist. Liver tissue be extracted, frozen, and shipped to an analytical laboratory for analysis by high performance liquid chromatography (HPLC). Because so few anticoagulant screens are conducted, exposure of birds to anticoagulants is likely much more widespread than the number of incidents suggests. Most rodenticide incidents likely go undetected except in those rare instances when a predator carcass happens to be exposed in an open area (e.g., roadside) where it is observed by someone willing to take the time and effort to report it to the proper authorities (McDonald et al. 1998, Newton et al. 1999). In many situations, carcasses might not be detected, death may be attributed to natural mortality, or an incident may not be reported for a variety of reasons, including ignorance, apathy, or failure of authorities to investigate and confirm the cause of death (Rymph 1994, Vyas 1999).

The incidents reported in the EIIS are based on confirmed exposure to a rodenticide. Anticoagulants are detected from residue analysis of liver tissue, supplemented by gross pathological findings. According to Stone et al. (1999), the most frequent pathological signs observed in birds (>50% of individuals examined) exposed to anticoagulants are subcutaneous hemorrhage and overall pallor. Occasional signs (10 to 50% of individuals) include inter/intra-muscular hemorrhage, free hemorrhage in the body cavity, excessive bleeding from minor wounds, and low blood volume in the heart and major blood vessels. Toxicosis resulting from exposure to non-anticoagulants may be more difficult to confirm than for an anticoagulant. Zinc phosphide is generally detected by the presence of dyed bait in the crop, stomach, or alimentary canal. The presence of an acetylene odor also is diagnostic of zinc phosphide toxicity but can be detected only if intact carcasses are sent to an examining laboratory soon after death (Michigan Wildlife Diseases Manual, undated). Little information is available on methodology for detecting bromethalin or cholecalciferol in body tissues.

Anticoagulant rodenticides, especially brodifacoum, have been detected in numerous predators and scavengers. Avian species most commonly exposed are great horned owls and red-tailed hawks. Multiple incidents also have been reported for golden and bald eagles, corvids, barn owl, eastern screech-owl, northern spotted owl, Cooper's hawk (*Accipiter cooperii*), red-shouldered hawk, sharp-shinned hawk (*Accipiter striatus*), peregrine falcon (*Falco peregrinus*), American kestrel, and vultures. Other incidents have included a long-eared owl, a barred owl (*Strix varia*), a snowy owl (*Nyctea scandiaca*), and a spotted owl (*Strix occidentalis*). Carnivores exposed include coyotes, various foxes (including the endangered kit fox), raccoons, bobcats, skunks, mountain lions, and a weasel. Brodifacoum was detected most often, followed by bromadiolone, chlorophacinone, and diphacinone. Difethialone was detected in 1 dead bobcat.

The American Society for Prevention of Cruelty to Animals (ASPCA) Poison Control Center also has some incident information for pets, mostly dogs. The Center reports 2334 cases involving potential exposure of 2685 animals from November 01, 2001 to June 16, 2003 (S. Hansen, Senior Vice President, pers comm.). By rodenticide, the number of cases were 1161 for brodifacoum,

511 for bromadiolone, 218 for zinc phosphide, 206 for diphacinone, 66 for bromethalin, 48 each for difethialone and warfarin, 42 for chlorophacinone, and 34 for cholecalciferol. EFED does not assess risks to pets, and these data are not a component of the EIIS. However, they do augment the wildlife incident data in demonstrating that nontarget animals are being exposed to some rodenticides, despite product-label use directions to apply bait in locations out of reach of children, pets, domestic animals and nontarget wildlife, or in tamper-resistant bait stations.

The Rodenticide Registrants Task Force (Kaukeinen et al.2000) believe that rodenticide incidents are few when compared to other sources of wildlife mortality. They note that diseases accounted for most of the mortality reported by the National Wildlife Health Center (NWHC) from July 1998 through March 1999 and that there is only a single rodenticide incident. This is not surprising, because the NWHC focuses on diseases and does not analyze wildlife carcasses for rodenticide residues (A. Schrader, NWHC, pers comm.). The Rodenticide Registrants Task Force also contend that bird deaths from collisions with television and radio towers, starvation, and parasitism far exceed deaths attributable to rodenticides. However, small birds such as sparrows, starlings, and other songbirds far outnumber predatory birds such as owls, hawks, and eagles in such incidents. The latter are more likely to comprise incidents attributed to rodenticide toxicity and are more likely to be found and reported. Based on an analysis of the EIIS by Mastrota (1999), brodifacoum was surpassed only by diazinon in the number of wildlife incidents reported for pesticides from 1994 through 1998, the latest period analyzed.

New York State Raptor Incidents

Stone et al. (1999, 2003) provide some perspective on the extent of exposure on some raptor species. They reported 26 cases of anticoagulant poisoning of raptors in New York State from 1994 to 1997, of which 23 (88%) involved brodifacoum. The incidents comprised 17% of all diagnoses for great horned owls (n = 59) and 6% of all diagnoses (n = 114) for red-tailed hawks during that period. For the period 1998 through 2001, they detected anticoagulant rodenticide in 49% of the 265 raptors analyzed in New York State (Table 44). Brodifacoum was detected in 84% of the positive cases and bromadiolone in 22%. One or more anticoagulants were detected in 12 of 19 species examined, with most detections made in great horned owls (81%), red-tailed hawks (58%), Cooper's hawks (36%), and screech owls (45%). Mean residue levels in those 4 raptor species are presented in Table 45. The data are not sufficient to determine if these exposures are impacting local or state-wide populations of these species via mortality or reduced reproductive success, but they do indicate a need for a sound monitoring program to determine potential adverse effects of such exposure.

Table 44. Detection of Anticoagulant Rodenticides in Liver Tissue of Raptors and Vultures In New York State From 1998 Through 2001 (from Stone et al. 2003)

Species	no. analyzed	no. with anticoagulant rodenticide	% positive detects
Red-tailed hawk	78	45	58
Great horned owl	53	43	81
Cooper's hawk	50	18	36
Screech owl	22	10	45
Barred owl	13	3	23
Long-eared owl	7	2	29
Turkey vulture	2	2	100
Golden eagle	1	1	100
Bald eagle	5	1	20
Sharp-shinned hawk	11	1	9
Saw-whet owl	3	1	33
Peregrine falcon	2	1	50
Broad-winged hawk	11	0	0
Snowy owl	2	0	0
Northern goshawk	1	0	0
Rough-legged hawk	1	0	0
Merlin	1	0	0
Short-eared owl	1	0	0
Black vulture	1	0	0

Table 45. Anticoagulant Rodenticide Residues In Four Raptor Species Analyzed by Stone et al. (2003)

Anticoagulant/ Raptor species	no. detects	Ō liver residue (ppm)	liver residue range (ppm)
Brodifacoum:			
Red-tailed hawk	42	0.21	0.006-1.28
Great horned owl	42	0.21	0.007-0.97
Screech owl	8	0.16	0.007-0.47
Cooper's hawk	12	0.10	0.008-0.22
Bromadiolone:			
Red-tailed hawk	6	0.23	0.08-0.50
Cooper's hawk	5	0.35	0.04-0.60
Diphacinone:			
Red-tailed hawk	1	0.34	
Cooper's hawk	1	0.10	
Warfarin:			
Great horned owl	1	0.73	
Cooper's hawk	1	0.10	
Chlorophacinone:			
Red-tailed hawk	1	0.18	

Endangered San Joaquin kit fox

Of particular concern are findings over the past several years that the endangered San Joaquin kit fox is being exposed to rodenticides, especially brodifacoum. From 1999 to 2003, liver tissue from 32 dead kit foxes has been screened for rodenticide residues by the Pesticide Investigations Unit of the California Department of Fish and Game and by the U. S. Fish and Wildlife Service (R. Hosea, pers. comm.). Anticoagulant rodenticide was detected in the liver of 27 (84%) foxes. Brodifacoum was detected in all 27 individuals. Bromadiolone also was detected along with brodifacoum in 2 of those foxes, and chlorophacinone and pival were found with brodifacoum in 1 fox each. Pival is no longer registered but may have been used under existing-stocks provisions.

Liver residue levels

Uncertainty exists as to what liver concentration might corroborate death or other adverse effects from anticoagulant exposure or even if such a cause-effect relationship is appropriate. The Rodenticide Registrants Task Force proposes a "threshold of toxicity" of 0.7 ppm for brodifacoum in liver tissue (Kaukeinen et al. 2000, Anonymous 2001). However, the proposed threshold level is based on only 2 laboratory studies with a total of 8 barn owls and some selected field surveys. Variation in susceptibility of different bird species, mammals, and other rodenticides is not addressed. Brodifacoum concentrations less than 0.7 ppm have been associated with toxicosis. Eason et al. (1996), for example, dosed 6 brushtail possums with a dose of 0.1 mg ai/kg and reported that 1 animal that died had a liver concentration of only 0.1 ppm brodifacoum. In another study, possums were offered brodifacoum baits for 3 nights (C. Eason, pers comm.). Mean bait consumption of 165.1 g, equivalent to 0.86 ± 0.04 mg ai/kg brodifacoum (range 0.33 to 1.09 mg ai/kg), provided a lethal dose. Extensive hemorrhaging was observed. The mean concentration in the liver was 0.56 mg ai/kg (range 0.17 to 1.04 mg ai/kg), and most animals that died had a liver concentration below the Rodenticide Registrants Task Force's proposed threshold level of 0.7 mg ai/kg. Hegdal and Colvin (1988) collected dead screech-owls during a brodifacoum-baiting study in Virginia; 8 of 9 dead owls with detectable residue had a level <0.7 ppm, and most had hepatic concentrations ranging from 0.3 (the limit of detection) to 0.5 ppm. Those authors also note that other wildlife has been killed in which brodifacoum liver residues were as low as 0.05 ppm (e.g., Rammell et al. 1984). Brown et al. (1996), in their review entitled "*Identification of pesticide poisoning in wildlife*", state that anticoagulant residues remaining after death are usually above or around 0.1 ppm.

A recent incident in Georgia correlates low levels of liver residue with deaths of a red-tailed hawk and a barn owl. These birds and several other raptors were housed in mews at the Amicalola Falls State Park. In November of 2003, the hawk and owl began showing abnormal physical and behavioral symptoms, and both birds died within a few days. Two other great horned owls later showed similar symptoms and were treated with vitamin K. A dead rat was also discovered in a hole in the back of one of the raptor cages. Second-generation anticoagulant rodenticides were in used at the park at the time of the incident to control rats around a lodge and intern housing. Necropsy of the bird carcasses by the Southeastern Cooperative Wildlife Disease Study, The University of Georgia, found moderate to severe clavarial hemorrhage in both birds and moderate focal myocardial hemorrhage in the barn owl. Microscopic examination also showed moderate to severe multifocal hemorrhage in the owl. Microbiological tests were negative. A fresh liver and kidney samples from each bird were screened for heavy metals and organic chemicals, including anticoagulant rodenticides. The only chemical detected in either bird was brodifacoum, with concentrations measured in the at 0.077 ppm in the hawk and 0.007 ppm in the owl. Despite the very low levels detected, the evidence of this case strongly indicates that the birds died from secondary poisoning by feeding on rats exposed to brodifacoum.

Hosea et al. (2001) demonstrate the importance of a proper necropsy in a case where a low liver-residue concentration (0.04 ppm) in the liver determined that brodifacoum caused the death of a golden eagle in California:

> "The carcass of an adult Golden Eagle was recovered from its breeding territory in Contra Costra County on March 11, 1999 (DFG case accession # P-2060A). The bird had been part of a long term radio telemetry study of eagles in the area. Based on telemetry data the breeding territory consisted mainly of open rangeland and random outbuildings with some areas of urban development.

> "The bird was not recovered in the vicinity of power lines and the feathers did not have the "singed" odor characteristic of accidental electrocution. The necropsy indicated no other evidence of physical trauma. The animal was skinned to determine the presence of puncture wounds from conflicts with other eagles or from a gunshot. The pericardial sac contained serum and blood. Approximately 65% of the surface of the heart muscle was haemorrhagic. The major vessels associated with the heart contained unclotted blood. The lung tissue was haemorrhagic, bleeding from a cut surface. the cerebro-spinal fluid was blood stained, indicating cranial haemorrhage. These clinical signs were consistent with previously published symptoms of anticoagulant toxicosis in raptors (Hegdal et al. 1988, Mendenhall and Pank 1980, Newton et al. 1990, Radvanyi et al. 1988). Liver tissue was analyzed for residues of anticoagulant rodenticides. Kidney tissue was also analyzed for lead concentrations. Kidney tissue had a lead concentration of 1.1 ppm, well below the level that would indicate acute toxicosis (Aiello 1998). Liver tissue had a brodifacoum concentration of 0.04 ppm. The presence of the rodenticide in liver tissue alone does not support a diagnosis of anticoagulant toxicosis. However, if considered in conjunction with the observed clinical signs consistent with anticoagulant toxicosis, a diagnosis of anticoagulant toxicosis is supported."

C. Eason (pers comm.) provided data depicting the range of brodifacoum concentration in various birds collected dead in areas where brodifacoum was applied in New Zealand. A total of 66 (63%) out of 105 birds found dead and 33 (40%) out of 82 collected alive contained brodifacoum residue (Table 44). As might be expected, brodifacoum residues were found in higher concentrations in birds found dead than in birds collected alive. Many dead birds had a liver concentration <0.7 ppm.

Taken together, findings from the field and the incident data indicate that the liver is an appropriate organ for determining exposure of birds and mammals to anticoagulant rodenticides. However, establishing a toxicity threshold of 0.7 ppm seems to be inappropriate and is not supported by the available data on mortality. Moreover, a toxicity threshold would need to account for adverse sublethal effects (e.g., reproductive, chronic).

Table 44. Brodifacoum Residues Detected In the Liver of Birds In New Zealand (compiled by C. Eason; data obtained from the New Zealand National Vertebrate Pesticide Database and Towns et al. 1994, Morgan et al. 1996, Ogilvie et al. 1997, Dowding et al. 1999, Empson and Miskelly 1999, Robertson et al. 1999, and Stephenson et al. 1999)

Species	Collected alive				Collected dead			
	No. tested	No. positive	mg ai/kg in positives		No. tested	No. positive	mg ai/kg in positives	
			mean	range			mean	range
Astralaian harrier	1	0			2	2	0.64	0.61-0.66
Australasian magpie	10	2	0.25	0.08-0.41	10	2	0.47	0.08-0.99
Bellbird	1	0						
Blackbird	6	6	0.10	0.01-0.20	7	7	0.55	0.01-1.10
Chaffinch					3	3	1.43	0.12-2.31
Paradise shelduck					4	4	0.56	0.24-0.80
Grey duck					1	1	0.91	
Mallard					2	2	1.07	0.90-1.23
Fantail	1	0						
Kaka (parrot)					3	3	2.87	1.20-4.10
Kakariki (parakeet)					2	1	0.03	
Kereru (pigeon)					5	0		
Brown kiwi					29	14	0.09	0.01-0.69
Kokako (wattlebird)					4	0		
Morepork (owl)	1	1	0.61		3	3	1.84	0.97-3.44
Myna					3	3	0.80	0.54-1.27
Pukeko (gallinule)					8	8	0.86	0.52-1.35
Robin, Chatham Island					1	1	0.35	
Robin, North Island					1	1	0.58	
Saddleback					4	2	0.33	0.05-0.60

Species	Collected alive				Collected dead			
	No. tested	No. positive	mg ai/kg in positives		No. tested	No. positive	mg ai/kg in positives	
			mean	range			mean	range
Silvereye					1	0		
Southern black-backed gull					1	1	0.58	
Spotless crake					1	1	0.04	
Tomtit	5	0			1	0		
Tui (honeyeater)					1	0		
Weka (rail)	48	24	0.25	0.01-0.95	7	7	1.08	0.11-2.30
Whitehead	5	0			1	0		

The liver is only one of many organs and tissues in which anticoagulant residue accumulates in the body. Concentrations in the liver are often, but not always, higher than in other tissues (e.g., Tables 39, 40, 46, 47). However, because the liver comprises only about 4 to 7% of the weight of a rat or mouse (Newton et al. 1990, Howald et al. 1999), most residue actually may be stored in other parts of the body. For example, Newton et al. (1990) reported a much higher mean residue concentration in liver (2.13 ppm) than in the remainder of the carcass (0.36 ppm) of 10 mice fed brodifacoum bait. However, the mean total amount of residue in the carcass (excluding the liver) was 11.85 µg ai versus only 3.51 µg ai in the liver (Table 47).

Table 46. Tissue Residues in Nine Captive Coyotes Killed With a Single Oral Dose of Diphacinone (adapted from Savarie et al. 1979)

Dose (mg ai/kg)	Tissue residue (ppm)					
	liver	small intestine	kidney	heart	muscle	fat
10	1.2	1.8	0.6	0.5	0.2	<0.1
10	0.7	0.3	0.5	0.2	<0.1	0.3
5	1.8	4.7	1.7	1.5	0.7	<0.1
5	0.5	0.4	<0.1	<0.1	<0.1	<0.1
2.5	0.6	1.3	0.9	0.5	<0.1	<0.1
2.5	0.6	1.0	0.6	0.2	<0.1	<0.1
1.25	1.1	0.5	0.7	0.2	<0.1	<0.1
0.63	1.0	0.3	0.5	0.1	<0.1	<0.1
0.63	0.6	0.2	0.2	<0.1	<0.1	<0.1

Table 47. Brodifacoum Residue in the Liver and Carcass of Mice Fed 20 ppm Bait For 1 Day (adapted from Newton et al. 1990)

Mouse	Liver		Carcass minus liver	
	μg ai	ppm (μg ai/g)	μg ai	ppm (μg ai/g)
1	0.14	0.07	15.39	0.45
2	1.73	1.66	16.07	0.53
3	4.06	3.03	13.13	0.42
4	4.44	2.39	7.44	0.22
5	5.52	2.70	5.10	0.16
6	1.69	1.10	14.48	0.47
7	5.67	3.64	9.77	0.28
8	6.72	2.85	19.83	0.58
9	2.70	1.86	5.37	0.18
10	2.44	1.97	11.88	0.35
mean	3.51 ± 0.66	2.13 ± 0.33	11.85 ± 1.54	0.36 ± 0.05

The "threshold of toxicity" concept (Kaukeinen et al. 2000, Anonymous 2001) also assumes that mortality is the only endpoint of concern. A sublethal dose of anticoagulant can produce significant clotting abnormalities and some hemorrhaging (Eason and Murphy 2001), and such effects might be especially detrimental if combined with other stressors that have additive or synergistic adverse effects. Jaques (1959) reported that stress is a hemorrhagic factor in rabbits and rats, and it could be induced by a variety of factors (e.g., frostbite, insulin, NACL). Only 6% of his rats died after 5 days of exposure to an anticoagulant compound (dicoumarol), but 50% died when exposed to the anticoagulant and additional stressors. Others have speculated that birds exposed to anticoagulants may become more susceptible to environmental stressors, such as adverse weather conditions, food shortages, and predation (Hegdal 1985, Hegdal and Colvin 1988, LaVoie 1990). Newton et al. (1999) have speculated that sublethal levels of rodenticide might predispose death from other causes (e.g., collisions with automobiles, starvation) or may reduce the chance of recovery from accidents.

Three golden eagles (*Aquila chrysactos*) recently died in captivity during relocation from the California Channel Islands (J. Linthicum, The Santa Cruz Predatory Bird Research Group [TSCPBRG], pers. comm.). Necropsies were performed and tissues analyzed for a variety of contaminants. Hemorrhaging in lung and brain tissue was reported in 2 birds, and brodifacoum was detected in the liver (0.004 to 0.026 ppm) of all 3 birds. TSCPBRG has trapped hundreds of golden and bald eagles as part of various studies and never previously had an injury or fatality. SCPBRG noted that "Birds of prey, in particular golden eagles, are hardy, tough animals." and

"Nothing in our experience or other's we have spoken to suggest that these birds should have died under these circumstances." Brodifacoum can't be directly implicated in the deaths of the 3 golden eagles, but concern exists. These birds might have succumbed to brodifacoum when augmented by additional stresses from handling and captivity.

Papworth (1959), in discussing the mechanism of anticoagulant toxicity, speculated that a slight scratch, bruise, or even a minor internal injury might lead to death from hemorrhage if clotting is inhibited over an injured surface. Some incidents reported to the Agency suggest that raptors exposed to anticoagulants can be in danger of excessive bleeding from minor wounds caused by their prey. Such wounds, not normally life-threatening, may cause prolonged bleeding and mortality when blood-clotting mechanisms are disrupted. One great horned owl exposed to brodifacoum (0.64 ppm liver residue) was collected near death on a farm where brodifacoum bait had been applied in barns and sheds. This owl was almost completely exsanguinated from a small laceration on a toe. Other owls and hawks found dead had bled excessively from minor wounds, usually on their feet, likely inflicted by prey (see Attachment D). A partially eaten muskrat was found by one dead owl that appeared to have bled excessively from a puncture wound extending from between the eyes into the sinuses. Brodifacoum was detected in the liver of these raptors at concentrations ranging from 0.08 to 0.80 ppm. Bromadiolone also was detected in 1 owl.

Some of the concerns and uncertainties regarding possible adverse sublethal effects can be addressed through avian reproduction studies, which the Agency will require for all pesticides with outdoor uses. The no-observable-adverse-effects concentration (NOAEC) established from these studies will be a more appropriate indicator of a toxicity threshold than is the liver residue in dead animals.

Conclusions

The available information indicates that differences exist among these rodenticides in their potential risks (primary and secondary) to birds and nontarget mammals. Based on the comparative analysis model, comparing measures of effect for primary and secondary risks to birds and mammals, brodifacoum, zinc phosphide, and difethialone are ranked as the rodenticides posing the greatest potential overall risk (Table 48, Figure 6).

Table 48. Comparative Analysis Model Results for Overall Risk to Birds and Mammals. Tabulated values are weighted measures of effect.

Rodenticide	mg ai/kg bait	Primary risks		Secondary risks		Summary values
		birds	mammals	birds	mammals	
Brodifacoum	50	5.58	1.25	8.60	6.76	5.55
Bromadiolone	50	0.10	0.71	3.03	4.40	2.06
Bromethalin	100	0.10	0.10	2.20	0.44	0.71
Chlorophacinone	100	0.14	0.16	0.03	7.62	1.99
Chlorophacinone	50	0.07	0.08	0.03	7.62	1.95
Cholecalciferol	750	0.12	0.18	2.00	2.00	1.07
Difethialone	25	4.15	0.45	6.29	4.82	3.93
Diphacinone	100	0.01	0.43	3.18	8.42	3.01
Diphacinone	50	0.01	0.22	3.18	8.42	2.96
Warfarin	250	0.04	0.83	1.72	1.32	0.98
Zinc Phosphide	20,000	7.81	10.00	0.00	0.69	4.63

Figure 6. Comparative Analysis Model Summary Values For Overall Risks to Birds and Nontarget Mammals
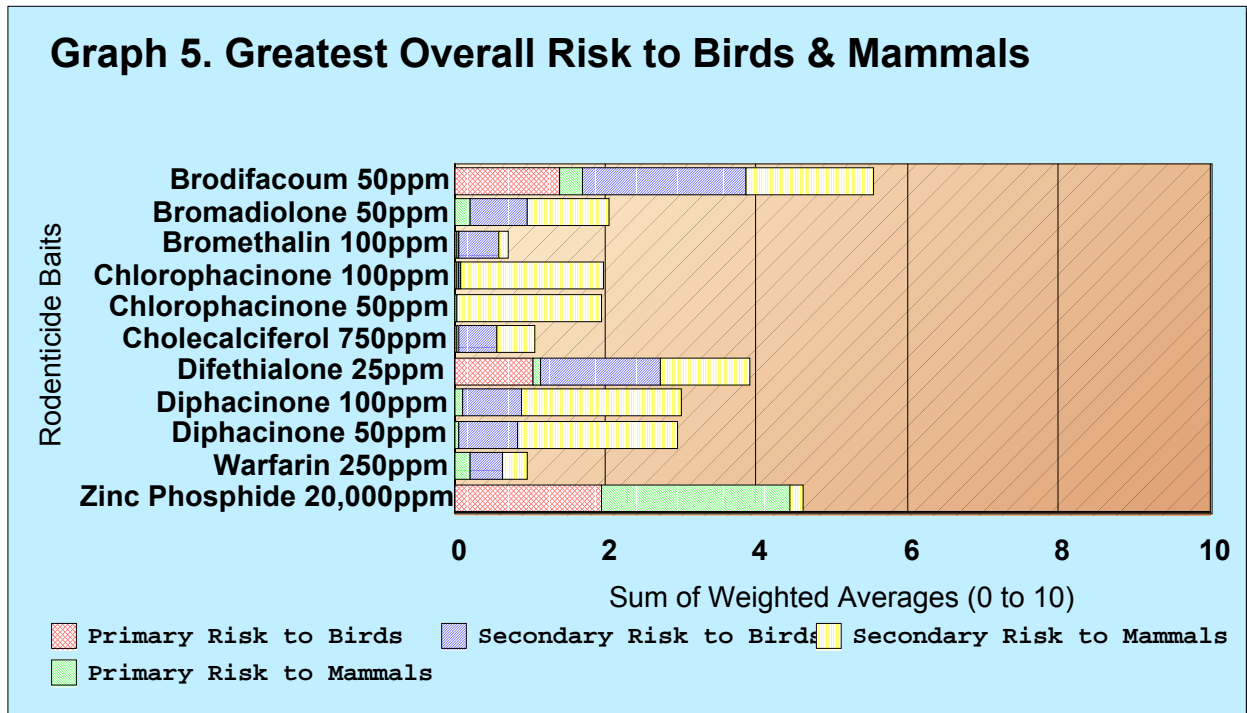
The approach taken for the overall analysis is to analyze each risk type separately, then analyze the summary values for each of the four risk types together. Each type of risk included variable and unequal numbers of measures of effect. Analyzing them separately and using summary values to derive an overall risk value eliminates unequal weighting of one risk over another due to differences in the number of measures of effect. An alternate approach is to consider all measures of effect in a single step and ignore unequal weighting. This alternate approach did not result in a change in the rankings (see Fig. 6).

Figure 7. Comparative Analysis Model Results Summary Values For Overall Risks When All Measures of Effect Are Considered in One Step

Graph 8. Comparing Summary Risk Values
Sum of Each Risk Type vs Separate MEs
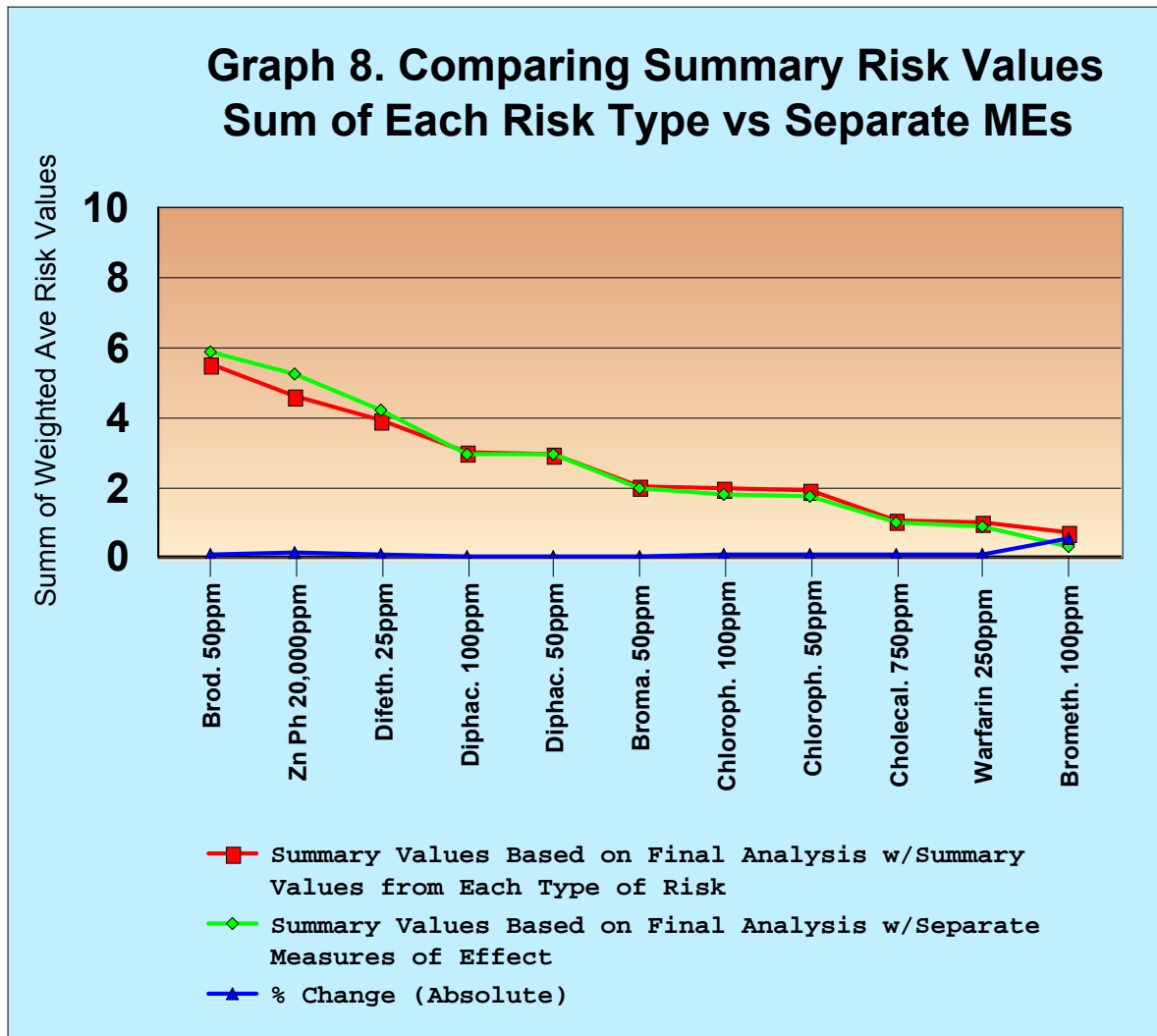
The sensitivity analysis (Fig. 7) indicates that the comparative analysis model rankings are robust, especially for brodifacoum, zinc phosphide and difethialone. Their ranking as the three rodenticides posing the greatest overall potential risk do not change when values for the measures of effect are varied by ±50%. See Appendix C for additional details of the sensitivity analysis.

Figure 8. Sensitivity Analysis of Measure-of-effect Values Used in the Comparative Analysis Model. Each measure-of-effect value is separately decreased by 50% and then increased by 50%.

Graph 6
Results from Sensitivity Analysis

Sum of Weighted Averages

Calculations for + 50% [#s 1 to 77] and - 50% [#s 78 to 154] Change in RQs

- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm
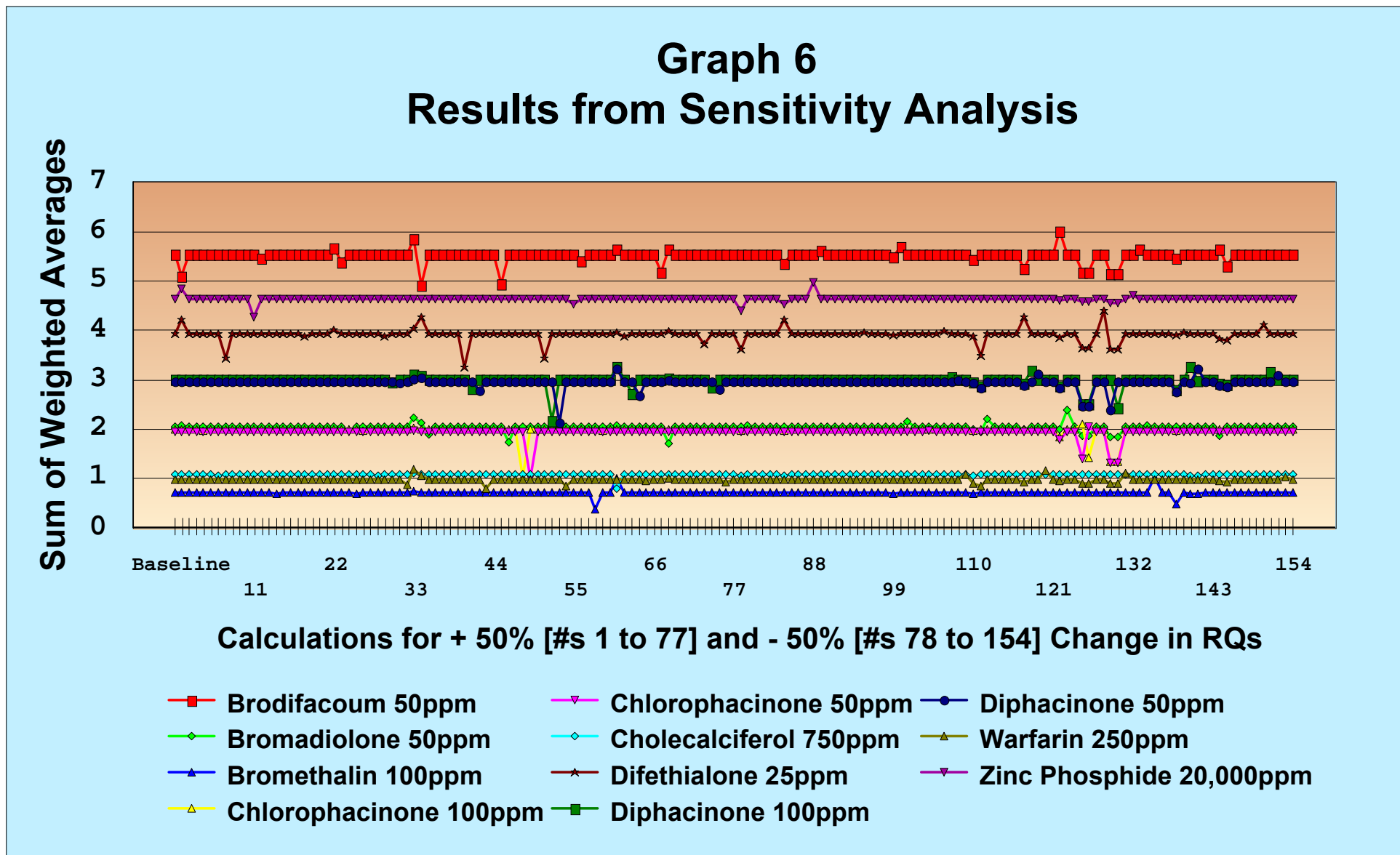
Lack of data for some rodenticides accounts for the most uncertainty in the comparative analysis model results. Data gaps include no secondary-hazards data for difethialone and few for bromethalin and cholecalciferol. For difethialone, which is highly similar to brodifacoum but used at a lower ai in baits (50 ppm vs 25 ppm), an assumption is made that secondary mortality would be about 80% of that reported for brodifacoum. Data are sufficient to distinguish differences in potential primary risks between 50 ppm and 100 ppm chlorophacinone and diphacinone baits but are insufficient to assess differences in secondary risks. Also, few if any data are available regarding retention time in blood and/or liver for some rodenticides, especially first-generation anticoagulants and the non-anticoagulants.

The incident data are not included in the comparative analysis model results but are meaningful for characterizing risk. A comparison of incidents versus the summary risk values for each rodenticide bait is depicted in Figure 9 (see graphs 9 and 10 in Attachment C for separate plots for birds and mammals). The baits with the most incidents and highest risk values are in the upper left, whereas those with the fewest incidents and lowest risk values are in the lower right portion of the graph. Brodifacoum is distinguished by its high summary value and high number of incidents in relation to the other rodenticides. Distinctions cannot be made between the 50 ppm and 100 ppm chlorophacinone and diphacinone baits in the incident data, but the 100 ppm baits are likely to present greater risk than the 50 ppm baits.

Figure 9. Plot of Summary Risk Values Versus Number of Incidents For Each Rodenticide

Graph 11. Plot of Summary Risk Values vs All Incidents
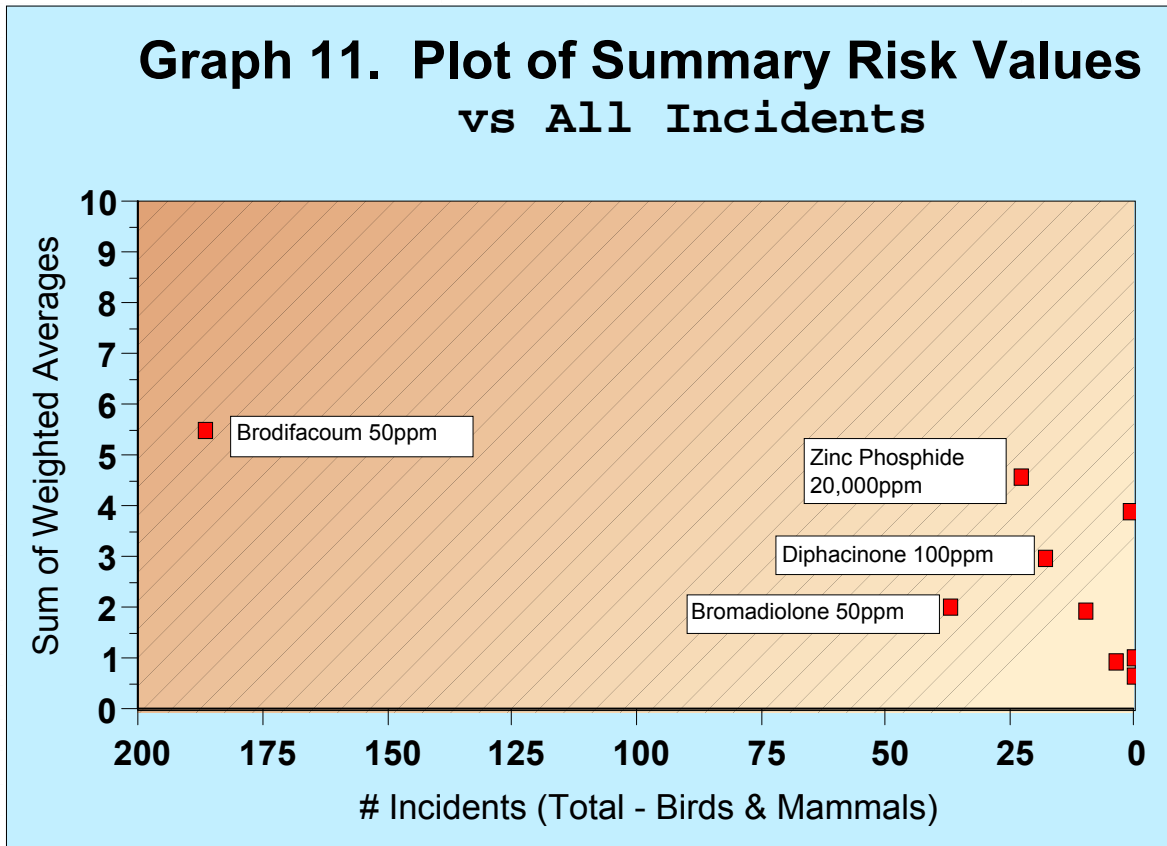
A "lines-of-evidence" assessment was performed based on the available data and supporting information. Each rodenticide is assigned a rating of high, moderate, or low for primary risk to birds, primary risk to nontarget mammals, secondary risk to birds, and secondary risk to mammals (Table 49). Differences among the rodenticides in their potential primary and secondary risks to birds are pronounced. Brodifacoum, and possibly difethialone, baits present the highest potential overall primary and secondary risks to birds and nontarget mammals. Brodifacoum is hazardous to birds and mammals, is persistent, and is widely used for commensal rodent control (see Table 2 for over-the-counter sales in 1996 and 1997). Difethialone is also hazardous to birds and mammals and it is very similar to brodifacoum (e.g., chemical structure, acute-toxicity profile). However, some uncertainty exists when comparing difethialone risks to brodifacoum risks, because market-share and use information and secondary-hazards data are lacking.

Based on the lines-of-evidence assessment, potential primary risks to birds are highest for zinc phosphide, brodifacoum, and difethialone. A small bird finding and eating a pellet or two of any of these baits is likely to ingest a lethal dose, and just a few pellets could provide a lethal dose to larger birds. In contrast, it seems highly unlikely that any small bird could eat 100 to 1000 pellets in a single feeding, which would be needed to provide an LD50 dose from a first-generation anticoagulant, bromadiolone, or cholecalciferol bait. Avian dietary RQs for zinc phosphide, brodifacoum, and difethialone greatly exceed the Agency's LOC for acute risk to birds, whereas they are not or only slightly exceeded for other rodenticides. The dietary RQ provides some useful information for comparing potential risks among rodenticide baits but is based on birds feeding continuously on rodenticide bait for several days. Although some birds might do so, others might only find one or a few pellets in a foraging bout. Therefore, the number of pellets needed to be eaten to provide an LD50 dose may be a more appropriate approximation of potential risk than is the dietary RQ. Nevertheless, the characterization of risk does not change based on the method used to estimate potential risk.

Brodifacoum and difethialone clearly present a greater potential risk to raptors and avian scavengers than do the other rodenticides. Risks posed by brodifacoum are apparent from experimental and other control applications in outdoor settings and from many incidents involving owls, hawks, eagles, corvids and other birds. Concern about risks of second-generation anticoagulants to avian predators and scavengers is widely expressed in the rodenticide literature (Colvin et al. 1988; Hegdal and Colvin 1988; Joermann 1998; Howald et al. 1999; Stephenson et al. 1999; Stone et al. 1999), and the need to monitor residues and population trends is evident (Newton et al. 1990, 1999). This need is especially critical for brodifacoum, because it is so widely used for commensal-rodent control and because it may pose a greater potential risk compared to the other rodenticides.

Rodenticide baits are not selective to the target species. Some baits pose a greater hazard than others, but all rodenticides pose a risk to small nontarget mammals that eat bait, and many pose a potential risk to mammals that prey or scavenge dead or dying rodents that have eaten bait. Baits are formulated to be lethal to small mammals, and many small nontarget mammals are likely to

find and eat bait available around the outside of buildings, inside barns and farm or utility shed, or in other outdoor settings.

Table 49. Primary and Secondary Risk Presumptions For Birds and Nontarget Mammals

Rodenticide	Primary risks		Secondary risks	
	birds	mammals	birds	mammals
Second-generation anticoagulants				
Brodifacoum	high	high	high	high
Difethialone	high	high	high	high
Bromadiolone	low to moderate	high	moderate	high
First-generation anticoagulants				
Diphacinone	low	high	moderate	high
Chlorophacinone	low to moderate	high	low	high
Warfarin	low	high	low	moderate
Others (non-anticoagulants)				
Bromethalin	moderate to high	high	insufficient data available	
Zinc phosphide	high	high	low	low
Cholecalciferol	low to moderate	high	insufficient data available	

The anticoagulants present a potential secondary risk to mammals, although warfarin probably to a lesser extent than the others. The incident data in Attachment D helps characterize and corroborate these risks. Zinc phosphide potentially poses minimal risks to either predatory birds or mammals, but insufficient data are available for bromethalin and cholecalciferol.

Eason et al. (2001) assessed risks of brodifacoum to nontarget birds and mammals in New Zealand, where brodifacoum is widely used to control rodents and possums. They conclude that ". . . the recorded mortality of birds after some control operations, coupled with the detection of brodifacoum residues in a range of wildlife including native birds and feral game animals raises

serious concerns about the long-term effects of the targeted field use of brodifacoum or its use around farms where wildlife might encounter poisoned carcasses." Eason et al. (in prep.) also note: "On an international level we note that the reports of non-target wildlife mortality and contamination in raptors and mustelids from anticoagulants are on the increase (Shore *et al.*, 1999; Howald *et al.* 1999; Stone *et al.* 1999; B. Hosea, pers. comm.) and we strongly recommend that residue-monitoring programmes are established in those countries where anticoagulants are used in the field or extensively around farm buildings. An improved understanding of the risk associated with this class of compound will be achieved when there is a better understanding of whether or not food-chain contamination is occurring. The development of 'biomarkers' of exposure for different bird species will assist those agencies involved in wildlife protection."

More information also is needed on the potential adverse sublethal effects of rodenticides. Newton et al. (1990) note that ". . . there remains the possibility that sub-lethal levels of rodenticide may predispose death from other causes, or reduce the chance of recovery from accidents." Eason and Murphy (2001) emphasize that the risk of brodifacoum is magnified by its persistence, which could lead to accumulation on repeated exposure. A compound that is rapidly metabolized or excreted from a primary consumer may result in a lesser risk than one that bioaccumulates with repeated sublethal exposure, even if repeated exposure occurs weeks or even months after the initial exposure. Those compounds more rapidly cleared from the body are less likely to pose such long-term risk. Unfortunately, most laboratory tests and risk assessments do not consider the potential for bioaccumulation of the highly persistent anticoagulant compounds. Sublethal effects on reproduction will be considered when the data become available.

Uncertainty and Data Needs

A number of factors contribute uncertainty to the assessment. Those that appear to contribute the greatest uncertainty are: (1) missing data, including acute, chronic, and secondary toxicity as well as 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 nontarget 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 nontarget mammals frequenting baited areas and their 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 sublethal effects on reproduction and nontarget 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 sublethal exposures to bait or poisoned rodents utilized as food by predators and scavengers; and (8) lack of incident reporting.

The greatest reduction in uncertainty for these analyses is likely to come from addressing data gaps where data is missing or needs to be standardized because quality is variable, as well as obtaining specific use and exposure information. Some of the concerns about adverse sublethal effects can be addressed through reproduction studies, which the Agency will require for all pesticides with outdoor uses. The no-observable-adverse-effects concentration (NOAEC) established from these studies will be a more appropriate indicator of a toxicity threshold than is the liver residue in dead animals.

Endangered Species Considerations

In response to a formal consultation requested by EPA (1991b) under Section 7 of the Endangered Species Act, the United States Fish and Wildlife Service issued a Biological Opinion on *Effects of 16 Vertebrate Control Agents On Threatened and Endangered Species* in March, 1993 (USFWS 1993). The Biological Opinion included jeopardy determinations for mammals, birds, and reptiles potentially exposed via primary or secondary exposure to brodifacoum, bromadiolone, chlorophacinone, diphacinone, warfarin, bromethalin, zinc phosphide, and cholecalciferol. For each species addressed in the Biological Opinion, the Service determined either that use of the rodenticide "is likely to jeopardize" or "is not likely to jeopardize" the continued existence of the species. For the likely-to-jeopardize determinations the Service provided "reasonable and prudent alternatives" that preclude jeopardy but still allow use of the rodenticide. These alternatives represent the Service's best professional judgement of the measures necessary to provide the appropriate level of protection to the species. The Service also provided "incidental take" statements and "reasonable and prudent measures" to minimize take. Table 50 indicates the number of species, by rodenticide, for which the Service made a likely-to-jeopardize determination. The species addressed, jeopardy and no-jeopardy determinations, and the Service's reasonable and prudent alternatives and/or measures are tabulated for each of the 8 rodenticides in Attachment E. Difethialone, first registered in 1995, is not addressed in this or any subsequent Biological Opinion, but EPA believes the jeopardy determinations for brodifacoum also would be applicable for difethialone.

Table 50. USFWS (1993) Jeopardy Determinations For Endangered and Threatened Species at Risk From Use of Each Rodenticide (Except Difethialone).

Rodenticide	no. species likely at jeopardy		
	mammals	birds	reptiles
Brodifacoum	10	2	0
Bromadiolone	7	0	0
Chlorophacinone	20	1	0
Diphacinone	28	1	0
Warfarin	10	0	0
Bromethalin	10	0	0
Zinc phosphide	16	9	0
Cholecalciferol	10	0	0
Total no. species	29	11	0

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Attachment A: Chemical Structures and Selected Physical/Chemical Properties of the Rodenticides

Brodifacoum:

Chemical name: 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one

Chemical structure:
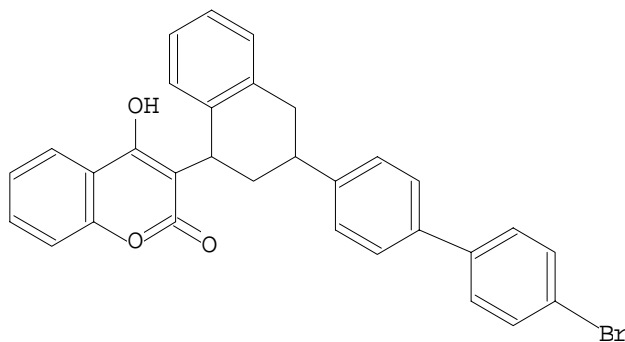
Class: coumarin anticoagulant

Molecular formula: $C_{31}H_{23}BrO_3$

Molecular weight: 523.4

Physical state: solid

Melting point: 228-232° C

Solubility: <10 ppm in water at 20° C, pH 7

Difethialone:

Chemical name: 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-

Chemical structure:
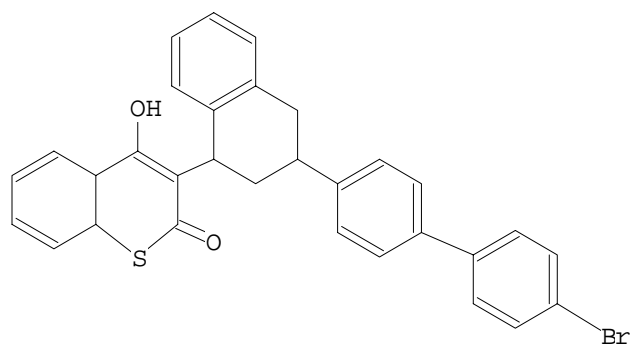
Class: coumarin anticoagulant

Molecular formula: $C_{31}H_{24}BrO_2S$

Molecular weight: 539.5

Physical state: solid

Melting point: 230° C

Solubility: 0.39 ppm in water at 25° C

Bromadiolone:

Chemical name: 3-[3-(4'-bromo[1,1'-biphenyl]-3-hydroxy-1-phenylpropyl]-4-
                   hydroxy-2H-1-benzopyrane-2-one

Chemical structure:
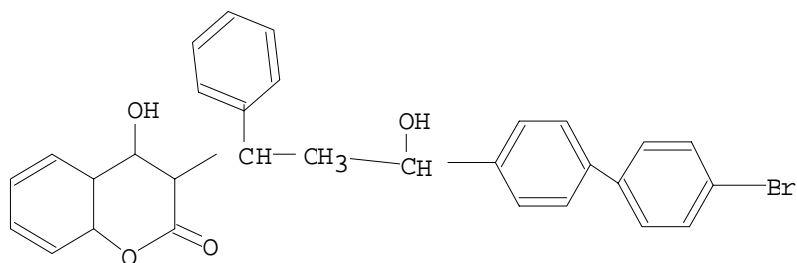
Class: coumarin anticoagulant

Molecular formula: $C_{30}H_{23}BrO_4$

Molecular weight: 527.4

Physical state: solid

Melting point: 200-210° C

Solubility: 12 ppm in water at 20° C

Chlorophacinone:

Chemical name: 2-[(4-chlorophenyl)phenylacetyl]-1H-indene-1,3(2H)-dione

Chemical structure:
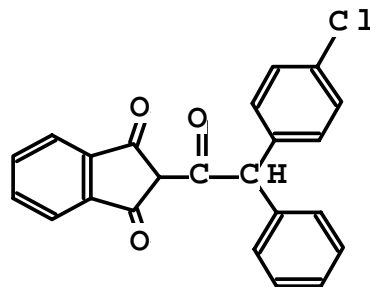
Class: indandione anticoagulant

Molecular formula: $C_{23}H_{14}O_3Cl$

Molecular weight: 373.8

Physical state: solid

Melting point: 140° C

Solubility: 20-34 ppm

Diphacinone:

Chemical name: 2-(diphenylacetyl]-1H-indene-1,3(2H)-dione

Chemical structure:
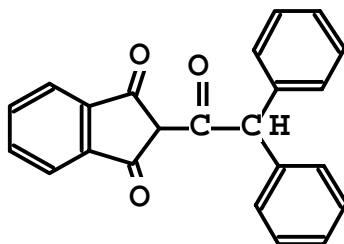
Class: indandione anticoagulant

Molecular formula: $C_{23}H_{16}O_3$

Molecular weight: 340.4

Physical state: solid

Melting point: 141-145° C

Solubility: 17-30 ppm in water (not verified)

Warfarin:

Chemical name: 4-hydroxy-3-(3-oxo-1-phenylbutyl)-2H-1-benzopyran-2-one

Chemical structure:
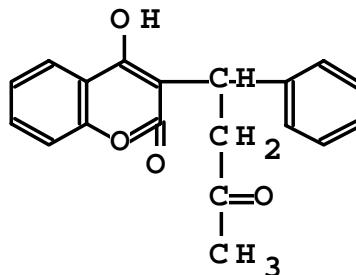
Class: coumarin anticoagulant

Molecular formula: $C_{19}H_{16}O_4$
                            $C_{19}H_{15}NaO_4$ (sodium salt)

Molecular weight: 308.4
                            330.1 (sodium salt)

Physical state: solid

Melting point: 159-165° C

Solubility: 0.196 ppm in water at 25° C

Bromethalin:

Chemical name: N-methyl-2,4-dinitro-N-(2,4,6-tribromophenyl)-6-(trifluoromethyl)-benzenamine

Chemical structure:
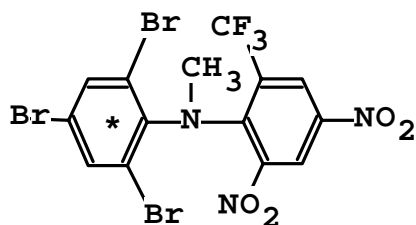
Class: diphenylamine

Molecular formula: $C_{13}H_7Br_3F_3N_3O_4$

Molecular weight: 578.0

Physical state: solid

Melting point: 148-152ºC

Solubility: 3.8 ppb at 25°C

Zinc phosphide:

Chemical name: zinc phosphide

Chemical structure:
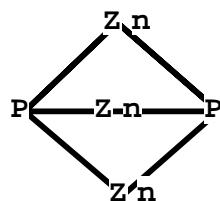
Class: inorganic compound

Molecular formula: Zn_3P_2

Molecular weight: 258.09

Physical state: solid

Melting point: 420° C

Solubility: reported to be insoluble in water

Cholecalciferol:

Chemical name: 9,10-Secocholesta-5,7,10(19)-trien-3 beta-ol

Chemical structure:
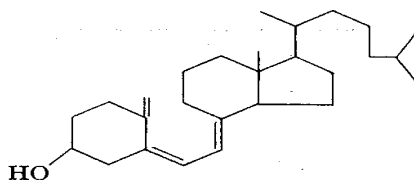
Class: sterol

Molecular formula: $C_{27}H_{44}O$

Molecular weight: 384.6

Physical state: solid

Melting point: 84-85º C

Solubility: no data available, but reported to be insoluble in water

Attachment B: Common and Scientific Names of the Birds and Mammals Cited in the Assessment

Order/ Common name	Scientific name	Family
Waterfowl (Anseriformes)		
Mallard	*Anas platyrhynchos*	Anatidae
Canada goose	*Branta canadensis*	Anatidae
White-fronted goose	*Anser albifrons*	Anatidae
Snow goose	*Chen caerulescens*	Anatidae
Paradise shelduck	*Tadorna variegata*	Anatidae
Grey duck	*Anas superciliosa*	Anatidae
Gallinaceous birds (Galliformes)		
Northern bobwhite	*Colinus virginianus*	Phasianidae
Ring-necked pheasant	*Phasianus colchicus*	Phasianidae
California quail	*Callipepla californica*	Phasianidae
Japanese quail	*Coturnix coturnix*	Phasianidae
Chukar	*Alectoris chukar*	Phasianidae
Gray partridge	*Perdix perdix*	Phasianidae
Turkey (wild)	*Meleagris gallopavo*	Phasianidae
Owls (Strigiformes)		
Barn owl	*Tyto alba*	Tytonidae
Great-horned owl	*Bubo virginianus*	Strigidae
Spotted eagle owl	*Bubo africanus*	Strigidae
Northern saw-whet owl	*Aegolius acadicus*	Strigidae
Eastern screech-owl	*Otus asio*	Strigidae
Long-eared owl	*Asio otus*	Strigidae
Short-eared owl	*Asio flammeus*	Strigidae
Spotted owl	*Strix occidentalis*	Strigidae
Tawny owl	*Strix aluco*	Strigidae
Barred owl	*Strix varia*	Strigidae
Snowy owl	*Nyctea scandiaca*	Strigidae
Morepork	*Ninox novaeseelandiae*	Strigidae

Order/ Common name	Scientific name	Family
Diurnal birds of prey (Falconiformes)		
Red-tailed hawk	*Buteo jamaicensis*	Accipitridae
Red-shouldered hawk	*Buteo lineatus*	Accipitridae
Eurasian buzzard	*Buteo buteo*	Accipitridae
Broad-winged hawk	*Buteo platypterus*	Accipitridae
Rough-legged hawk	*Buteo lagopus*	Accipitridae
Cooper's hawk	*Accipiter cooperii*	Accipitridae
Sharp-shinned hawk	*Accipiter striatus*	Accipitridae
Northern goshawk	*Accipiter gentilis*	Accipitridae
Golden eagle	*Aquila chrysactos*	Accipitridae
Bald eagle	*Haliaeetus leucocephalus*	Accipitridae
Eurasian harrier	*Circus pygargus*	Accipitridae
Australasian harrier	*Circus approximans*	Accipitridae
Kite	*Milvus migrans*	Accipitridae
American kestrel	*Falco sparverius*	Falconidae
Merlin	*Falso columbarius*	Falconidae
Peregrine falcon	*Falco peregrinus*	Falconidae
New Zealand falcon	*Falco novaeseelandiae*	Falconidae
Turkey vulture	*Cathartes aura*	Cathartidae
Black vulture	*Coragyps atratus*	Cathartidae
Herons (Ciconiformes)		
Great blue heron	*Ardea herodias*	Ardeidae
White stork	*Ciconia ciconia*	Ciconiidae
Gulls and shorebirds (Charadriiformes)		
Southern black-backed gull	*Larus dominicans*	Laridae
Laughing gull	*Larus atricilla*	Laridae
Black-billed gull	*Larus bulleri*	Laridae
Franklin's gull	*Larus pipixcan*	Laridae
Brown skua	*Catharacta skua*	Stercorariidae
New Zealand dotterel	*Charadrius obscurus*	Charadriidae
Variable oystercatcher	*Haematopus unicolor*	Haematopodidae

Order/ Common name	Scientific name	Family
Rails (Gruiformes)		
Weka	*Gallirallus australus*	Rallidae
Pukeko (purple gallinule)	*Porphyrio porphyrio*	Rallidae
Spotless crake	*Porzana tabuensis*	Rallidae
Parrots (Psittaciformes)		
Kaka	*Nestor meridionalis*	Psittacidae
Kakariki	*Cyanoramphus* sp.	Psittacidae
Pigeons/doves (Columbiformes)		
Mourning dove	*Zenaida macroura*	Columbidae
Kereru	*Hemiphaga novaeseelandiae*	Columbidae
Kiwi (Apterygiformes)		
Brown kiwi	*Apteryx mantelli*	Apterygidae
Perching Birds (Passeriformes)		
American crow	*Corvus brachyrhynchos*	Corvidae
Carrion crow	*Corvus corone*	Corvidae
Common raven	*Corvus corax*	Corvidae
Northwestern crow	*Corvus caurinus*	Corvidae
Fish crow	*Corvus ossifragus*	Corvidae
Black-billed magpie	*Pica pica*	Corvidae
Blue jay	*Cyanocitta cristata*	Corvidae
Australian magpie	*Gymnorhina tibicen*	Cracticidae
Myna	*Acridotheres tristis*	Sturnidae
House sparrow	*Passer domesticus*	Passeridae
Horned lark	*Eremophila alpestris*	Alaudidae
Lincoln's sparrow	*Melospiza lincolnii*	Emberizidae
Song sparrow	*Melospiza melodia*	Emberizidae
Red-winged blackbird	*Agelaius phoeniceus*	Emberizidae
Canary	*Serinus canarius*	
Chaffinch	*Fringilla coelebs*	Fringillidae
Robin (New Zealand)	*Petroica australis*	Eopsalttriidae

Order/ Common name	Scientific name	Family
Tomtit	*Petroica macrocephala*	Eopsalttriidae
Fantail	*Rhipidura fuliginosa*	Monarchidae
Bellbird	*Anthornis melanura*	Meliphagide
Tui	*Prosthemadera novaeseelandiae*	Meliphagide
Saddleback	*Philesturnus carunculatus*	Callaeidae
Kokako	*Callaeas cinerea*	Callaeidae
Whitehead	*Mohoua ochrocephala*	Pachycephalidae
Silvereye	*Zosterops lateralis*	Zosteropidae
Blackbird (Eurasian)	*Turdus merula*	Muscicapidae

Rodents (Rodentia)

Norway rat	*Rattus norvegicus*	Muridae
Roof rat (black rat, ship rat)	*Rattus rattus*	Muridae
Polynesian rat	*Rattus exulans*	Muridae
House mouse	*Mus musculus*	Muridae
Deer mouse	*Peromyscus maniculatus*	Muridae
Meadow vole	*Microtus pennsylvanicus*	Muridae
Pine vole	*Microtus pinetorum*	Muridae
Water vole	*Arvicola terrestris*	Muridae
Muskrat	*Ondatra zibethicus*	Muridae
Heermann's kangaroo rat	*Dipodomys heermanni*	Heteromyidae
Banner-tailed kangaroo rat	*Dipodomys spectabilis*	Heteromyidae
San Joaquin pocket mouse	*Perognathus inornatus*	Heteromyidae
Botta's pocket gopher	*Thomomys bottae*	Geomyidae
California ground squirrel	*Spermophilus beecheyi*	Sciuridae
Richardson's ground squirrel	*Spermophilus richardsonii*	Sciuridae
Rock squirrel	*Spermophilus variegatus*	Sciuridae
Black-tailed prairie dog	*Cynomys ludovicianus*	Sciuridae
Gray squirrel	*Sciurus carolinensis*	Sciuridae
Fox squirrel	*Sciurus niger*	Sciuridae
Eastern chipmunk	*Tamias striatus*	Sciuridae

Order/ Common name	Scientific name	Family
Nutria (coypu)	*Myocastor coypus*	Myocastoridae
Insectivores (Insectivora)		
Dusky shrew (montane shrew)	*Sorex monticolus*	Soricidae
Rabbits/hares (Lagomorpha)		
Cottontail rabbit	*Sylvilagus floridanus*	Leporidae
Desert cottontail	*Sylvilagus auduboni*	Leporidae
Black-tailed jack rabbit	*Lepus californicus*	Leporidae
European rabbit	*Oryctolagus cuniculus*	Leporidae
European hare	*Lepus capensis*	Leporidae
Carnivores (Carnivora)		
Coyote	*Canis latrans*	Canidae
Red fox	*Vulpes vulpes*	Canidae
San Joaquin kit fox	*Vulpes macrotis mutica*	Canidae
Gray fox	*Urocyon cinereoargenteus*	Canidae
Mountain lion	*Felis concolor*	Felidae
Bobcat	*Lynx rufus*	Felidae
Lynx	*Lynx lynx*	Felidae
Badger	*Meles meles*	Mustelidae
Ermine (stoat)	*Mustela erminea*	Mustelidae
European ferret	*Mustela putorius furo*	Mustelidae
Siberian ferret	*Mustela eversmanni*	Mustelidae
Mink	*Mustela vison*	Mustelidae
Least weasel	*Mustela nivalis*	Mustelidae
Long-tailed weasel	*Mustela frenata*	Mustelidae
Polecat	*Mustela putorius*	Mustelidae
Striped skunk	*Mephitis mephitis*	Mustelidae
Stone marten	*Martes foina*	Mustelidae
Raccoon	*Procyon lotor*	Procyonidae
Mongoose	*Herpestes auropunctatus*	Herpestidae

Order/ Common name	Scientific name	Family
Marsupials (Marsupialia)		
Opossum	*Didelphis virginiana*	Didelphidae
Brushtail possum	*Trichosurus vulpecula*	Phalangeridae
Ungulates (Artiodactyla)		
White-tailed deer	*Odocoileus virginianus*	Cervidae
Roe deer	*Capreolus capreolus*	Cervidae
Boar (pig)	*Sus scrofa*	Suidae

Attachment C: Comparing Potential Risks of Rodenticide Baits to Birds and Mammals Using A Comparative Analysis Model

Prepared by: Douglas J. Urban, Senior Scientist, EFED

Executive Summary

The standard comparative analysis modeling technique often used in decision-analysis called the simple multi-attribute rating technique or SMART is adapted for comparing the risks of rodenticide baits based on a number of measures of effect values for primary and secondary risk to birds and mammals. Of the 11 rodenticide baits considered in the main document, three are considered to pose the greatest overall potential risk to birds and mammals: brodifacoum, zinc phosphide, and difethialone. Based on this analysis, brodifacoum poses the greatest potential risk to birds and mammals, and by a substantial margin over the other rodenticide baits. Brodifacoum has higher summary risk values than zinc phosphide for both secondary risk to birds and secondary risk to mammals. Zinc phosphide has higher summary risk values than difethialone for both primary risk to birds and primary risk to mammals.

A sensitivity analysis is performed to identify the most sensitive measure of effect(s) and to determine if changes of 50% or more in these sensitive measures of effect would change the results of the analysis. The results of this analysis show that the ranking for the rodenticide baits which pose the greatest potential risk to birds and mammals is robust when the measures of effect are changed by +/- 50%. The ranking is generally robust when the measures of effect are changed by +/- 99%, with the following exceptions: a reduction of greater than 67% in the Mean Dietary Risk Quotient for brodifacoum, 64% in the Mean (%) Mortality of Secondary Lab Studies on Birds for brodifacoum, and 76% in the Mean (%) Mortality of Secondary Lab Studies on Mammals for brodifacoum, would result in zinc phosphide moving ahead of brodifacoum as posing the greatest overall risk to birds and mammals; and, an increase of 99% in the Mean (%) Mortality of Secondary Lab Studies on Mammals for difethialone would result in difethialone moving ahead of zinc phosphide as posing the second greatest overall risk to birds and mammals. Thus, with few exceptions, the sensitivity analysis shows that brodifacoum poses the greatest overall potential risk to birds and mammals, followed by zinc phosphide and difethialone.

Acute toxicity reference values for rodenticides to birds and an alternative approach are also considered. The toxicity reference values from a recent publication are substituted for the avian LD50 values for bobwhite quail and mallard ducks used in one of the avian measures of effect for Primary Risk to Birds. The results show that the overall ranking remains the same and the use of these toxicity values does not affect the analysis. When unequal weighting of measures of effect for each type of risk is ignored and all measures of effect are considered together, again the results show that the overall ranking does not change. Unequal weighting of one type of risk over another, at least in this case, does not appear to have a significant effect on the overall ranking.

Two factors are identified as contributing the greatest uncertainty to the analysis: (1) missing data, especially secondary mortality data for difethialone, bromethalin, and cholecalciferol, and blood and liver retention values for a number of rodenticides; and (2) the assumption that field mortality to birds and mammals due to difethialone would likely equal 80% of that reported for brodifacoum. This assumption is based on the many chemical similarities between these two rodenticides, because difethialone bait is formulated at a lower % a.i. than brodifacoum, and the fact that compared to brodifacoum less difethialone is used.

The available incidents for birds and mammals are analyzed and compared to the summary of the weighted average risk values. The results confirm that brodifacoum is the rodenticide bait that poses the greatest potential overall risk to birds and mammals, but they also identify bromadiolone and zinc phosphide as potential concerns for birds, and bromadiolone, diphacinone (100 ppm), and chlorophacinone (100 ppm) as potential concerns for mammals.

Introduction

Comparative risk assessment can be a daunting process when risk assessors are faced with risks for a number of alternative pesticides covering multiple endpoints. When attempting to decide which pesticides present the greatest overall risk and having to consider many different endpoints that lead to a matrix of comparisons, many risk assessors rely on individual or group intuition. The inability to simultaneously track risk values assigned to multiple endpoints among many alternative pesticides as well as the varying importance of each to the assessment can easily result in paralysis (indecision).

The Agency attempted to address such situations in a December 1998 presentation to the Federal Insecticide, Fungicide and Rodenticide (FIFRA) Science Advisory Panel (SAP) titled, "*A Comparative Analysis of Ecological Risks from Pesticides and Their Use: Background, Methodology, Case Study*"[1]. The Panel noted the many scientific uncertainties in the method, yet agreed that it was a useful screening tool that provides a rough estimate of relative risk. The Panel also made a number of helpful suggestions to improve the utility of the methodology presented for use in comparative analyses of ecological risk from pesticides. There are, however, two recommendations that the panel thought critical for valid results: risk quotients - risk indices which are used to express risk from pesticides to nontarget organisms, should never be combined (added); and, a sensitivity analysis should always be included. Following this advice, no risk quotients or indices have been added together for this analysis, and a sensitivity analysis has been included. An early draft of this analysis was submitted for additional peer review by experts outside the Agency. Their comments and suggestions are very helpful and have also been incorporated, to the extent possible, into the updated analysis and this final report.

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[1]See http://www.epa.gov/scipoly/sap/1998/index.htm#december8

Endpoint and Data Selection

This comparative analysis of the potential risks from eleven rodenticide baits is based on the available primary and secondary toxicity data and persistence information for the nine rodenticides which are presented the main document *"Potential Risks of Nine Rodenticides to Birds and Nontarget Mammals: A Comparative Approach"*. Henceforth, this will be referred to as the "main document". These eleven baits are compared based on four types of risk: primary risk to birds, primary risk to mammals, secondary risk to birds, and secondary risk to mammals. Each type of risk is quantitatively evaluated by one to three measures of effect:

Type or Risk	Measures of Effect (ME)
Primary Risk to Birds	1) <u>Mean Dietary Risk Quotient</u> (RQ = the ppm ai in the rodenticide bait/LC50). See Table 29 in the main document. When more than one dietary RQ is available, the mean is calculated and used.
	2) Inverse of the <u>No. of Bait Pellets Needed for 100-g Bird to Ingest LD50 Dose at a Single Feeding</u> See Table 28 in the main document and the 'no. bait pellets' column under 100-g non-passerine. All > values are assumed to be = values.
Primary Risk to Mammals	1) Inverse of the <u>No. of Bait Pellets Needed for 100-g Mammal to Ingest LD50 Dose at a Single Feeding</u> See Table 31 in the main document and the 'no. bait pellets' column under 100-g rodent. All > values are assumed to be = values.
Secondary Risk to Birds	1) <u>Mean % Mortality of Secondary Lab Studies (Birds)</u>. See Tables 11-12, 14-16, 18-19 in the main document and the '% dead' column. Missing data are not considered in the analysis. Difethialone is considered a special case due to it's similarity to brodifacoum. While missing data, it is given a % equal to 80% of that for brodifacoum. Bait specific data is not available; thus, where there are two baits (chlorophacinone, diphacinone), the % dead is applied to both baits.
	2) <u>Blood Retention Time (days)</u>. See Tables 13 and 17 in the main document and the 'Blood $t_{1/2}$' column. Missing data are not considered in the analysis. Where multiple half-lives existed, the mean is calculated and used. Bait specific data are not available; thus, where there are two

baits (chlorophacinone, diphacinone), the half-life is applied to both baits.

3) <u>Liver retention Time (days)</u>. See Tables 13 and 17 in the main document and the 'Liver $t_{1/2}$' column. Missing data are not considered in the analysis. Where multiple half-lives existed, the mean is calculated and used. Bait specific data is not available; thus, where there are two baits (chlorophacinone, diphacinone), the half-life is applied to both baits.

Secondary Risk to Mammals 1) <u>Mean % Mortality of Secondary Lab Studies (Mammals)</u>. See Tables 20-27 in the main document and the '% dead' column. Missing data are not considered in the analysis. Difethialone is considered a special case due to it's similarity to brodifacoum. It is given a % equal to 80% of that for brodifacoum. Bait specific data is not available; thus, where there are two baits (chlorophacinone, diphacinone), the % dead is applied to both baits.

2) <u>Blood Retention Time (days)</u>. See Tables 13 and 17 in the main document and the 'Blood $t_{1/2}$' column. Missing data are not considered in the analysis. Where multiple half-lives existed, the mean is calculated and used. Bait specific data is not available; thus, where there are two baits (chlorophacinone, diphacinone), the half-life is applied to both baits.

3) <u>Liver retention Time (days)</u>. See Tables 13 and 17 in the main document and the 'Liver $t_{1/2}$' column. Missing data are not considered in the analysis. Where multiple half-lives existed, the mean is calculated and used. Bait specific data is not available; thus, where there are two baits (chlorophacinone, diphacinone), the half-life is applied to both baits.

Table 1 contains the data for each of the measures of effect used in the analysis.

Method & Approach[2]

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[2]Much of the software description is based on a software review by Len Tashman and Sara Munro, 1997.

During the 1998 SAP presentation, commercially available software called *DecideRight® (Version 1.2)*[3] was presented as an useful tool designed to aid comparative analysis and support decision-making. This user friendly software is designed primarily for use in business, but it can be applied to many situations where risk assessors and decision-makers must choose among alternatives when many factors must be considered. The underlying methodology used in the software is called the simple multi-attribute rating technique or SMART (Goodwin and Wright, 1998). This technique was developed approximately 30-years ago and has become a standard in decision modeling. When faced with a number of alternatives pesticide baits and a number of types of risk with measures of effect, SMART prescribes that (1) each alternative pesticide be rated on each measure of effect, (2) each measure of effect be assigned a measure of importance to the decision-maker, and (3) a summary score for each alternative pesticide be calculated as a weighted average of the ratings, where the weights represent the relative importance of the measure of effect for each type of potential risk. In the end, the higher the summary score, the higher the potential risk for that alternative pesticide. The result of this process has proved to be superior to the alternative of reliance on intuition.

SMART is not rooted in probability and ignores any interaction or correlation between criteria. The assigned ratings are assumed to be based on full knowledge of the type of risk. However, some uncertainty can be dealt with in the ratings by a sensitivity analysis. In this case, two scenarios are developed where the individual risk ratings are varied to see the effect on the overall ranking. This results of this analysis is included.

To begin, the problem must be formulated as a question. In this analysis, the question being asked is: "*Which of the 11 Rodenticide Baits Pose the Greatest Overall Risk to Birds and Mammals Based on their Primary and Secondary Risk Characteristics?*" The following basic equation is used to calculate the summary values for the risk comparison:

Equation 1.

$$\textbf{Summary Value}_{\textbf{(scale from 0 to 10)}} = \sum f(ME_i)(ME_{max})^{-1} \cdot f(Weight) \, (\sum Weights)^{-1} \cdot (10)$$

where ME_i is the measure of effect value for one of the eleven rodenticide baits and ME_{max} is the maximum ME for all rodenticide baits; **Weight** is the importance value placed on each measure of effect, with high = 10 to 6.67, medium = 6.68 to 3.33, and low = 3.34 to 0; and, $\sum$**Weights** is the sum of all the weights for all the measures of effect.

For this analysis, potential risk increased as all measures of effect values increased. For two measures: No. Bait Pellets Needed for 100-g Bird to Ingest LD50 Dose at a Single Feeding; and,

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[3]*DecideRight®* was developed by Avantos Performance Systems of Emertville, California. The company has since closed; however, the software is still available from Performance Management Solutions, LLC, 1198 Pacific Coast Hwy., D515 Seal Beach, CA. 90740 [Ph. 562/430-7096 Ext. 0 - Fax. 800/645-6618]. Also, see http://www.performancesolutionstech.com/default.htm . Mention of this commercial product does not constitute a recommendation or endorsement by EPA.

No. Bait Pellets Needed for 100-g Mammal to Ingest LD50 Dose at a Single Feeding, the inverse of the number of bait pellets was used in order to correctly calculate the weighted averages and avoid skewed results. Further, the weights given to all measures of effect are high (=10) since we did not have any scientific reason to differentiate between the importance of the measures, except for the two measures of retention or persistence in prey. The half-life in blood and liver are each given a weight of medium (2.5) for the secondary risk to birds and the secondary risk to mammals since we believe that the overall importance of the persistence should equal that of the mortality observed in the toxicity studies (2.5 x 4 = 10). Finally, summary values for each of the four risk types (i.e., primary risk to birds, primary risk to mammals, secondary risk to birds, secondary risk to mammals) are calculated separately and then these summary values are analyzed together in a final overall analysis. An alternate approach is considered where all measure of effects are considered in one step. The results of different approaches are compared and discussed later in this appendix. Basically, the approach using separate risk calculations is chosen because it eliminated unequal weighting of one risk over another due to differences in the number of measures of effect.

The *DecideRight*® software is not used for the analysis; rather, *Lotus SmartSuite 1-2-3*® is used for all calculations .

Table 1. Input Data for Comparative Analysis of Risk from 11 Rodenticide Baits

	Type of Risk								
	Primary Risk to Birds		*Primary Risk to Mammals*	*Secondary Risk to Birds*			*Secondary Risk to Mammals*		
	Measures of Effect		**Measure of Effect**	**Measures of Effect**			**Measures of Effect**		
Alternative Pesticides	**Mean Dietary Risk Quotient (ppm bait/LC50)**	**Inverse of the No. Bait Pellets Needed for 100gm Bird to Ingest LD50 Dose**	**Inverse of the No. Bait Pellets Needed for 100gm Mammal to Ingest LD50 Dose**	**Mean Mortality (%)of Secondary Lab Studies (Birds)**	**Blood Retention Time (days)**	**Liver Retention Time (days)**	**Mean Mortality (%) of Secondary Lab Studies (Mammals)**	**Blood Retention Time (days)**	**Liver Retention Time (days)**
Brodifacoum 50 ppm	44.00	0.3846	0.25	42.00	7.30	217.00	42.00	7.30	217.00
Bromadiolone 50 ppm	0.85	0.0007	0.14	8.00	1.40	248.00	23.00	1.40	248.00
Bromethalin 100 ppm	0.35	0.0435	0.02	No Data	5.60	No Data	0.00	5.60	No Data
Chlorophacinone 100 ppm	1.20	0.0008	0.03	0.00	0.40	No Data	55.00	0.40	No Data
Chlorophacinone 50 ppm	0.60	0.0004	0.02	0.00	0.40	No Data	55.00	0.40	No Data
Cholecalciferol 750 ppm	1.00	0.0025	0.04	0.00	25.50	No Data	0.00	25.50	No Data
Difethialone 25 ppm	34.00	0.1923	0.09	33.60	2.50	117.70	33.60	2.50	117.70
Diphacinone 100 ppm	0.10	0.0005	0.09	9.00	17.50	90.00	58.00	17.50	90.00
Diphacinone 50 ppm	0.10	0.0003	0.04	9.00	17.50	90.00	58.0	17.50	90.00
Warfarin 250 ppm	0.35	0.0008	0.17	9.00	0.82	35.00	9.00	0.82	0.35.00
Zinc Phosphide 20,000 ppm	24.75	3.3333	2.00	0.00	No Data	No Data	4.00	No Data	No Data

Results of the Comparative Analysis Model

As noted above, the summary values for each of the four risk types are calculated separately and then these summary values are analyzed together in a final overall analysis. Decision tables and graphs of the sums of the weighted averages for each of the four risk types are presented separately below. At the end, the decision table and graph for the overall potential risk analysis is presented.

By way of example, a detailed explanation of how the comparative analysis model results presented in Table 2. - Greatest Primary Risk to Birds - are calculated, is provided here in a series of steps. The measure of effect values come from Table 1.

Step 1. <u>Give a Weight (Importance Value) to each Measure of Effect</u>

Both Measures of Effect for Primary Risk to Birds are given a weight of high =10.

Step 2. <u>Normalize the Assigned Weights for each Measure of Effect</u>

Divide each weight by the sum of the all weights, i.e. 10/20 = 0.5, and multiply the result by 10. Thus, the weight for each Measure of Effect = 5.

Step 3. <u>Calculate the Weighted Average Values for Each Measure of Effect and each Bait</u>

Substep A. The first measure of effect is the Mean Dietary Risk Quotient (ppm bait/LC50). The calculation for each rodenticide bait is: The RQ value for that rodenticide is divided by the Maximum RQ value for all the rodenticides; and, the result is multiplied by the normalized wight for the measure of effect. Specifically, for each rodenticide bait, the calculations are as follows:

Brodifacoum 50 ppm:	$(44.0/44.0)*5 = 5.00$
Bromadiolone 50 ppm:	$(0.85/44.0)*5 = 0.10$
Bromethalin 100 ppm:	$(0.35/44.0)*5 = 0.04$
Chlorophacinone 100 ppm:	$(1.20/44.0)*5 = 0.14$
Chlorophacinone 50 ppm:	$(0.60/44.0)*5 = 0.07$
Cholecalciferol 750 ppm:	$(1.00/44.0)*5 = 0.11$
Difethialone 25 ppm:	$(34.0/44.0)*5 = 3.86$
Diphacinone 100 ppm:	$(0.10/44.0)*5 = 0.01$
Diphacinone 50 ppm:	$(0.10/44.0)*5 = 0.01$
Warfarin 250 ppm:	$(0.35/44.0)*5 = 0.04$
Zinc Phosphide 20,000 ppm:	$(24.75/44.0)*5 = 2.81$

Substep B. The second measure of effect is the No. Bait Pellets Needed for a 100 g Bird to Ingest LD50 Dose at a Single Feeding. The inverse of this measure of effect was used in order to correctly calculate the weighted averages and avoid skewed results. The Inverse of the No. Bait Pellets value for each rodenticide is divided by the Maximum

Inverse of the No. Bait Pellets value; then, this result is multiplied by the normalized weight for the measure of effect. Specifically, for each rodenticide bait, the calculations are as follows:

Brodifacoum 50 ppm: (0.3846/3.3333)*5 = 0.58
Bromadiolone 50 ppm: (0.0007/3.3333)*5 = 0.00
Bromethalin 100 ppm: (0.0435/3.3333)*5 = 0.07
Chlorophacinone 100 ppm: (0.0008/3.3333)*5 = 0.00
Chlorophacinone 50 ppm: (0.0004/3.3333)*5 = 0.00
Cholecalciferol 750 ppm: (0.0025/3.3333)*5 = 0.00
Difethialone 25 ppm: (0.1923/3.3333)*5 = 0.29
Diphacinone 100 ppm: (0.0005/3.3333)*5 = 0.00
Diphacinone 50 ppm: (0.0003/3.3333)*5 = 0.00
Warfarin 250 ppm: (0.0008/3.3333)*5 = 0.00
Zinc Phosphide 20,000 ppm: (3.3333/3.3333)*5 = 5.00

Step 4. <u>Sum the Weighted Average Values for Both Measures of Effect for each Rodenticide Bait</u>

The weighted average values calculated above are summed for each rodenticide bait to arrive at the sum of the weighted average values for primary risk to birds.

Brodifacoum 50 ppm: 5.00+0.58 = 5.58
Bromadiolone 50 ppm: 0.10+0.00 = 0.10
Bromethalin 100 ppm: 0.04+0.07 = 0.10
Chlorophacinone 100 ppm: 0.14+0.00 = 0.14
Chlorophacinone 50 ppm: 0.07+0.00 = 0.07
Cholecalciferol 750 ppm: 0.11+0.00 = 0.12
Difethialone 25 ppm: 3.86+0.29 = 4.15
Diphacinone 100 ppm: 0.01+0.00 = 0.10
Diphacinone 50 ppm: 0.01+0.00 = 0.01
Warfarin 250 ppm: 0.04+0.00 = 0.04
Zinc Phosphide 20,000 ppm: 2.81+5.00 = 7.81

The summary values above, in ranked order from highest to lowest, are found in Table 2, and Figure 1 presents a graph of the calculations. Rounding affects some of the calculations.

Results of Comparative Analysis for Primary Risk to Birds

The question *"Which of the 11 Rodenticide Baits Pose the Greatest Primary Risk to Birds?"* is analyzed by the comparative model and the results are presented in a table (Table 2). The sum of the weighted average values for primary risk to birds is found in the 'Summary Values" column in Table 2, and graphically shown in Figure 1. The results are based on two measures of effect: Mean Dietary Risk Quotient (ppm bait/LC50) and the Inverse of the No. Bait Pellets Needed for 100-g Bird to Ingest LD50 at Single Feeding. Of all the rodenticide baits considered, three are considered to pose the greatest potential primary risk to birds:

> Zinc Phosphide 20,000 ppm
> Brodifacoum 50 ppm
> Difethialone 25 ppm

Based on this analysis, zinc phosphide poses the greatest potential primary risk to birds. The Inverse of the No. Bait Pellets Needed for 100-g Bird to Ingest LD50 at Single Feeding appears to be the most significant measure of effect leading to the conclusion that zinc phosphide poses greater risk to birds than brodifacoum. It also appears to be the most significant measure of effects leading to the conclusion that zinc phosphide poses greater potential primary risk to birds than difethialone. Brodifacoum has a higher summary risk value for one of the two measures of effect, mean dietary risk quotient (ppm ai bait/LC50), than both zinc phosphide and difethialone. Difethialone also has a higher summary risk value for one of the two measures of effect, mean dietary risk quotient (ppm ai bait/LC50), than zinc phosphide.

Table 2. Decision Table: Greatest Primary Risk to Birds.

Alternative Pesticides	Mean Dietary Risk Quotient (ppm bait/ LC50)	Inverse of No. Bait Pellets Needed for 100gm Bird to Ingest LD50 Dose at Single Feeding	Summary Values
	Measure of Effect Values		
Brodifacoum 50ppm	44.00	0.38	5.58
Bromadiolone 50ppm	0.85	0.00	0.10
Bromethalin 100ppm	0.35	0.04	0.10
Chlorophacinone 100ppm	1.20	0.00	0.14
Chlorophacinone 50ppm	0.60	0.00	0.07
Cholecalciferol 750ppm	1.00	0.00	0.12
Difethialone 25ppm	34.00	0.19	4.15
Diphacinone 100ppm	0.10	0.00	0.01
Diphacinone 50ppm	0.10	0.00	0.01
Warfarin 250ppm	0.35	0.00	0.04
Zinc Phosphide 20,000ppm	24.75	3.33	7.81

**Graph 1. Greatest Primary Risk to Birds
Sum of Weighted Averages of Measures of Effect**

Rodenticide Baits:
Brodifacoum 50ppm
Bromadiolone 50ppm
Bromethalin 100ppm
Chlorophacinone 100ppm
Chlorophacinone 50ppm
Cholecalciferol 750ppm
Difethialone 25ppm
Diphacinone 100ppm
Diphacinone 50ppm
Warfarin 250ppm
Zinc Phosphide 20,000ppm

Sum of Weighted Averages (0 to 10)

Legend:
Mean Dietary Risk Quotient (ppm a bait/LC50)
Inverse of No. Bait Pellets Needed for 100gm Bird to Ingest LD50 Dose at Sing Feeding

Results of Comparative Analysis for Primary Risk to Mammals

The question *"Which of the 11 Rodenticide Baits Pose the Greatest Primary Risk to Mammals?"* is analyzed by the comparative model and the results are presented in a table (Table 3). The sum of the weighted average values for primary risk is found in the 'Summary Values" column in Table 3, and graphically shown in Figure 2. The results are based on a single measure of effect: Inverse of the No. Bait Pellets Needed for 100-g Mammal to Ingest an LD50 Dose at a Single Feeding. Of all the rodenticide baits considered, one is considered to pose the greatest potential primary risk be mammals:

Zinc Phosphide 20,000 ppm

Based on this analysis, zinc phosphide poses the greatest potential primary risk to mammals by a substantial margin over the other rodenticide baits. Warfarin and brodifacoum are in distant second and third place.

Table 3. Greatest Primary Risk to Mammals.		
	Inverse of No. Ba Pellets Needed for 100gm Mammal to Ingest LD50 Dose at Single Feeding	*Summary Values*
Alternative Pesticides	Measure of Effect Value	
Brodifacoum 50ppm	0.25	1.25
Bromadiolone 50ppm	0.14	0.71
Bromethalin 100ppm	0.02	0.10
Chlorophacinone 100ppm	0.03	0.16
Chlorophacinone 50ppm	0.02	0.08
Cholecalciferol 750ppm	0.04	0.18
Difethialone 25ppm	0.09	0.45
Diphacinone 100ppm	0.09	0.43
Diphacinone 50ppm	0.04	0.22
Warfarin 250ppm	0.17	0.83
Zinc Phosphide 20,000ppm	2.00	10.00

Graph 2. Greatest Primary Risk to Mammals
Sum of Weighted Averages of Measure of Effect
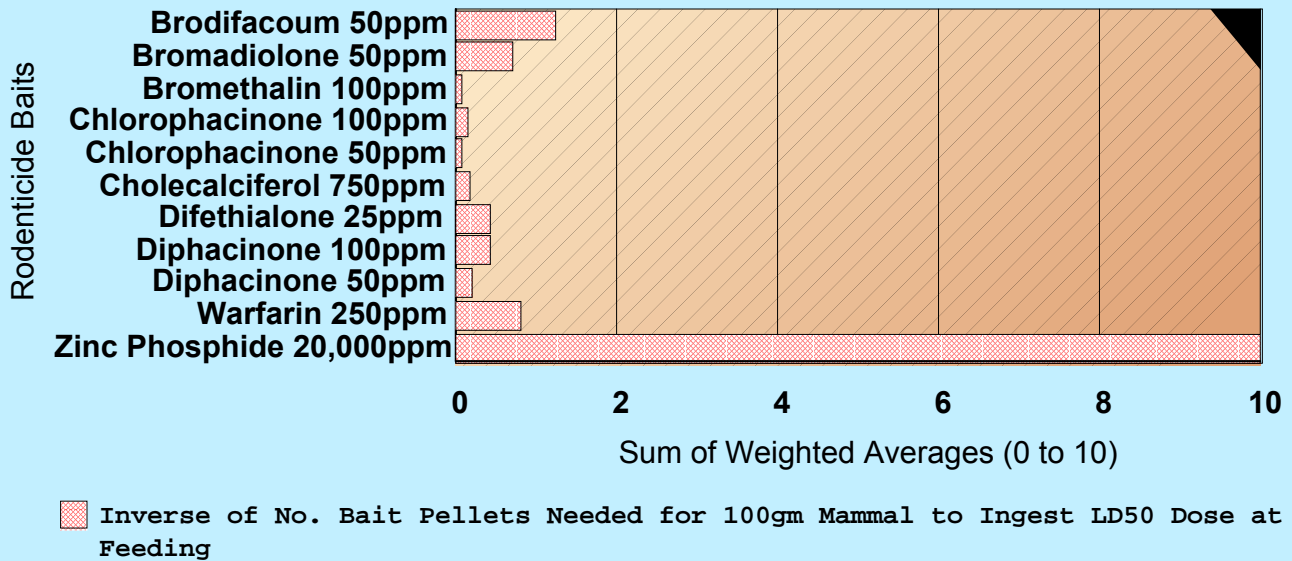
Rodenticide Baits (y-axis, top to bottom):
- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

x-axis: 0, 2, 4, 6, 8, 10

Sum of Weighted Averages (0 to 10)

Inverse of No. Bait Pellets Needed for 100gm Mammal to Ingest LD50 Dose at Feeding

Results of Comparative Analysis for Secondary Risk to Birds

The question *"Which of the 11 Rodenticide Baits Pose the Greatest Secondary Risk to Birds ?"* is analyzed by the comparative model and the results are presented in a table (Table 4). The sum of the weighted average values for secondary risk to birds is found in the 'Summary Values" column in Table 4, and graphically shown in Figure 3. The results are based on three measures of effect: Mean % Mortality of Secondary Lab Studies, Blood Retention Time (Days), Liver Retention Time (Days). Of all the rodenticide baits considered, two are considered to pose the greatest potential secondary risk to birds:

> Brodifacoum 50 ppm
> Difethialone 25 ppm

Based on this analysis, brodifacoum poses the greatest potential secondary risk to birds, and by a substantial margin over difethialone. Brodifacoum had higher summary values for all three measures of effect. Mean (%) Mortality of Secondary Lab Studies appears to be the most significant measure of effect leading to the conclusion that brodifacoum poses greater risk than difethialone.

Table 4. Greatest Secondary Risk to Birds.

Alternative Pesticides Measures of Effect Value	Mean Mortality of Secondary Lab Studies	Blood Retention Time (days)	Liver Retention Time (days)	*Summary* *Values*
Brodifacoum 50ppm	42.00	7.30	217.00	8.60
Bromadiolone 50ppm	8.00	1.40	248.00	3.03
Bromethalin 100ppm	No Data	5.60	No Data	2.20
Chlorophacinone 100ppm	0.00	0.40	No Data	0.03
Chlorophacinone 50ppm	0.00	0.40	No Data	0.03
Cholecalciferol 750ppm	0.00	25.50	No Data	2.00
Difethialone 25ppm	33.60	2.50	117.70	6.29
Diphacinone 100ppm	9.00	17.50	90.00	3.18
Diphacinone 50ppm	9.00	17.50	90.00	3.18
Warfarin 250ppm	9.00	0.82	35.00	1.72
Zinc Phosphide 20,000ppm	0.00	No Data	No Data	0.00

Results of Comparative Analysis for Secondary Risk to Mammals

Graph 3. Greatest Secondary Risk to Birds
Sum of Weighted Averages of Measures of Effect
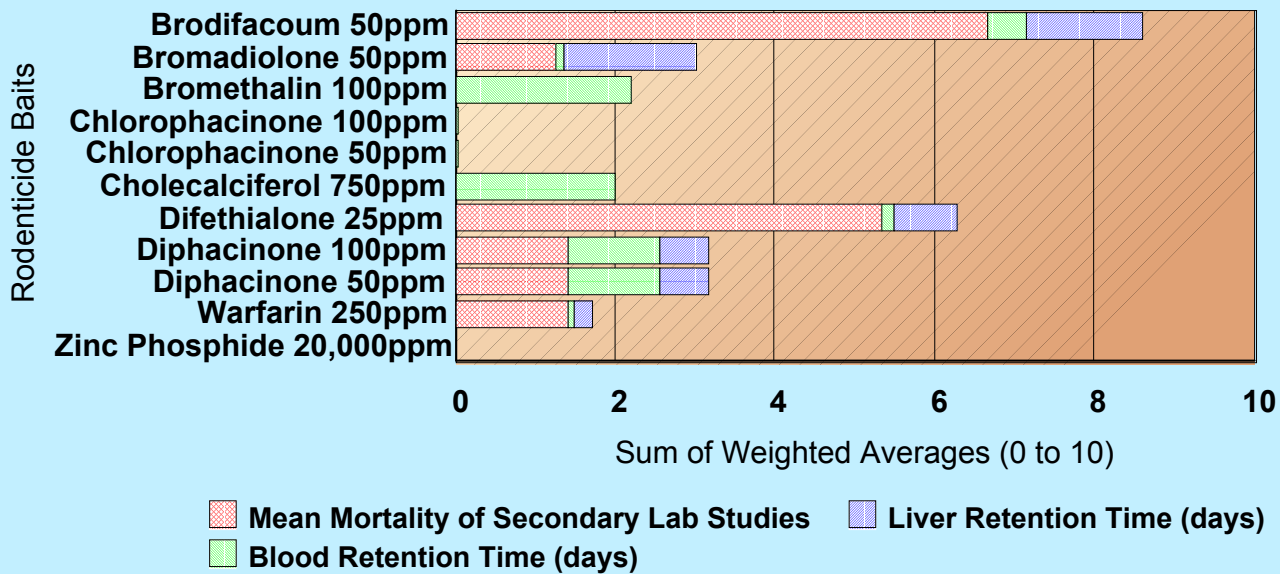
The question *"Which of the 11 Rodenticide Baits Pose the Greatest Secondary Risk to Mammals?"* is analyzed in the comparative analysis model and the results are presented in a table (Table 5). The sum of the weighted average values for secondary risk to mammals is found in the 'Summary Values" column in Table 5, and graphically shown in Figure 4. The results are based on three measures of effect: Mean % Mortality of Secondary Lab Studies, Blood Retention Time (Days), Liver Retention Time (Days). Of all the rodenticide baits considered, five are considered to pose the greatest potential secondary risk to mammals:

> Diphacinone 100 ppm
> Diphacinone 50 ppm
> Chlorophacinone 100 ppm
> Chlorophacinone 50 ppm
> Brodifacoum 50 ppm

Based on this analysis, diphacinone (100 ppm and 50 ppm baits) pose the greatest potential secondary risk to mammals. Both rodenticide baits had identical summary risk values. Blood Retention Time (days) appears to be the most significant measure of effect leading to the conclusion that both of these diphacinone baits pose greater secondary risk to mammals than the

chlorophacinone baits (100 ppm and 50 ppm baits). Both of the chlorophacinone baits had identical summary risk values as well. Mean (%) Mortality of Secondary Lab Studies appears to be the most significant measure of effect leading to the conclusion that both baits of diphacinone and chlorophacinone pose greater secondary risk to mammals than brodifacoum.

Table 5. Greatest Secondary Risk to Mammals.				
	Mean Mortality of Secondary Lab Studies	Blood Retention Time (days)	Liver Retention Time (days)	*Summary Values*
Alternative Pesticides	Measures of Effect Value			
Brodifacoum 50ppm	42.00	7.30	217.00	6.76
Bromadiolone 50ppm	23.00	1.40	248.00	4.40
Bromethalin 100ppm	0.00	5.60	No Data	0.44
Chlorophacinone 100ppm	55.00	0.40	No Data	7.62
Chlorophacinone 50ppm	55.00	0.40	No Data	7.62
Cholecalciferol 750ppm	0.00	25.50	No Data	2.00
Difethialone 25ppm	33.60	2.50	117.70	4.82
Diphacinone 100ppm	58.00	17.50	90.00	8.42
Diphacinone 50ppm	58.00	17.50	90.00	8.42
Warfarin 250ppm	9.00	0.82	35.00	1.32
Zinc Phosphide 20,000ppm	4.00	No Data	No Data	0.69

Graph 4. Greatest Secondary Risk to Mammals
Sum of Weighted Averages of Measures of Effect

Rodenticide Baits (y-axis):
- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

X-axis: Sum of Weighted Averages (0 to 10) — 0, 2, 4, 6, 8, 10

Legend:
- Mean Mortality of Secondary Lab Studies
- Liver Retention Time (days)
- Blood Retention Time (days)
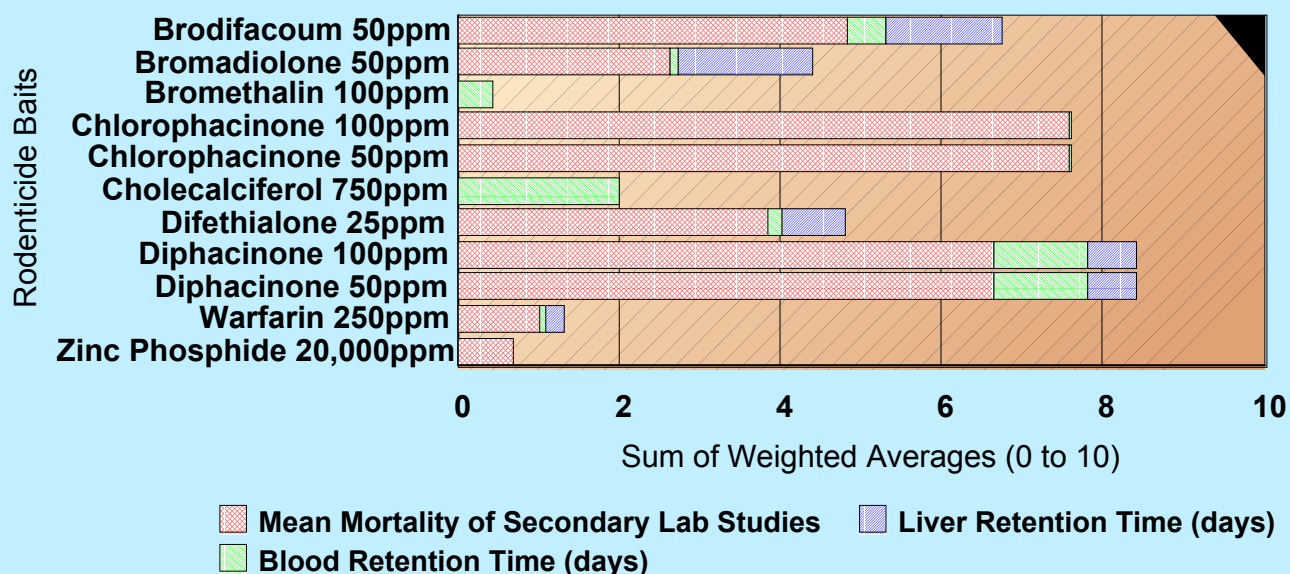
Results of Comparative Analysis for Overall Risk to Birds and Mammals

The question *"Which of the 11 Rodenticide Baits Pose the Greatest Overall Risk to Birds and Mammals?"* is analyzed by the comparative analysis model and the results are presented in a table (Table 6). The sum of the weighted average values for overall risk to birds and mammals is found in the 'Summary Values" column in Table 6, and graphically shown in Figure 5. The results are based on four types of risk, which in this case are the four measures of effect: Primary Risk to Birds, Primary Risk to Mammals, Secondary Risk to Birds, and Secondary Risk to Mammals. Of all the rodenticide baits considered, three are considered to pose the greatest potential overall risk to birds and mammals:

> Brodifacoum 50 ppm
> Zinc Phosphide 20,000 ppm
> Difethialone 25 ppm

Based on this analysis, brodifacoum poses the greatest overall potential risk to birds and mammals and by a substantial margin over the other rodenticide baits. Brodifacoum has higher summary risk values than zinc phosphide for two of the four measures of effect. Secondary Risk

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to Birds and Secondary Risk to Mammals appear to be the most significant measures of effect leading to the conclusion that brodifacoum poses greater overall potential risk to birds and mammals than zinc phosphide. Zinc phosphide has higher summary risk values than difethialone for two of the four measures of effect, and Primary Risk to Mammals and Primary Risk to Birds appear to be the most significant measures of effect leading to the conclusion that zinc phosphide poses greater overall risk to birds and mammals than difethialone. Difethialone has higher summary risk values than both diphacinone baits (100 ppm and 50 ppm) for three of the four measures of effect, and Primary Risk to Birds appears to be the most significant measure of effect leading to the conclusion that difethialone poses greater overall potential risk to birds and mammals than both diphacinone baits.

Table 6. Greatest Overall Risk to Birds and Mammals.

	Primary Risk to Birds	Primary Risk to Mammals	Secondary Risk to Birds	Secondary Risk to Mammals	Summary Values
Alternative Pesticide	Measures of Effect Value				
Brodifacoum 50ppm	5.58	1.25	8.60	6.76	5.55
Bromadiolone 50ppm	0.10	0.71	3.03	4.40	2.06
Bromethalin 100ppm	0.10	0.10	2.20	0.44	0.71
Chlorophacinone 100ppm	0.14	0.16	0.03	7.62	1.99
Chlorophacinone 50ppm	0.07	0.08	0.03	7.62	1.95
Cholecalciferol 750ppm	0.12	0.18	2.00	2.00	1.07
Difethialone 25ppm	4.15	0.45	6.29	4.82	3.93
Diphacinone 100ppm	0.01	0.43	3.18	8.42	3.01
Diphacinone 50ppm	0.01	0.22	3.18	8.42	2.96
Warfarin 250ppm	0.04	0.83	1.72	1.32	0.98
Zinc Phosphide 20,000ppm	7.81	10.00	0.00	0.69	4.63

Graph 5. Greatest Overall Risk to Birds & Mammals Sum of Weighted Averages of Measures of Effect

Chart with vertical axis labeled "Rodenticide Baits" listing the following categories (top to bottom):

- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

Horizontal axis labeled "Sum of Weighted Averages (0 to 10)" with scale: 0, 2, 4, 6, 8, 10.

Legend:
- Primary Risk to Birds
- Secondary Risk to Birds
- Secondary Risk to Mammals
- Primary Risk to Mammals

Results of Sensitivity Analysis

As previously noted, the FIFRA SAP recommended performing a sensitivity analysis. Specifically, they suggested that *"it would be useful to test the rankings by changing the values of the input variables...to lend insight to the robustness of the rankings, increase the confidence in the predictions, and move toward a better understanding of the effect that varying levels of uncertainty can have on the predictions."* This is also a recommendation from a number of the peer reviewers. Therefore, to study how changes in each measure of effect value could affect the overall summary risk results presented above (Table 6 and Graph 5), a simple sensitivity analysis is performed using two scenarios: (1) vary each individual risk rating +50%, and -50%; and , (2) select certain risk rating that appeared to show a sensitivity to change, extend the change up to 90% (+ or -) or more. Thus, for the first scenario, each measure of effect value is separately decreased by 50%, and then increased by 50%. The percentage 50% is chosen arbitrarily, with the intention of choosing greater percentages for change in the second scenario after viewing these results. The changes in the overall summary risk values found in Table 6 as a result of the change in each measure of effect value, are recorded. The overall summary risk values in Table 6 are the baseline values. The results of the 154 changes in the summary risk values are presented in Graph 6.

Graph 6
Results from Sensitivity Analysis
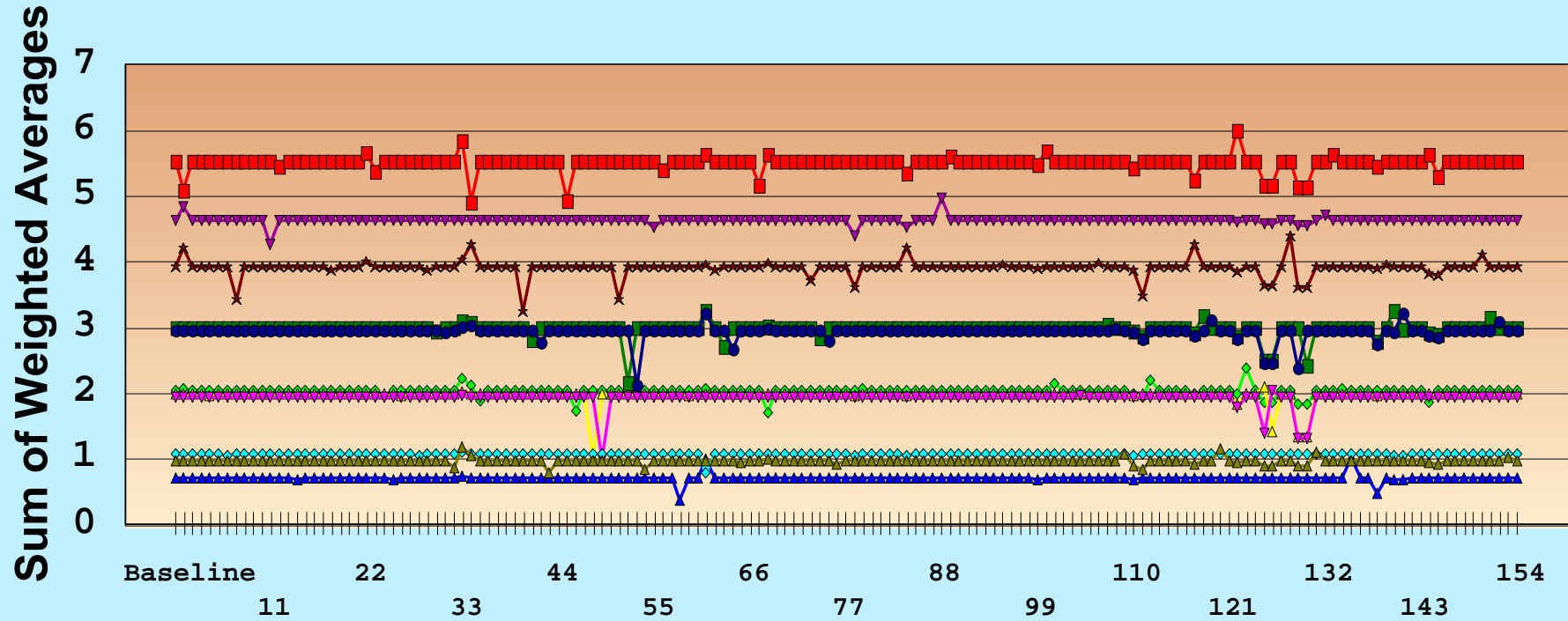
Calculations for + 50% [#s 1 to 77] and - 50% [#s 78 to 154] Change in RQs

Legend:
- Brodifacoum 50ppm
- Bromadiolone 50ppm
- Bromethalin 100ppm
- Chlorophacinone 100ppm
- Chlorophacinone 50ppm
- Cholecalciferol 750ppm
- Difethialone 25ppm
- Diphacinone 100ppm
- Diphacinone 50ppm
- Warfarin 250ppm
- Zinc Phosphide 20,000ppm

Y-axis: Sum of Weighted Averages

X-axis: Baseline, 11, 22, 33, 44, 55, 66, 77, 88, 99, 110, 121, 132, 143, 154

With a 50 % (+ or -) change in the measure of effect values, the ranked positions for brodifacoum, zinc phosphide, and difethialone do not change, indicating that the ranking is robust at this level of change. However, the ranked positions of the other rodenticide baits change numerous times, as indicated by the numerous times the lines cross each other. A few of the changes do result in lower values for brodifacoum, such as #s 1, 34, 45 and 67, or higher values for zinc phosphide, such as #s 1 and 88, or higher values for difethialone, such as # 128. To further test the rankings, the measures of effect values for these numbers are increased to 90% (+ or -) or greater and the resultant overall summary risk values are presented below:

> #1, Reduction in the Mean Dietary Risk Quotient (ppm bait/LC50), one measure of effect for primary risk to birds for brodifacoum, of 50%, 67%, 70% and 90% resulted in the following ranking of overall summary risk values:

Alternative Pesticides	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values
Brodifacoum 50ppm	5.11	4.83	4.78	4.46
Bromadiolone 50ppm	2.07	2.07	2.07	2.07
Bromethalin 100ppm	0.71	0.71	0.71	0.71
Chlorophacinone 100ppm	2.00	2.00	2.00	2.00
Chlorophacinone 50ppm	1.95	1.95	1.95	1.95
Cholecalciferol 750ppm	1.08	1.08	1.08	1.08
Difethialone 25ppm	4.21	4.21	4.21	4.21
Diphacinone 100ppm	3.01	3.01	3.01	3.01
Diphacinone 50ppm	2.96	2.96	2.96	2.96
Warfarin 250ppm	0.98	0.98	0.98	0.98
Zinc Phosphide 20,000ppm	4.83	4.83	4.83	4.83
	50%	67%	70%	90%

> Results: A reduction in the Mean Dietary Risk Quotient, one of two measures of effect for primary risk to birds for brodifacoum, of greater than 67% would result in zinc phosphide moving ahead of brodifacoum as the rodenticide bait posing the greatest overall potential risk to birds and mammals.

> #34, Reduction in the Mean (%) Mortality of secondary Lab Studies on Birds, one measure of effect for secondary risk to birds for brodifacoum, of 50%, 64%, 70 and 90%, resulted in the following ranking of overall summary risk values:

Alternative Pesticides	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values	Brodifacoum 50ppm Summary Values
Brodifacoum 50ppm	4.92	4.63	4.51	4.09
Bromadiolone 50ppm	2.14	2.14	2.14	2.14
Bromethalin 100ppm	0.71	0.71	0.71	0.71
Chlorophacinone 100ppm	1.99	1.99	1.99	1.99
Chlorophacinone 50ppm	1.95	1.95	1.95	1.95
Cholecalciferol 750ppm	1.07	1.07	1.07	1.07
Difethialone 25ppm	4.26	4.26	4.26	4.26
Diphacinone 100ppm	3.10	3.10	3.10	3.10
Diphacinone 50ppm	3.04	3.04	3.04	3.04
Warfarin 250ppm	1.07	1.07	1.07	1.07
Zinc Phosphide 20,000ppm	4.63	4.63	4.63	4.63
	50%	64%	70%	90%

Results: A reduction in the Mean (%) Mortality of Secondary Lab Studies on Birds, one of two measures of effect for secondary risk to birds for brodifacoum, of greater than 64% would result in zinc phosphide moving ahead of brodifacoum as the rodenticide bait posing the greatest overall potential risk to birds and mammals.

#45, Reduction in the Mean (%) Mortality of secondary Lab Studies on Mammals, one measure of effect for secondary risk to mammals for brodifacoum, of 50%, 76% and 90%, resulted in the following ranking of overall summary risk values:

Alternative Pesticides	Summary Values	Summary Values	Summary Values
Brodifacoum 50ppm	4.94	4.63	4.46
Bromadiolone 50ppm	2.06	2.06	2.06
Bromethalin 100ppm	0.71	0.71	0.71
Chlorophacinone 100ppm	1.99	1.99	1.99
Chlorophacinone 50ppm	1.95	1.95	1.95
Cholecalciferol 750ppm	1.07	1.07	1.07
Difethialone 25ppm	3.93	3.93	3.93
Diphacinone 100ppm	3.01	3.01	3.01
Diphacinone 50ppm	2.96	2.96	2.96
Warfarin 250ppm	0.98	0.98	0.98
Zinc Phosphide 20,000ppm	4.63	4.63	4.63
	50%	76%	90%

Results: A reduction in the Mean (%) Mortality of Secondary Lab Studies on Mammals, one of two measures of effect for secondary risk to mammals for brodifacoum, of greater

than 76% would result in zinc phosphide moving ahead of brodifacoum as the rodenticide bait posing the greatest overall potential risk to birds and mammals.

#128, Increase in the Mean (%) Mortality of secondary Lab Studies on Mammals, one measure of effect for secondary risk to mammals for difethialone, of 50% and 99%, resulted in the following ranking of overall summary risk values:

Alternative Pesticides	Difethialone 25ppm Summary Values	Difethialone 25ppm Summary Values
Brodifacoum 50ppm	5.55	5.39
Bromadiolone 50ppm	2.06	1.97
Bromethalin 100ppm	0.71	0.71
Chlorophacinone 100ppm	1.99	1.74
Chlorophacinone 50ppm	1.95	1.70
Cholecalciferol 750ppm	1.07	1.07
Difethialone 25ppm	4.41	4.63
Diphacinone 100ppm	3.01	2.79
Diphacinone 50ppm	2.96	2.73
Warfarin 250ppm	0.98	0.94
Zinc Phosphide 20,000ppm	4.63	4.60
	50%	99%

Results: An increase in the Mean (%) Mortality of Secondary Lab Studies on Rodents, one of two measures of effect for secondary risk to mammals for difethialone, of 99% would result in difethialone moving ahead of zinc phosphide as the rodenticide bait posing the second greatest overall potential risk to birds and mammals.

None of the following changes resulted in changes in rankings of brodifacoum, zinc phosphide or difethialone: a 99% reduction in Liver Retention Time (days) for brodifacoum (#67); a 99% increase in the Mean Avian Dietary Risk Quotient for zinc phosphide (#88); a 99% increase in the Mean (%) Mortality of secondary Lab Studies on Mammals for difethialone.

The sensitivity analysis shows that the ranking for the rodenticide baits which pose the greatest potential risk to birds and mammals is robust when the measures of effect are changed by +/-50%. The ranking is generally robust when the measures of effect are changed by +/- 99%. However, a reduction of greater than 67% in the Mean Dietary Risk Quotient for brodifacoum, 64% in the Mean (%) Mortality of Secondary Lab Studies on Birds for brodifacoum, and 76% in the Mean (%) Mortality of Secondary Lab Studies on Mammals f or brodifacoum, would result in zinc phosphide moving ahead of brodifacoum as posing the greatest overall risk to birds and mammals. In addition, an increase of 99% in the Mean (%) Mortality of Secondary Lab Studies

on Mammals for difethialone would result in difethialone moving ahead of zinc phosphide as posing the second greatest overall risk to birds and mammals. Thus, the sensitivity analysis shows that the ranking for the rodenticide baits is generally robust. With few exceptions we can confidently say that brodifacoum poses the greatest overall potential risk to birds and mammals, followed by zinc phosphide and difethialone.

Results Using Toxicity Reference Values for Birds

Mineau *et al* (2001) state that *"when carrying out comparative assessments for pesticides, it is essential to use the most unbiased data possible."* They suggest a distribution approach for avian LD50 data, modified (1) to incorporate body-weight scaling, and (2) to use extrapolation factors for pesticides for which there are insufficient data from which to derive a distribution. *"A distribution-based approach uses the pesticide-specific data available to define the shape of the distribution through the estimation of a mean and variance for the distribution."* As the authors note, *"Working with a distribution allows one to set a desired percentile, or threshold LD50 value sufficiently protective for an arbitrarily chosen portion of the entire population of bird species."* They follow other authors and arbitrarily set the protection level at the 5th percentile of the species distribution, which they term the Hazardous Dose 5% or HD_5. Further, they fixed the level of certainty at 50%. Thus, the $HD_5(50\%)$ reference value is the 5% tail of the avian LD50 toxicity distribution calculated with 50% probability of overestimation. They believe that this *"approach of using reference values based on species specific extrapolation factors represents the most unbiased attempt to date to compare the toxicity of pesticides for which many data points are available with those about which we know very little."*

Since $HD_5(50\%)$ reference values are available for all rodenticides but diphacinone (Table 3 in Mineau *et al*), these values are substituted for the LD50 values for bobwhite quail or mallard duck used in the measure of effect - Inverse the No. Bait Pellets Needed for a 100-g Bird LD50 Dose at a Single Feeding in the comparative analysis for Primary Risk to Birds.

Rodenticide	$HD_5(50\%)$
Brodifacoum 50 ppm	0.81
Bromadiolone 50 ppm	53.26
Bromethalin 100 ppm	0.83
Chlorophacinone 100 ppm	3.32
Chlorophacinone 50 ppm	4.98
Cholecalciferol 750 ppm	192.68
Difethialone 25 ppm	0.31
Diphacinone 100 ppm	No Data
Diphacinone 50 ppm	No Data
Warfarin 250 ppm	120.21
Zinc Phosphide 20,000 ppm	5.45

Since bait-specific $HD_5(50\%)$s are not available, the $HD_5(50\%)$ value from Mineau *et al* is applied to the highest active ingredient concentration of two baits, and it is reduced by the

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proportion difference in active ingredient concentrations between baits and applied to the bait with the lower active ingredient concentration. Lacking slope data, this assumes a linear relationship between the active ingredient in the bait and the acute toxicity to birds. Finally, the overall summary values for risk to birds and mammals are calculated and compared to the baseline in Table 6 and Graph 5. The results of the analysis are presented in Graph 7.

This analysis shows that the ranking remains the same and the use of the $HD_5(50\%)$ values from Mineau *et al* in place of the LD50 values for bobwhite quail or mallard duck does not have any affect on ranking of the rodenticide baits posing the greatest overall potential risk to birds and mammals. Missing $HD_5(50\%)$ data for diphacinone adds uncertainty to this conclusion.

Graph 7. Comparing Summary Risk Values BWQ & MD LD50s vs HD5(50%)s

Res
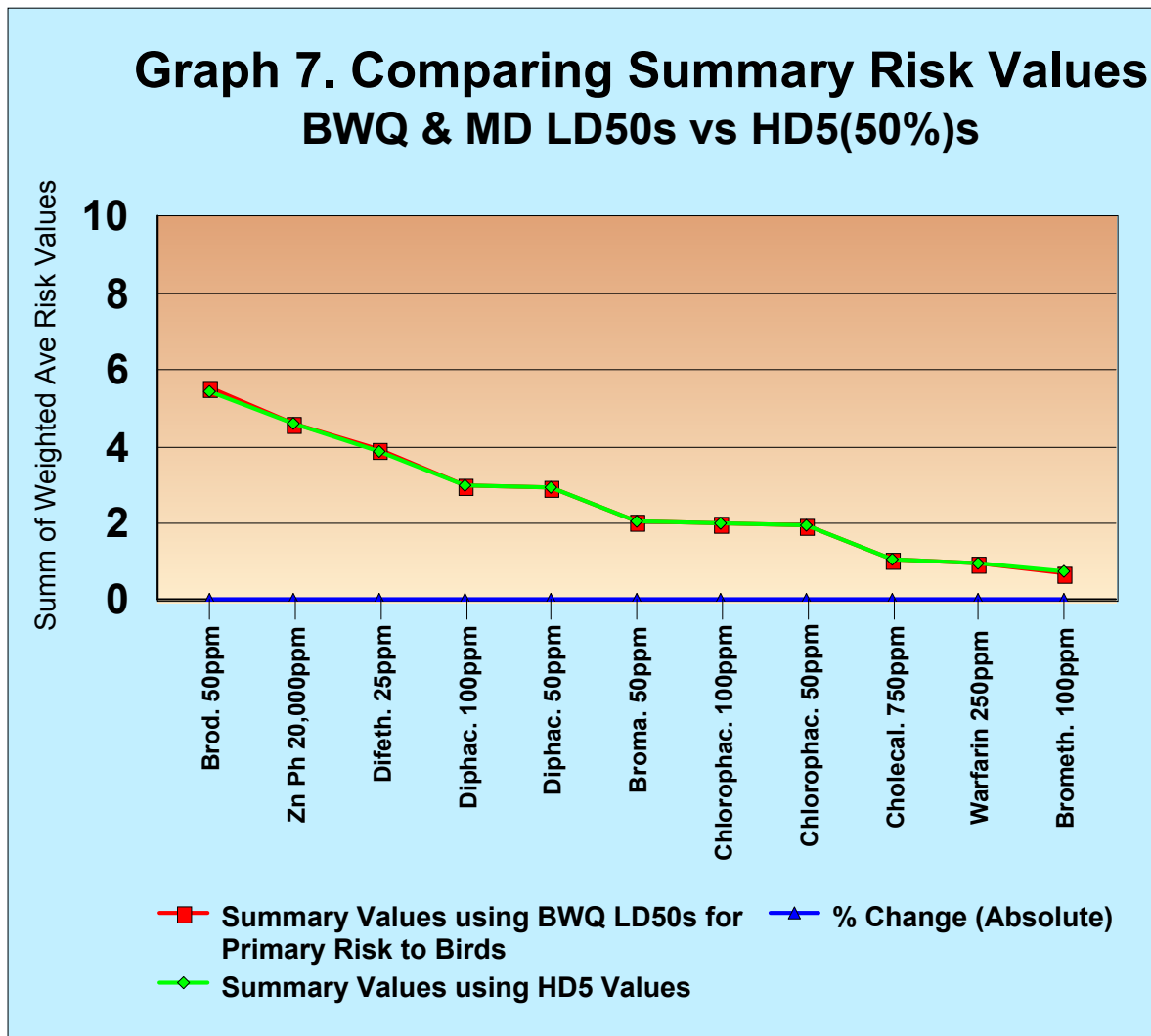
ults Using An Alternative Approach

As noted previously, the approach taken for this analysis is to separately analyze the risk for each risk type, then analyze the summary values for each of the four risk types together in a final overall analysis. Each type of risk included variable and unequal numbers of measures of effect. Analyzing them separately and then using their summary values to arrive at an overall risk value eliminated unequal weighting of one type of risk over another due to differences in the number of measures of effect.

An alternate approach is considered where the unequal weighting is ignored and all measure of effects are considered in one step. The weights are all rated high (10.0), except for blood retention and liver retention, which are weighted medium (5.0) so that the total contribution of persistence is rated equal to the other measures of effect (10.0). The overall summary risk values are calculated and compared to the baseline results in Table 5 and Graph 6. The results of this analysis is presented in Graph 8. The rankings for overall risk to birds and mammals do not change. Thus in this case, the unequal weighting of one type of risk over another due to differences in the number of measures of effect does not appear to have a significant effect on the overall ranking.

Graph 8. Comparing Summary Risk Values Sum of Each Risk Type vs Separate MEs

Summ of Weighted Ave Risk Values

Brod. 50ppm
Zn Ph 20,000ppm
Difeth. 25ppm
Diphac. 100ppm
Diphac. 50ppm
Broma. 50ppm
Chloroph. 100ppm
Chloroph. 50ppm
Cholecal. 750ppm
Warfarin 250ppm
Brometh. 100ppm

- ■ Summary Values Based on Final Analysis w/Summary Values from Each Type of Risk
- ◆ Summary Values Based on Final Analysis w/Separate Measures of Effect
- ▲ % Change (Absolute)

175
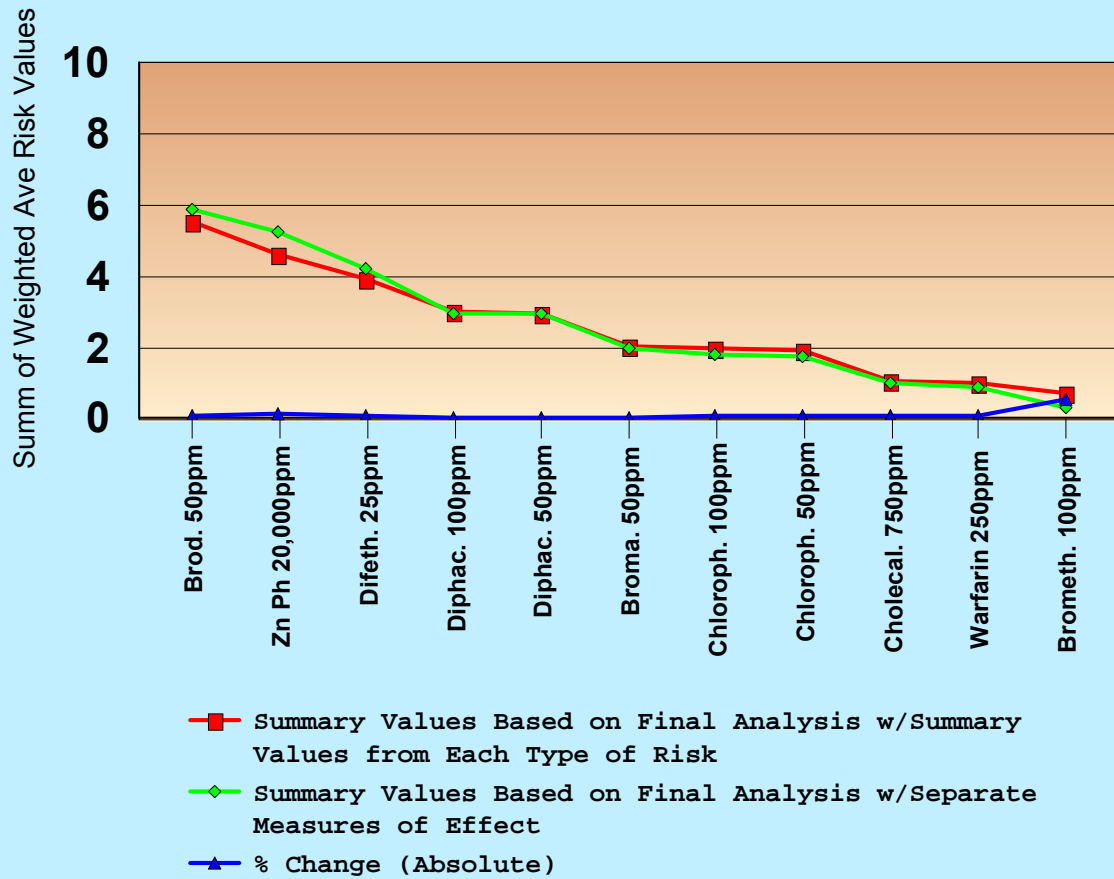
Incidents

Bird and mammal incidents provide additional information to further characterize the risk of rodenticide baits. The collection and reporting of incidents is not systematic, and the presence or absence of incidents is also affected by the extent of use of the rodenticide bait as well as other factors. Thus, the existence of incidents for a rodenticide bait can be viewed as confirming the risk, where as the absence of them says little about the risk. Further, without more information than is typically available for most incident reports, it can sometimes be difficult to separate the incidents based on primary or secondary effects.

Based on Table 42 in the main document, there are a large number of bird and mammal incidents reported for rodenticide baits (161 birds; 119 mammal; 280 total). Reported mortality is attributed to both primary and secondary effects. The incidents reported for each rodenticide bait (where two baits are included in the analysis, the one with the highest concentration in the bait formulation is used) are plotted on the x-axis against the summary values of the weighted averages for the overall risk to birds and mammals (See summary values, Table 6) on the y-axis. The incidents are 'turned around' so that the rodenticide baits with the greatest number of reported incidents and the largest summary risk values should appear in the upper left of the graph. Tables 7, 8 and 9 show the input values for the following graphs. Graph 9 presents the bird incidents; Graph 10, the mammal incidents; and Graph 11, both combined.

The graphs confirm that brodifacoum is the rodenticide bait that poses the greatest overall potential risk to birds and mammals. In addition to brodifacoum, Graph 9 also identifies bromadiolone and zinc phosphide as potential concerns for birds, while Graph 10 identifies bromadiolone, diphacinone, and chlorophacinone as potential risk concerns for mammals.

Table 7. Input values for Graph 9	# Incidents – Birds	Summary Values
Brodifacoum 50ppm	111	5.55
Zinc Phosphide 20,000ppm	21	4.63
Difethialone 25ppm	1	3.93
Diphacinone 100ppm	5	3.01
Bromadiolone 50ppm	19	2.06
Chlorophacinone 100ppm	1	1.99
Cholecalciferol 750ppm	0	1.07
Warfarin 250ppm	3	0.98
Bromethalin 100ppm	0	0.71
Sum	161	

Table 8. Input Values for Graph 10.	# Incidents - Mammals	Summary Values
Brodifacoum 50ppm	76	5.55
Zinc Phosphide 20,000ppm	2	4.63
Difethialone 25ppm	0	3.93
Diphacinone 100ppm	13	3.01
Bromadiolone 50ppm	18	2.06
Chlorophacinone 100ppm	9	1.99
Cholecalciferol 750ppm	0	1.07
Warfarin 250ppm	1	0.98
Bromethalin 100ppm	0	0.71
Sum	119	

Table 9. Input Values for Graph 11.	# Incidents - Total	Summary Values
Brodifacoum 50ppm	187	5.55
Zinc Phosphide 20,000ppm	23	4.63
Difethialone 25ppm	1	3.93
Diphacinone 100ppm	18	3.01
Bromadiolone 50ppm	37	2.06
Chlorophacinone 100ppm	10	1.99
Cholecalciferol 750ppm	0	1.07
Warfarin 250ppm	4	0.98
Bromethalin 100ppm	0	0.71
Sum	280	

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Graph 9. Plot of Summary Risk Values vs Birds Incidents

Graph 10. Plot of Summary Risk Values
vs Mammal Incidents

Sum of Weighted Averages (y-axis): 0 to 10

Incidents (Mammals) (x-axis): 80 to 0

Brodifacoum 50ppm
Diphacinone 100ppm
Bromadiolone 50ppm
Chlorophacinone 100ppm

Graph 11. Plot of Summary Risk Values vs All Incidents

X-axis: # Incidents (Total - Birds & Mammals)
Y-axis: Sum of Weighted Averages

Labeled points:
- Brodifacoum 50ppm
- Zinc Phosphide 20,000ppm
- Diphacinone 100ppm
- Bromadiolone 50ppm
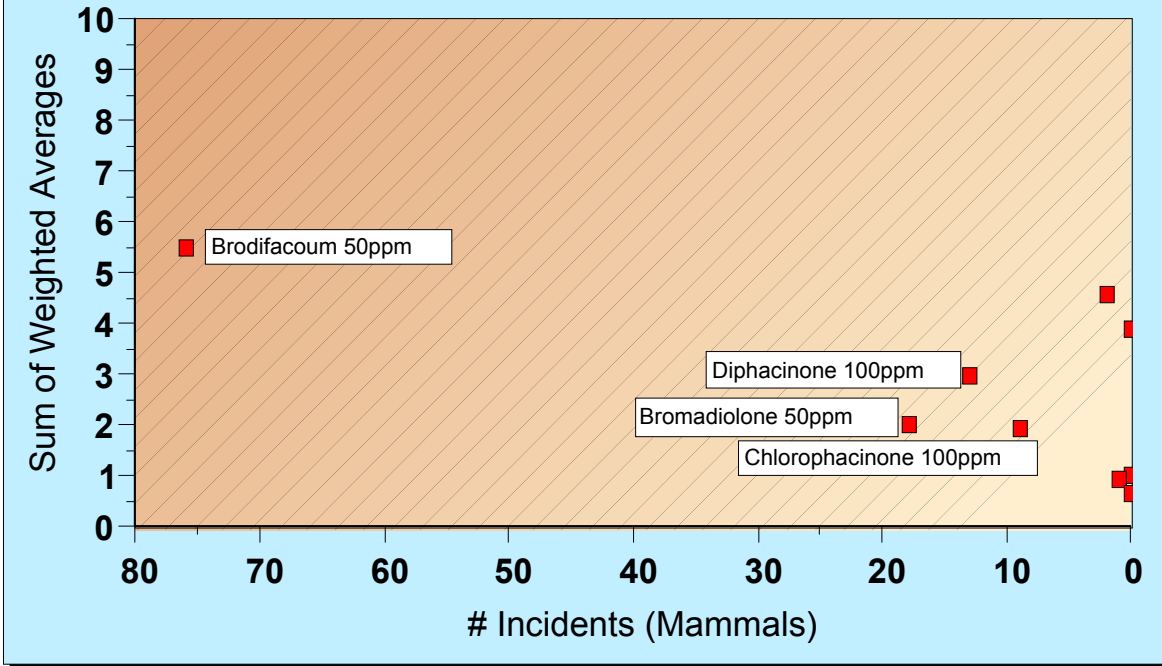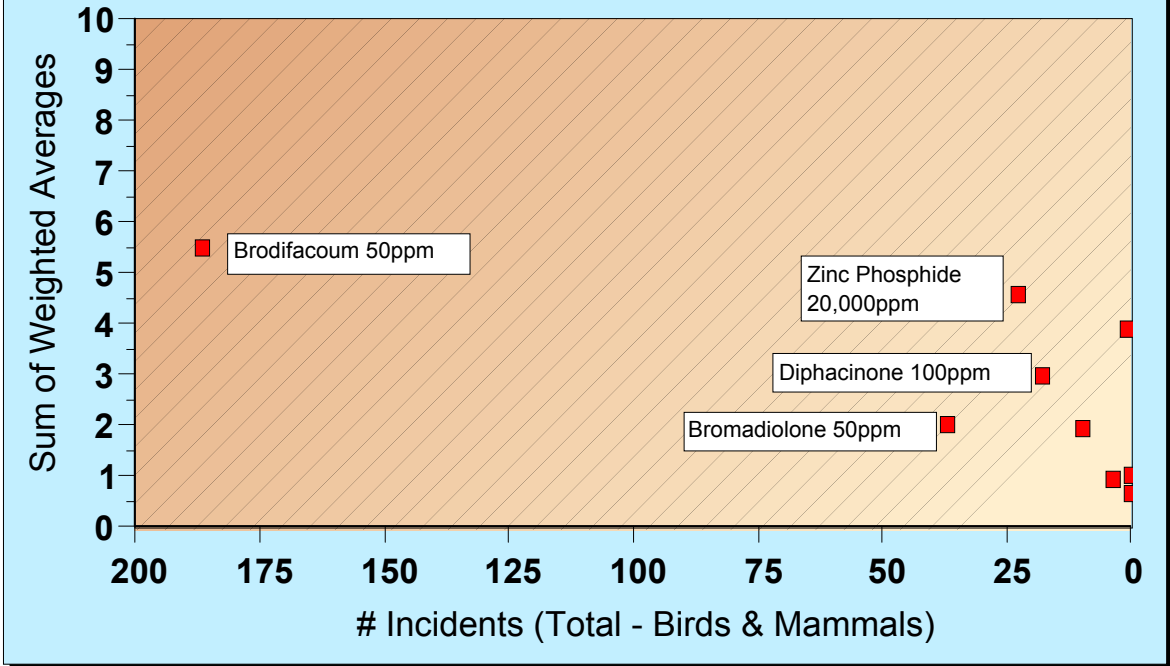
Conclusions

Based on the comparative analysis model called the simple multi-attribute rating technique or SMART, the potential risks of 11 rodenticide baits are compared based on a number of measures of effect values for primary and secondary risk to birds and mammals. Of all the rodenticide baits considered, three are considered to pose the greatest overall potential risk to birds and mammals: brodifacoum, zinc phosphide, and difethialone. Brodifacoum poses the greatest overall potential risk to birds and mammals, and by a substantial margin over the other rodenticide baits. Brodifacoum has higher summary risk values than zinc phosphide for both secondary risk to birds and secondary risk to mammals. Zinc phosphide has higher summary risk values than difethialone for both primary risk to birds and primary risk to mammals.

A sensitivity analysis is performed to identify the most sensitive measure of effect(s) and to determine if changes of 50% or more in these sensitive measures of effect would change the results of the analysis. This analysis shows that the ranking for the rodenticide baits which pose the greatest risk to birds and mammals is robust when the measures of effect are changed by +/- 50%. The ranking is generally robust when the measures of effect are changed by +/- 99%, with the following exceptions: a reduction of greater than 67% in the Mean Dietary Risk Quotient for brodifacoum, 64% in the Mean (%) Mortality of Secondary Lab Studies on Birds for brodifacoum, and 76% in the Mean (%) Mortality of Secondary Lab Studies on Mammals for brodifacoum, would result in zinc phosphide moving ahead of brodifacoum as posing the greatest overall risk to birds and mammals; and, an increase of 99% in the Mean (%) Mortality of Secondary Lab Studies on Mammals for difethialone would result in difethialone moving ahead of zinc phosphide as posing the second greatest overall potential risk to birds and mammals. Thus, the sensitivity analysis shows that the ranking for the rodenticide baits is generally robust. With few exceptions, we can say that brodifacoum poses the greatest overall potential risk to birds and mammals, followed by zinc phosphide and difethialone.

Acute toxicity reference values for rodenticides to birds and an alternative approach are also considered. The toxicity reference values from a recent publication are substituted for the avian LD50 values for bobwhite quail and mallard ducks that were used in one of the avian measures of effect. The results show that the overall ranking remains the same and the use of these toxicity reference values do not affect the analysis. When unequal weighting of measures of effect for each type of risk is ignored and all measures of effect are considered together, again the results show that the overall ranking does not change. Unequal weighting of type of risk over another, in this case, does not appear to have a significant effect on the overall ranking.

There are two factors which could contribute the greatest uncertainty to the analysis: (1) missing data, especially field mortality data for difethialone, and blood and liver retention values for a number of rodenticides; and (2) the assumption that field mortality to birds and mammals due to difethialone would likely equal 80% of that reported for brodifacoum. This assumption is based on the many chemical similarities between these two rodenticides, because difethialone is formulated at a lower % ai than brodifacoum, and the fact that less difethialone is used compared to brodifacoum.

The available incidents for birds and mammals are analyzed and compared the summary of the weighted average risk values. The resul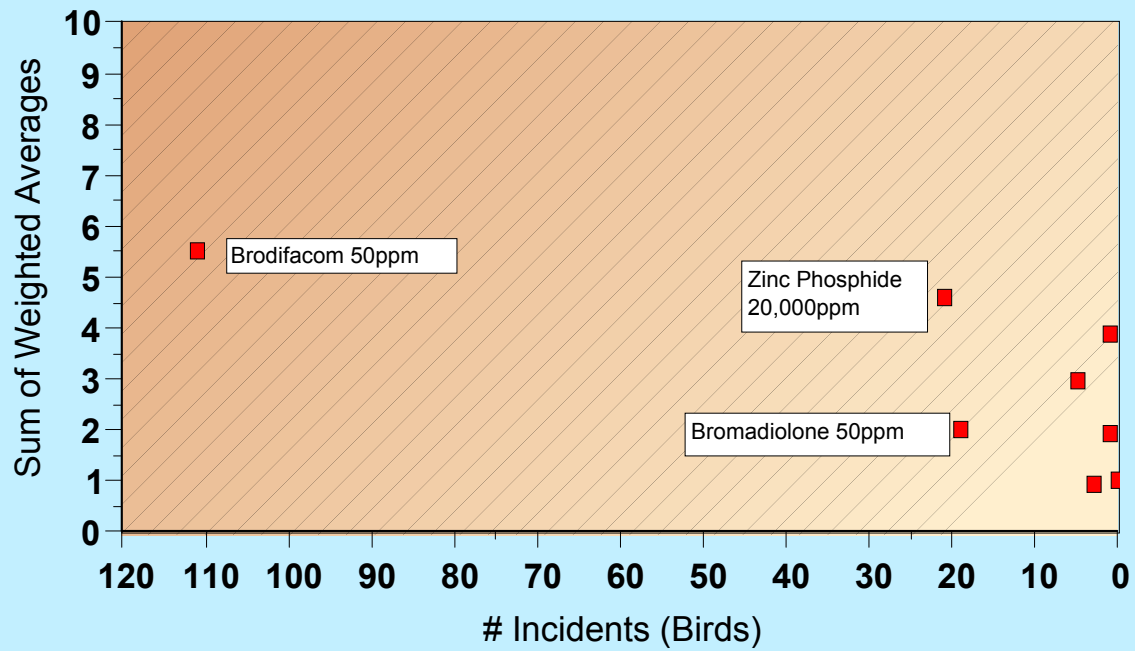ts confirm that brodifacoum is the rodenticide bait that poses the greatest overall potential risk to birds and mammals, but they also identify bromadiolone and zinc phosphide as potential concerns for birds, and bromadiolone, diphacinone (100 ppm), and chlorophacinone (100 ppm) as potential concerns for mammals.

References

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2.   Goodwin, P. and G. Wright. 1998. Decision analysis for management judgement, 2nd Ed. John Wiley & Sons, England. pp.454.

3.   Mineau, P. A. Baril, B. T. Collins, J. Duffe, G. Joerman, R. Littik. 2001. Pesticide acute toxicity reference values. Rev. Environ. Contam. Toxicol. 170: 13-74.

Attachment D: Incident Data For Birds and Nontarget Mammals

The incidents reported here are summarized for each rodenticide from incident reports in the EPA/OPP Environmental Fate and Effect Division's Ecological Incidents Information System. Unless otherwise noted, an incident is included here only if confirmation of exposure is reported. For the anticoagulants, detection of residue in the liver is the criterion of exposure unless otherwise stated. Hemorrhaging and other signs of toxicosis also generally are included in incident reports, but details are not tabulated here (see Stone et al. 1999, 2003; Hosea 2000). For the non-anticoagulants, detection of bait in the stomach or crop contents are typical evidence of exposure. Most of the incidents are based on carcass recovery; however, as noted, 3 incidents involved mammals that were live-trapped and sacrificed. Reported residue levels are provided only as confirmation that animals were exposed to a rodenticide. There are no incident data for bromethalin and cholecalciferol.

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Owls						
Great horned owl	NY	Erie	4/04	1	0.026	the owl was observed on the ground in a lethargic state for 3 days before its death
Great horned owl	NY	Saratoga	2/02	1	0.44	"Little blood in heart (blood watery)"
Great horned owl	NY	Erie	12/01	1	0.82	
Great horned owl	NY	Delaware	10/01	1	0.84	
Great horned owl	NY	Rockland	9/01	1	0.24	
Great horned owl	NY	Ulster	4/01	1	0.49	
Great horned owl	CA	Los Angeles	2000	1	0.34	
Great horned owl	CA	Los Angeles	2000	1	0.05	also bromadiolone (0.8 ppm)

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Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Great horned owl	NY	Rensselaer	11/00	1	0.09	
Great horned owl	NY	Warren	10/00	1	0.15	also bromadiolone (0.32 ppm)
Great horned owl	NY	Suffolk	7/00	1	0.37	also bromadiolone (0.4 ppm)
Great horned owl	NY	Albany	10/99	1	0.14	
Great horned owl	CA	San Bernardino	10/99	1	0.35	also bromadiolone (0.065 ppm)
Great horned owl	NY	Washington	7/99	1	0.42	bird was a fledgling
Great horned owl	NY	Dutchess	2/99	1	0.64	brodifacoum also detected in an egg (0.008 ppm)
Great horned owl	NY	Suffolk	2/99	1	0.23	
Great horned owl	NY	Ontario	2/99	1	0.16	
Great horned owl	NY	Nassau	2/99	1	0.08	brodifacoum also detected in skeletal muscle (0.02 ppm); 4 dead rats found in owl's nest
Great horned owl	NY	Columbia	1/99	1	0.036	small mammal hair in stomach
Great horned owl	NY	Oswego	12/98	1	0.30	owl may have bled excessively from puncture wound between eyes and into the sinuses, possibly caused by its prey (partially-eaten muskrat carcass found nearby)
Great horned owl	NY	Albany	12/98	1	0.08	also bromadiolone (0.27 ppm); "The owl died from hemorrhaging of minor wounds inflicted by prey";

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Great horned owl	CA	Contra Costa	8/98	1	0.04	also diphacinone (0.6 ppm)
Great horned owl	NY	Niagara	7/98	1	0.03	also bromadiolone (0.77 ppm) and warfarin (0.73 ppm)
Great horned owl	NY	Rensselaer	7/98	1	0.12	a dead rat found nearby owl
Great horned owl	NY	Saratoga	5/98	1	0.06	also bromadiolone (0.24 ppm)
Great horned owl	GA	White	2/98	2	0.099 0.23	
Great horned owl	NY	Dutchess	6/97	1	0.22	
Great horned owl	NY	Genesee	4/97	1	0.09	
Great horned owl	NY	Greene	2/97	1	0.08	
Great horned owl	NY	Monroe	6/96	1	0.35	vole remains in stomach; small laceration on foot
Great horned owl	NY	Chenango	2/96	1	0.36	
Great horned owl	NY	Suffolk	8/95	1	0.53	also bromadiolone (0.14 ppm)
Great horned owl	CA	San Joaquin	1995	1	0.015	
Great horned owl	NY	Albany	12/94	1	0.1	
Great horned owl	NY	Orleans	11/94	1	0.73	bled from punctures on feet
Great horned owl	NY	Erie	10/94	1	0.41	
Great horned owl	NY	Albany	6/94	1	0.64	blood on feet from hole on left foot; brodifacoum bait applied nearby
Great horned owl	NY	Niagara	3/94	1	0.53	

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Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Great horned owl	NY	Suffolk	10/89	1	0.2	
Great horned owl	NY	Putnam	3/89	1	0.01	
Long-eared owl	NY	Bronx	3/99	1	0.30	
Eastern screech-owl	NY	Suffolk	2/03	1	0.30	unidentified mammal hair and bones in the stomach
Eastern screech-owl	NY	Niagara	9/02	1	0.65	
Eastern screech-owl	NY	New York	1/02	1	0.91	
Eastern screech-owl	NY	Albany	2/00	1	0.16	
Eastern screech-owl	NY	Schenectady	10/99	1	0.16	
Eastern screech-owl	NY	Erie	10/97	1	0.8	
Eastern screech-owl	NY	Suffolk	2/97	1	0.34	
Barn owl	GA	Dawson	11/03	1	0.035	a red-tailed hawk also died, and vitamin K was administered to 2 great horned owls that showed signs of poisoning
Barn owl	CA	Sacramento	11/02	1	0.03	brodifacoum also detected in the ventriculus (4.90 ppb), along with mammal hairs, and in a blood sample taken from the thoracic cavity and ventriculus lining

Brodifacoum[a]

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Barn owl	CA	San Bernardino	10/99	3	0.35 0.21 0.07	also bromadiolone (0.38 ppm) also bromadiolone (0.31 ppm)
Barn owl	GA	Madison	11/95	2	0.85 0.75	
Barred owl	NY	Albany	11/01	1	0.04	
Northern spotted owl	WA	Chelan	4/91	1	0.1	NWHC[b] database (case 10128)
Northern spotted owl	WA	Kittitas	7/95	1	0.05	NWHC[b] database (case 13799)
Diurnal Birds of Prey						
Golden eagle	CA	Ventura	2000	3	0.026 0.01 0.004	the 3 eagles were live-trapped for relocation but died in captivity
Golden eagle	CA	Alameda	11/99	1	0.01	
Golden eagle	CA	Contra Costa	11/99	1	trace	
Golden eagle	CA	Stanislaus	7/99	1	0.02	
Golden eagle	CA	Contra Costa	3/99	1	0.04	
Golden eagle	CA	Alameda	2/99	1	0.04	
Golden eagle	NY	Washington	12/97	1	0.016	
Golden eagle	CA	Alameda	11/97	1	0.08	
Golden eagle	CA	Santa Clara	5/97	1	trace	
Golden eagle	CA	San Benito	12/96	1	0.13	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Golden eagle	NY	Monroe	4/96	1	0.03	tissue analyzed 7 months after death
Bald eagle	WI	Sawyer	10/98	1	detected	residue level reported as "moderate"
Bald eagle	ID	Boise	1/86	1	38	reported by the NWHC[b] (case 6372)
Red-tailed hawk	NY	Schenectady	3/04	1	0.50	probable bite injury on left foot likely source of blood on belly plumage
Red-tailed hawk	GA	Dawson	11/03	1	0.08	residue from unspecified fresh tissue
Red-tailed hawk	NY	Suffolk	3/02	1	0.57	
Red-tailed hawk	NY	New York	3/02	1	0.4	
Red-tailed hawk	NY	Albany	3/01	1	0.03	bled severely from foot lacerations probably inflicted by prey
Red-tailed hawk	WI	LaCrosse	2/01	1	0.02	
Red-tailed hawk	WI	Dane	1/01	1	0.04	unidentified meat/muscle in crop
Red-tailed hawk	WI	LaCrosse	1/01	1	0.11	
Red-tailed hawk	WI	Outagamie	1/01	2	0.008	6 other hawks found alive but ill
Red-tailed hawk	WI	Iowa	1/01	1	0.04	
Red-tailed hawk	CA	San Luis Obispo	1/01	1	0.015	

Brodifacoum[a]

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Red-tailed hawk	AL	Morgan	1/01	4	0.01	8 red-tailed hawks and 24 undidentified hawks reported in this incident in the NWHC[b] database (case 13799)
Red-tailed hawk	WI	Buffalo	12/00	1	0.014	rodent hair, meat, bones in crop
Red-tailed hawk	NY	Rockland	12/00	1	0.32	
Red-tailed hawk	CA	San Joaquin	12/00	1	0.12	
Red-tailed hawk	WI	Dane	8/00	1	0.009	
Red-tailed hawk	WI	Adams	7/00	1	0.003	
Red-tailed hawk	WI	Columbia	5/00	1	0.02	
Red-tailed hawk	NY	Rensselaer	4/00	1	0.94	
Red-tailed hawk	NY	New York	3/00	1	0.24	small mammal hair and bone in stomach
Red-tailed hawk	NY	Westchester	3/00	1	0.377	
Red-tailed hawk	NY	Westchester	3/00	1	0.08	
Red-tailed hawk	WI	Manitowoc	3/00	1	0.03	
Red-tailed hawk	WI	Columbia	2/00	1	detected	residue level not reported
Red-tailed hawk	WI	Vernon	1/00	1	detected	residue level not reported
Red-tailed hawk	WI	Dane	1/00	1	detected	residue level not reported
Red-tailed hawk	NY	Rensselaer	6/99	1	0.69	
Red-tailed hawk	NY	Albany	4/99	1	0.32	

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Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Red-tailed hawk	CA	Stanislaus	3/99	1	0.01	
Red-tailed hawk	NY	Nassau	3/99	1	1.28	
Red-tailed hawk	NY	Suffolk	2/99	1	0.80	this hawk apparently "bled out" through a minor leg wound possibly inflicted by its prey
Red-tailed hawk	NY	New York	1/99	1	0.23	
Red-tailed hawk	NY	Suffolk	1/99	1	0.13	
Red-tailed hawk	NY	Saratoga	1/99	1	0.16	severe blood loss may have been from minor bites on feet
Red-tailed hawk	NY	Albany	10/98	1	0.04	
Red-tailed hawk	NY	Nassau	1/98	1	0.56	
Red-tailed hawk	NY	Suffolk	10/96	1	0.5	mouse parts in GI tract
Red-tailed hawk	NY	Onondaga	6/96	1	0.65	small mammal fur in stomach
Red-tailed hawk	NY	Suffolk	12/95	1	1.6	blood stains on right foot and belly; rodenticide applied nearby
Red-tailed hawk	NY	Nassau	3/95	1	0.76	bled from foot punctures "probably inflicted by prey"
Red-tailed hawk	NY	Richmond	1/95	1	0.43	
Red-tailed hawk	NY	Westchester	12/94	1	0.23	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Red-tailed hawk	NY	Westchester	11/94	1	0.46	"The bird seemed to have exsanguinated through a minor toe wounds"
Red-shouldered hawk	NY	Westchester	4/02	1	0.23	
Red-shouldered hawk	CA	Stanislaus	3/99	2	0.15 0.01	also bromadiolone (0.28 ppm)
Cooper's hawk	NY	Dutchess	9/03	1	0.28	
Cooper's hawk	NY	Rensselaer	2/02	1	0.37	
Cooper's hawk	NY	Schenectady	2/01	1	0.18	
Cooper's hawk	NY	Albany	9/00	1	0.21	
Cooper's hawk	CA	Los Angeles	2000	1	0.03	
Cooper's hawk	WI	Manitowoc	3/00	1	0.03	
Sharp-shinned hawk	NY	Steuben	1/02	1	0.023	
Sharp-shinned hawk	NY	Schenectady	1/00	1	0.17	
Black vulture	NY	Westchester	4/02	1	0.13	
Turkey vulture	NY	Ulster	3/01	1	0.26	

Perching Birds

Raven	NY	Rensselaer	4/96	1	1.04	
American crow	NY	Albany	1/02	1	1.73	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
American crow	NY	Oneida	10/01	1	1.9	
American crow	NY	Chautaugun	10/01	1	0.07	
American crow	NY	Erie	9/01	1	0.70	
American crow	NY	Oneida	9/01	1	1.5	
American crow	NY	Erie	7/01	1	0.52	
American crow	NY	Erie	6/01	1	0.35	
American crow	NY	Erie	5/01	1	1.3	
American crow	NY	Albany	3/01	1	0.45	
American crow	NY	Albany	2/01	1	0.4	
American crow	NY	Onondaga	8/00	1	0.08	
American crow	NY	Suffolk	6/00	1	1.0	
American crow	NY	Westchester	4/00	1	1.2	
Crow	NY	Dutchess	10/99	1	1.67	
Crow	NY	Westchester	9/98	2	0.14	pooled sample from both birds
Crow	CT	Norwalk	1/97	1	1.34	gizzard contained blue-green granular material believed to be bait

Other Birds

Geese	VA	Fauquier	10/92	2	not reported	VA Dept. Game and Inland Fisheries attributed deaths to brodifacoum; no residue values provided

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Rock dove	CA	Ventura	5/03	1	0.01	also diphacinone (0.9 ppm)
Denver Zoo:	CO		11/86- 1/87	10		liver residues were determined at the Denver Federal Center; deaths coincided with bait application and a massive mouse die-off
Plover					0.8	
Sissa					0.5	
Franklin's gull					1.5-1.6	
Laughing gull					1.6	
National Zoo:	VA		4/84	~12	confirmed	birds apparently died after eating crickets that had consumed bait; according to EPA memo, "residues in birds were confirmed by ICI, the registrant"; memo also notes that a similar incident occurred at the Philadelphia Zoo 3 years earlier
Avocet						
Ant pitta						
Golden plover						
Honey creeper						
Finch						
Thrush						
Warbler						
Crake						
Carnivores						
Coyote	CA	Los Angeles	2000	1	0.08	also bromadiolone (0.44 ppm)
Coyote	NY	Warren	5/99	1	0.93	
Coyote	CA	Santa Clara	2/99	5	0.47	also bromadiolone (0.46 ppm)
					0.36	also chlorophacinone (trace)
					0.30	also bromadiolone (0.07 ppm)
					0.23	also bromadiolone (0.09 ppm)
					0.33	all 5 coyotes were live-trapped and sacrificed

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Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Coyote	CA	Santa Clara	1999	1	0.07	
Coyote	CA	Santa Clara	1999	1	0.03	
Coyote	CA	Santa Clara	1999	1	0.28	
Coyote	CA	Santa Clara	1999	1	0.06	
Coyote	CA	San Mateo	1998	1	0.08	
Coyote	CA	Ventura	1998	1	0.04	
Coyote	CA	Los Angeles	1998	1	0.08	also chlorophacinone (0.43 ppm) and diphacinone (0.08 ppm); coyote live-trapped and sacrificed
Coyote	CA	Orange	1998	2	0.5 0.66	also bromadiolone (0.22 ppm); coyotes live-trapped and sacrificed
Coyote	CA	Los Angeles	12/97	1	0.28	also detected in blood (0.019 ppm)
Coyote	CA	Ventura	10/97	1	0.083	also diphacinone (1.3 ppm)
Coyote	CA	Los Angeles	8/97	2	0.054 trace	
Coyote	CA	Ventura	8/97	1	trace	
San Joaquin Kit Fox	CA	Kern	8/03	1	11.0	
San Joaquin Kit Fox	CA	Kern	2002	1	0.706	
San Joaquin Kit Fox	CA	Kern	2002	1	0.381	
San Joaquin Kit Fox	CA	Kern	2002	1	0.373	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
San Joaquin Kit Fox	CA	Kern	2002	1	0.296	
San Joaquin Kit Fox	CA	Kern	2002	1	0.161	
San Joaquin Kit Fox	CA	Kern	2002	1	0.132	
San Joaquin Kit Fox	CA	Kern	2002	1	0.191	also pival[c] (6.93 ppm) and coumatetralyl[d] (0.368 ppm)
San Joaquin Kit Fox	CA	Kern	2002	1	0.122	also coumatetralyl[d] (1.42 ppm)
San Joaquin Kit Fox	CA	Kern	2002	1	0.019	coumatetralyl[d] (0.4 ppm)
San Joaquin Kit Fox	CA	Kern	2002	1	0.091	coumatetralyl[d] (1.1 ppm)
San Joaquin Kit Fox	CA	Kern	2002	1	0.009	coumatetralyl[d] (0.134 ppm)
San Joaquin Kit Fox	CA	Kern	2002	1	0.008	
San Joaquin Kit Fox	CA	Kern	2002	1	0.007	
San Joaquin Kit Fox	CA	Kern	2002	1	trace	
San Joaquin Kit Fox	CA	Tulare	2001	1	0.042	
San Joaquin Kit Fox	CA	Kern	2001	1	0.18	
San Joaquin Kit Fox	CA	Kern	2001	1	0.075	
San Joaquin Kit Fox	CA	Kings	2001	1	trace	
San Joaquin Kit Fox	CA	Kern	2000	1	1.0	
San Joaquin Kit Fox	CA	Kern	2000	1	0.11	
San Joaquin Kit Fox	CA	Kern	2000	1	0.1	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
San Joaquin Kit Fox	CA	Kern	1/00	1	0.13	also bromadiolone (0.14 ppm); roadside carcass
San Joaquin Kit Fox	CA	Kern	12/99	1	0.67	roadside carcass
San Joaquin Kit Fox	CA	Kern	11/99	1	0.22	animal hit by car and died
San Joaquin Kit Fox	CA	Kern	8/99	1	0.47	also bromadiolone (0.72 ppm)
San Joaquin Kit Fox	CA	Kern	9/99	1	0.07	also chlorophacinone (0.27 ppm)
Red fox	NY	Suffolk	3/96	2	4.01 1.32	also detected in alimentary canal contents (0.34 ppm), which contained deer hair; 4 dead deer, not analyzed, also were found
Red fox	CA	Monterey	1999	1	0.04	
Red fox	CA	Fresno	8/97	2	0.05	rodent bones and hair, feathers, and grain present in stomach
Gray fox	NY	Albany	8/99	1	0.35	
Gray fox	NY	Delaware	3/98	1	0.02	small mammal skin and hair in stomach
Gray fox	CA	Los Angeles	1998	1	0.03	
Bobcat	CA	Los Angeles	2/01	1	0.024	
Bobcat	CA	Ventura	9/99	1	0.07	also bromadiolone (0.11 ppm)
Bobcat	CA	Riverside	6/99	1	0.018	
Bobcat	CA	Ventura	12/97	1	0.049	

Brodifacoum[a]

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Mountain lion	CA	Riverside	4/97	1	0.52	
Raccoon	NY	New York	5/00	1	0.14	
Raccoon	CA	Los Angeles	1998	1	0.082	also bromadiolone (1.1 ppm) and diphacinone (0.13 ppm); raccoon live-trapped and sacrificed
Raccoon	CA	Orange	1998	1	0.011	also bromadiolone (0.41 ppm); raccoon live-trapped and sacrificed
Raccoon	NY	Albany	3/97	1	0.32	
Raccoon	NY	Suffolk	3/96	1	1.0	blue-green granular material, probably bait, in stomach
Raccoon	NY	Nassau	9/92	3	5.3 4.6 3.1	
Raccoon	NY	Niagara	6/92	1	1.8	detected in stomach contents; dyed bait also present in stomach
Long-tailed weasel	NY	Rensselaer	1/00	1	0.07	
Striped skunk	NY	Albany	5/99	1	1.05	
Striped skunk	NY	Delaware	3/98	1	0.3	small mammal fur in stomach

Marsupials

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Opossum	NY	Albany	12/98	1	0.24	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Opossum	NY	Albany	4/97	1	0.18	
Ungulates						
White-tailed deer	NY	Suffolk	12/97	1	0.16	
White-tailed deer	NY	Suffolk	4/96	1	0.12	
White-tailed deer	NY	Suffolk	5/96	1	0.41	
White-tailed deer	NY	Suffolk	9/95	1	0.37	also coumatetralyl (0.5 ppm)
White-tailed deer	NY	Suffolk	10/94	1	0.38	
Rodents						
Gray squirrel	NY	Albany	2/02	1	0.82	third dead squirrel found in 2 weeks
Gray squirrel	NY	Dutchess	10/01	3	5.5 1.03	
Gray squirrel	NY	Livingston	8/01	1	3.45	second squirrel found dead in a week
Gray squirrel	NY	Schenectady	8/01	1	2.64	
Gray squirrel	NY	Rockland	6/01	1	0.35	
Gray squirrel	NY	New York	2/01	1	0.3	
Gray squirrel	NY	Albany	4/00	2	8.3 4.1	
Gray squirrel	NY	Suffolk	12/99	2	0.70 0.25	

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Gray squirrel	NY	Albany	11/99	1	2.1	
Gray squirrel	NY	Rensselaer	8/99	1	2.4	
Gray squirrel	NY	Albany	7/99	1	0.31	
Gray squirrel	NY	Westchester	5/99	1	6.3	
Gray squirrel	NY	Westchester	5/99	3	2.4	
Gray squirrel	NY	Albany	5/99	1	0.23	
Gray squirrel	NY	New York	5/99	1	3.12	
Gray squirrel	NY	Westchester	4/99	3	6.44 6.93 6.9	also detected in stomach (10.3 ppm)
Gray squirrel	NY	Oneida	9/98	5	detected	reportedly detected at "significant" levels
Gray squirrel	NY	Nassau	3/97	1	0.88	the squirrel was found dead on 3/97 but not necropsied until 1/99
Gray squirrel	WI	Calumet	4-5/97	3	detected	residue level reported as "significant"
Gray squirrel	NY	Albany	12/96	1	1.39	
Gray squirrel	WI	Calumet	9/96	2	detected	residue level not reported
Gray squirrel	WI	Calumet	8/95	1	1.8	~30 other dead squirrels found, but not analyzed, between 2-8/95 in a neighborhood in Appleton, WI

Brodifacoum[a]

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Gray squirrel	NY	Albany	9/93	1	25.8	detected in colon contents; dyed bait also present in alimentary canal
Gray squirrel	NY	Albany	8/93	1	0.53	also chlorophacinone (0.62 ppm)
Gray squirrel	NY	Monroe	6/93	3	5.1	pooled sample
Gray squirrel	VA	Henrico	6/93	4	detected	residue level reported as "significant"; a cat also was treated for poisoning
Gray squirrel	NY	Monroe	7/90	1	4.1	
Gray squirrel	NY	Westchester	6/90	1	0.7	
Fox squirrel	CA	Sacramento	5/99	8	3.1	apparent deliberate misuse
Chipmunk	WI	Oneida	9/98	3	detected	present at "significant levels" in a pooled sample
Chipmunk	NY	Albany	6/92	1	3.8	

[a] two additional incidents were submitted by Syngenta under 6(a)(2) aggregate reporting; the species and number of individuals involved were not reported

[b] National Wildlife Health Center, Madison, WI; incident information from the Center's diagnostic file of individual birds submitted for examination or from their epizootic database (K. Converse, pers comm.)

[c] pival, a first-generation anticoagulant, is no longer registered in the U.S. but might have been used under existing stocks provisions

[d] coumatetralyl, a second-generation anticoagulant, is not registered for use in the U.S.

Difethialone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Carnivores						
Bobcat	CA	Los Angeles	1999	1	trace	

Bromadiolone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Owls						
Great horned owl	NY	Warren	10/00	1	0.32	also brodifacoum (0.15 ppm)
Great horned owl	NY	Suffolk	7/00	1	0.4	also brodifacoum (0.37 ppm)
Great horned owl	NY	Albany	7/00	1	detected	
Great horned owl	CA	Los Angeles	2000	1	0.8	also brodifacoum (0.05 ppm)
Great horned owl	CA	San Bernardino	10/99	1	0.065	also brodifacoum (0.35 ppm)
Great horned owl	NY	Albany	12/98	1	0.27	also brodifacoum (0.08 ppm); "The owl died from hemorrhaging of minor wounds inflicted by prey"
Great horned owl	NY	Niagara	7/98	1	0.77	also warfarin (0.73 ppm) and brodifacoum (0.03 ppm)
Great horned owl	NY	Saratoga	5/98	1	0.24	also brodifacoum (0.06 ppm)
Great horned owl	NY	Suffolk	8/95	1	0.14	also brodifacoum (0.53 ppm)
Eastern screech-owl	NY	Cattaragus	1/00	1	4.29	
Eastern screech-owl	NY	Suffolk	3/99	1	0.05	
Northern saw-whet owl	NY	Cattaraugus	3/00	1	0.43	

Bromadiolone

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Barn owl	CA	San Bernardino	10/99	3	0.38 0.31 0.38	also brodifacoum (0.21 ppm) also brodifacoum (0.07 ppm) A total of 29 owls, 6 hawks, and 1 egret were found dead
Diurnal Birds of Prey						
Red-shouldered hawk	CA	Stanislaus	1999	1	0.28	also brodifacoum (0.01 ppm)
Red-tailed hawk	NY	not reported	10/98	1	0.08	
Cooper's hawk	NY	Erie	12/00	1	0.6	
Cooper's hawk	NY	Greene	2/99	1	0.24	several puncture wounds, coated with dried blood, on foot
American kestrel	CA	Yolo	1998	1	trace	detected in a nestling
Herons						
Great blue heron	NY	New York	1/99	1	0.1	
Perching Birds						
Fish crow	NY	Richmond	4/00	1	2.1	
Doves						
Mourning dove	NY	New York	10/99	1	0.42	

Bromadiolone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Carnivores						
San Joaquin Kit Fox	CA	Kern	1/00	1	0.14	also brodifacoum (0.13 ppm)
San Joaquin Kit Fox	CA	Kern	1999	1	0.72	also brodifacoum (0.47 ppm)
Coyote	CA	Los Angeles	2000	1	0.44	also brodifacoum (0.08 ppm)
Coyote	CA	Santa Clara	1999	3	0.46 0.09 0.07	also brodifacoum (0.47 ppm) also brodifacoum (0.23 ppm) also brodifacoum (0.30 ppm)
Coyote	CA	Orange	1998	1	0.22	also brodifacoum (0.66 ppm); coyote live-trapped and sacrificed
Bobcat	CA	Ventura	1999	1	0.11	also brodifacoum (0.07 ppm)
Raccoon	CA	Los Angeles	1998	1	1.1	also brodifacoum (0.082 ppm) and diphacinone (0.13 ppm); raccoon live-trapped and sacrificed
Raccoon	CA	Orange	1998	1	0.41	also brodifacoum (0.011 ppm); raccoon live-trapped and sacrificed
Striped skunk	NY	Westchester	4/96	3	0.2 0.29 0.08	
Marsupials						
Opossum	NY	Albany	11/96	1	0.8	

Bromadiolone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Rodents						
Gray squirrel	NY	New York	2/01	1	0.3	
Gray squirrel	NY	Suffolk	6/00	1	0.003	
Gray squirrel	NY		6/00	1	2.92	also detected (0.021 ppm) in stomach contents
Gray squirrel	NY	New York	4/00	3	8.84 3.14 2.46	
Gray squirrel	NY	Erie	11/99	3	2.88 1.43 1.01	all 3 squirrels had undergone considerable autolysis
Gray squirrel	NY	New York	2/99	1	0.05	
Gray squirrel	NY	Onondaga	9/98	1	0.12	
Gray squirrel	VA	Richmond	6/98	2	4.94	pooled sample from 2 of 8 squirrels found dead; also diphacinone (3.41 ppm); several unidentified birds also found dead

Chlorophacinone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Diurnal Birds of Prey						
Red-tailed hawk	NY	New York	7/99	1	0.18	
Gallinaceous Birds						
Turkey (wild)	KS	Cheyenne	4/02	2	0.69 0.40	bait present in gastrointestinal tract
Turkey (wild)	CA	Nevada	12/94	3	0	residues confirmed in gut contents; also detected in blood (5.5 ppm)
Carnivores						
Coyote	CA	Santa Clara	2/99	1	trace	also brodifacoum (0.36 ppm); the animal was live-trapped and sacrificed
Coyote	CA	Los Angeles	7/98	1	0.43	also brodifacoum (0.08 ppm) and diphacinone (0.081 ppm); the animal was live-trapped and sacrificed
Coyote	CA	Los Angeles	9/97	1	1.2	
San Joaquin kit fox	CA	Kern	9/99	1	0.27	also brodifacoum (0.07 ppm)
San Joaquin kit fox	CA	San Luis Obispo	8/90	4	detected	residue levels not reported

Chlorophacinone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Bobcat	CA	Marin	7/95	1	0.4	bobcat found dead 1 day after seen feeding on a dead owl; a rodent carcass was recovered in the crop of the owl
Rodents						
Gray squirrel	NY	New York	2/99	1	0.44	
Gray squirrel	NY	New York	1/99	1	0.47	
Gray squirrel	NY	New York	1/99	1	0.29	
Gray squirrel	NY	Albany	8/93	1	0.62	also brodifacoum (0.53 ppm)

Diphacinone

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Owls						
Barred owl	NY	Schenectady	11/99	1	0.62	immediate cause of death apparently was blunt trauma, possibly impact by an automobile
Great horned owl	CA	Contra Costa	8/98	1	0.6	also brodifacoum (0.04 ppm)
Snowy owl	NY	Dutchess	11/93	1	0.26	
Diurnal Birds of Prey						
Red-tailed hawk	NY	Nassau	6/99	1	0.34	
Turkey vulture	CA	Alameda	7/97	1	0.4	
Other Birds						
Rock dove	CA	Ventura	5/03	1	0.9	also brodifacoum (0.01 ppm)
Carnivores						
San Joaquin kit fox	CA	Kern	6/87	1	0.18	anticoagulant baits had been applied in the area for ground squirrel control
Coyote	CA	Ventura	10/97	1	1.3	also in thoracic-cavity blood (0.1 ppm) and stomach contents (0.16 ppm); also brodifacoum (0.083 ppm)

Diphacinone

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Coyote	CA	Los Angeles	1998	1	0.081	also chlorophacinone (0.43 ppm) and brodifacoum (0.08 ppm); the animal was live-trapped and sacrificed
Coyote	CA	Los Angeles	9/97	1	0.043	
Mountain lion	CA		11/86	1	see comment	45 ppm detected in blood
Raccoon	CA	Los Angeles	1998	1	0.13	also bromadiolone (1.1 ppm) and brodifacoum (0.082 ppm); the animal was live-trapped and sacrificed
Raccoon	CA		11/86	1	see comment	44 ppm detected in "blood and liver" sample
Ungulates						
White-tailed deer	NY	Suffolk	12/96	1	0.2	maggots in carcass suggest the deer had probably been dead for several weeks prior to analysis
White-tailed deer	NY	Suffolk	10/96	1	0.93	
Rodents						
Gray squirrel	NY	Albany	3/00	1	1.02	

Diphacinone

Order/species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Gray squirrel	VA	Richmond	6/98	2	3.41	pooled sample; also bromadiolone (4.94 ppm); 6 other squirrels and several unidentified birds also found dead
Gray squirrel	NY	Suffolk	4/97	1	2.0	
Heermann's kangaroo rat	CA	Merced	4/94	1	3.5	
Rabbits						
Cottontail rabbit	CA	Kern	8/89	12	not analyzed	reported by CA Dept. Fish and Game as "circumstantially indicated, but not conclusive" - dead rabbits found in area where diphacinone was applied; bleeding and hemorrhaging suggested anticoagulant poisoning

Warfarin

Order/ species	State	County	Date	No. animals analyzed	Liver residue (ppm)	Comments
Owls						
Great-horned owl	NY	Niagra	7/98	1	0.73	also bromadiolone (0.77 ppm) and brodifacoum (0.03 ppm)
Diurnal Birds of Prey						
Bald eagle	NY	Orleans	4/95	1	1.45	
Peregrine falcon	NJ	Sea Isle City	10/86	1	1.48	small bird parts were observed in the gizzard
Rodents						
Gray squirrel	NY	Niagara	9/81	1	0.23	

Zinc Phosphide

Order/ species	State	County	Date	No. animals examined	Comments
Gallinaceous Birds					
Turkey (wild)	NY	Wayne	2/00	2	detected in crop contents
Turkey (wild)	MI	Montcalm	12/97	3	detected in crop contents
Turkey (wild)	NY	Wayne	11/95	1	detected in crop contents
Turkey (wild)	WI	not reported	3/91	2	turkey found dead after bait applied in an orchard
Turkey (wild)	MI	Manistee	12/87	4	27 ppm
Turkey (wild)	MI	Leelanau	11/87	1	170 ppm in gizzard contents
Turkey (wild)	MI	Leelanau	4/87	1	28 ppm in gizzard contents
Turkey (wild)	MI	Missaukee	3/87	1	220 ppm in gizzard contents
Turkey (wild)	MI	Benzie	12/86	9	430 ppm in gizzard contents
Turkey (wild)	MI	Wexford	11/86	4	330 ppm in gizzard contents
Turkey (wild)	MI	Grand Traverse	11/86	4	confirmed by MI Dept. of Agric. lab. analysis
Waterfowl					
Canada goose	NY	Niagra	12/01	4-5	15 geese found dead, with phosphine odor present; 3 of 4 geese analyzed with Draeger apparatus tested positive for phosphine gas
Canada goose	NY	Ulster	12/96	4	phosphine gas detected in ingesta
Canada goose	UT	Summit	4/94	1	information obtained from epizootic database, National Wildlife Health Center, Madison, WI

Zinc Phosphide

Order/ species	State	County	Date	No. animals examined	Comments
Canada goose	CT	Fairfield	3/92	9	information obtained from epizootic database, National Wildlife Health Center, Madison, WI
Canada goose	MI	Grand Traverse	11/86	1	20 ppm residue in gizzard contents
Canada goose	MI	Oakland	12/82	30	confirmed by MI Dept. of Agric. lab. analysis
Canada goose	CA	Siskiyou	10/63	105	Keith and O'Neill[b]
White-fronted goose	CA	Siskiyou	10/63	325	Keith and O'Neill[b]
Snow goose	CA	Siskiyou	10/63	25	Keith and O'Neill[b]
White-fronted and Snow geese	CA	Siskiyou	4/84	~40	information obtained from epizootic database, National Wildlife Health Center, Madison, WI
Mallard	UT	Summit	10/93-4/94	29	information obtained from epizootic database, National Wildlife Health Center, Madison, WI
Carnivores					
Red fox	MI	Grand Traverse	6/87	2	"secondary poisoning from eating mice that had consumed Zn_phosphide treated grain"[a]
Other Mammals					
Eastern cottontail	VA	Augusta	1/04	1	>40 ppm in fresh tissues: ZP pellets had been applied in an orchard
Gray squirrel	MI	Calhoun	6/83	10	information obtained from epizootic database, National Wildlife Health Center, Madison, WI

[a] reported in Johnson and Fagerstone (1992) and Hegdal and Gatz (1977)

Attachment E. USFWS Jeopardy Determinations for Effects of 8 Rodenticides on Threatened and Endangered Species.

In response to a formal consultation requested by EPA (1991b) under Section 7 of the Endangered Species Act, the United States Fish and Wildlife Service issued a Biological Opinion on *Effects of 16 Vertebrate Control Agents On Threatened and Endangered Species* in March of 1993 (USFWS 1993). The Biological Opinion included jeopardy determinations for species potentially exposed (primary or secondary exposure) to brodifacoum, bromadiolone, chlorophacinone, diphacinone, warfarin, bromethalin, zinc phosphide, and cholecalciferol. For each species addressed in the Biological Opinion, the Service determined either that use of the rodenticide "is likely to jeopardize" or "is not likely to jeopardize" the continued existence of the species. For the likely to jeopardize determinations the Service provided "reasonable and prudent alternatives" that preclude jeopardy but still allow use of the rodenticide. These alternatives represent the Service's best professional judgement of the measures necessary to provide the appropriate level of protection to the species. The Service also provided "incidental take" statements and "reasonable and prudent measures" to minimize take. Difethialone, first registered in 1995, is not addressed in this or any subsequent Biological Opinion, but EPA believes the jeopardy determinations for brodifacoum also would be applicable to difethialone. The Service's determinations for each rodenticide are tabulated below. Only the common names of the species are presented in the table for each rodenticide, but scientific names are listed in a final table. Species not included in the tables were presumed by the Service to not be affected by the rodenticide of concern or to have no chance for exposure.

Brodifacoum

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which brodifacoum "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Salt marsh harvest mouse Fresno kangaroo rat	Prohibit use within 100 yards of these species' occupied habitat
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
Audubon's crested caracara	Prohibit use within this species' occupied habitat
San Clemente loggerhead shrike	Prohibit use on San Clemente Island, California

Brodifacoum

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which brodifacoum "is not likely to jeopardize" their continued existence:	
Giant kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Point Arena mountain beaver	Incidental take can be minimized by prohibiting outdoor use within 100 yards of these species' occupied habitat
Louisiana black bear	Incidental take can be minimized by prohibiting use within occupied habitat
San Joaquin kit fox	Incidental take can be minimized by requiring that outdoor applications be made in tamper-resistant bait boxes placed in areas not accessible to wildlife
Hawaiian hawk	Incidental take can be minimized by prohibiting use within 100 yards of this species' occupied habitat
Eastern indigo snake	Incidental take can be minimized by conducting laboratory studies using surrogate snake species to obtain toxicity data on the chemical's secondary poisoning hazard to snakes

Bromadiolone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which bromadiolone "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Salt marsh harvest mouse	Prohibit use within 100 yards of these species' occupied habitat
Species for which bromadiolone "is not likely to jeopardize" their continued existence:	
Fresno kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Point Arena mountain beaver	Incidental take can be minimized by prohibiting outdoor use within 100 yards of these species' occupied habitat

Bromadiolone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
San Joaquin kit fox	Incidental take can be minimized by requiring that outdoor applications be made in tamper-resistant bait boxes placed in areas not accessible to wildlife

Chlorophacinone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which chlorophacinone "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Stephen's kangaroo rat Amargosa vole Hualapai Mexican vole	Prohibit use within 100 yards of these species' occupied habitat
Salt marsh harvest mouse Tipton kangaroo rat Giant kangaroo rat Fresno kangaroo rat Point Arena mountain beaver	Prohibit outdoor use within 100 yards of these species' occupied habitat unless specific programs for chlorophacinone are approved by the Service and implemented
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
San Joaquin kit fox	Prohibit use within the kit fox range as determined by the Service, except for agricultural areas $\geq$1 mile from any kit fox habitat as determined by the California EPA in consultation with the Service, or areas where applicable surveys have been conducted and yielded negative results

Chlorophacinone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Florida panther	Prohibit use within 20 miles of the boundary of any Federal and State lands (e.g., National Wildlife Refuge, National Park, State Park, etc.) and Indian Reservations that provide suitable panther habitat south of Charlotte, Glades and Martin counties, Florida; incidental take can be minimized by removing and properly disposing of any dead or incapacitated animal likely to have been poisoned within and including the area extending 5 miles from the edge of the prohibited use zone
Jaguarundi Ocelot	Prohibit use within 3 miles of occupied habitat; incidental take can be minimized by conducting surveys prior to use to determine if habitat is occupied
Audubon's crested caracara	Prohibit use within this species' occupied habitat
Species for which chlorophacinone "is not likely to jeopardize" their continued existence:	
Louisiana black bear	Incidental take can be minimized by prohibiting use within occupied habitat
Grizzly bear Gray wolf Utah prairie dog	None specified
Puerto Rican boa Virgin Island tree boa	Incidental take can be minimized by prohibiting use within the known occupied habitat
Eastern indigo snake	Incidental take can be minimized by conducting laboratory studies using surrogate snake species to obtain toxicity data on the chemical's secondary poisoning hazard to snakes

Diphacinone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which diphacinone "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Key Largo cotton mouse Key Largo woodrat Southeastern beach mouse Morro Bay kangaroo rat Stephen's kangaroo rat Silver rice rat Hualapai Mexican vole Utah prairiedog	Prohibit use within 100 yards of these species' occupied habitat
Salt marsh harvest mouse Tipton kangaroo rat Giant kangaroo rat Fresno kangaroo rat Point Arena mountain beaver	Prohibit outdoor use within 100 yards of these species' occupied habitat unless specific programs for diphacinone are approved by the Service and implemented
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
San Joaquin kit fox	Prohibit use within the kit fox range as determined by the Service, except for agricultural areas ≥1 mile from any kit fox habitat as determined by the California EPA in consultation with the Service, or areas where applicable surveys have been conducted and yielded negative results
Florida panther	Prohibit use within 20 miles of the boundary of any Federal and State lands (e.g., National Wildlife Refuge, National Park, State Park, etc.) and Indian Reservations that provide suitable panther habitat south of Charlotte, Glades and Martin counties, Florida; incidental take can be minimized by removing and properly disposing of any dead or incapacitated animal likely to have been poisoned within and including the area extending 5 miles from the edge of the prohibited use zone

Diphacinone

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Jaguarundi Ocelot	Prohibit use within 3 miles of occupied habitat; incidental take can be minimized by conducting surveys prior to use to determine if habitat is occupied
Gray wolf Grizzly bear	Prohibit use within the geographic range of this species until the Service has determined the species is not in the vicinity of the treatment site
Louisiana black bear	Prohibit use within the current known occupied habitat
Black-footed ferret	Prohibit use within 7 km (4.34 mi) from a prairie dog town, except for black-tailed prairie dog colonies <80 acres in size or white-tailed prairie dog colonies <200 acres in size, or urban situations, or colonies that have been surveyed in coordination with the Service and determined that ferrets are absent
Lower Keys rabbit	Prohibit use within 100 yards of this species' occupied habitat
Audubon's crested caracara	Prohibit use within this species' occupied habitat
Species for which diphacinone "is not likely to jeopardize" their continued existence:	
Delmarva fox squirrel	Incidental take can be minimized by placing bait in bait boxes small enough to exclude fox squirrels
Puerto Rican boa Virgin Island tree boa	Incidental take can be minimized by prohibiting use within the known occupied habitat
Eastern indigo snake	Incidental take can be minimized by conducting laboratory studies using surrogate snake species to obtain toxicity data on the chemical's secondary poisoning hazard to snakes

Warfarin

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which warfarin "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Salt marsh harvest mouse Fresno kangaroo rat	Prohibit use within 100 yards of these species' occupied habitat
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
Species for which warfarin "is not likely to jeopardize" their continued existence:	
Giant kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Point Arena mountain beaver	Incidental take can be minimized by prohibiting outdoor use within 100 yards of these species' occupied habitat

Bromethalin

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which bromethalin "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat	Prohibit use within 100 yards of these species' occupied habitat
Salt marsh harvest mouse Fresno kangaroo rat	Prohibit use within 100 yards of these species' occupied habitat
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida

Bromethalin

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which bromethalin "is not likely to jeopardize" their continued existence:	
Giant kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Point Arena mountain beaver	Incidental take can be minimized by prohibiting outdoor use within 100 yards of these species' occupied habitat

Zinc phosphide

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which zinc phosphide "is likely to jeopardize" their continued existence:	
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Silver rice rat	Prohibit use within 100 yards of these species' occupied habitat
Fresno kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Giant kangaroo rat Salt marsh harvest mouse Point Arena mountain beaver	Prohibit outdoor use within 100 yards of occupied habitat unless a protection program has been approved by the Service and implemented
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
Black-footed ferret	Prohibit use within 7 km (4.34 mi) from a prairie dog town, except for black-tailed prairie dog colonies <80 acres in size or white-tailed prairie dog colonies <200 acres in size, or urban situations, or colonies that have been surveyed in coordination with the Service and determined that ferrets are absent
Hawaiian crow	Prohibit use within 100 yards of occupied habitat unless bait is placed in tamper-resistant bait boxes

Zinc phosphide

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Atwater's prairie chicken	Prohibit use within 100 yards of occupied habitat unless bait is placed in tamper-resistant bait boxes
Hawaiian coot Hawaiian duck	Prohibit use within 100 yards of any water or wetland on or adjacent to any golf course or turf farm on the islands of Kauai, Oahu, and Maui unless bait is placed in tamper-resistant bait boxes
Nene (Hawaiian goose) Mariana crow	Prohibit use in occupied habitat unless bait is placed in tamper-resistant bait boxes
Mississippi sandhill crane Puerto Rican plain pigeon Yellow-shouldered blackbird	Outdoor baiting must use tamper-resistant bait boxes within occupied habitat
Species for which zinc phosphide "is not likely to jeopardize" their continued existence:	
Gray wolf Grizzly bear	Incidental take can be minimized by applying bait in tamper-resistant bait boxes, or contacting the local Service office to ensure that these species are not in the vicinity of the treatment site
Utah prairie dog	None specified
San Joaquin kit fox	Incidental take can be minimized by requiring that outdoor applications be made in tamper-resistant bait boxes placed in areas not accessible to wildlife
San Clemente sage sparrow	Incidental take can be minimized by prohibiting use in occupied habitat unless bait is placed in tamper-resistant bait boxes
Whooping crane	Incidental take can be minimized by ensuring that cranes have not wandered into the treatment area

Cholecalciferol

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Species for which cholecalciferol "is likely to jeopardize" their continued existence:	

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Cholecalciferol

Species	Reasonable and Prudent Alternatives/ Reasonable and Prudent Measures
Alabama beach mouse Choctawhatchee beach mouse Perdido Key beach mouse Anastasia Island beach mouse Southeastern beach mouse Morro Bay kangaroo rat Salt marsh harvest mouse Fresno kangaroo rat	Prohibit use within 100 yards of these species' occupied habitat
Carolina northern flying squirrel	Prohibit outdoor use within this species' occupied habitat
Florida salt marsh vole	Prohibit use within 100 yards of the landward edge of this species' habitat in Levy County, Florida
Species for which cholecalciferol "is not likely to jeopardize" their continued existence:	
Giant kangaroo rat Stephen's kangaroo rat Tipton kangaroo rat Point Arena mountain beaver	Incidental take can be minimized by prohibiting outdoor use within 100 yards of these species' occupied habitat

Species addressed in the Biological Opinion[a]:

Mammals:

Alabama beach mouse (*Peromyscus polionotus amnobates*)

Amargosa vole (*Microtus californicus scirpensis*)

Anastasia Island beach mouse (*Peromyscus polionotus phasma*)

Black-footed ferret (*Mustela nigripes*)

Carolina northern flying squirrel (*Glaucomys sabrinus coloratus*)

Choctawhatchee beach mouse (*Peromyscus polionotus allophrys*)

Delmarva fox squirrel (*Sciurus niger cinereus*)

Florida salt marsh vole (*Microtus pennsylvanicus dukecampbelli*)

Florida panther (*Puma (=Felis) concolor coryi*)

Fresno kangaroo rat (*Dipodomys nitratoides exilis*)

Giant kangaroo rat (*Dipodomys ingens*)

Gray wolf (*Canis lupus*)

Grizzly bear (*Ursus arctos*)

Species addressed in the Biological Opinion[a]:

    Hualapai Mexican vole (*Microtus pennsylvanicus hualpaiensis*)

    Jaguarundi (*Herpailurus (=Felis) yagouaroundi cacomitli*)

    Jaguar (*Panthera onca*)

    Key Largo cotton mouse (*Peromyscus gossypinus allapaticola*)

    Key Largo woodrat (*Neotoma floridana smalli*)

    Lower Keys rabbit (*Sylvilagus palustris hefneri*)

    Louisiana black bear (*Ursus americanus luteolus*)

    Morro Bay kangaroo rat (*Dipodomys heermanni morroensis*)

    Ocelot (*Leopardus (=Felis) pardalis*)

    Perdido Key beach mouse (*Peromyscus polionotus trissyllepsis*)

    Point Arena mountain beaver (*Aplodontia rufa nigra*)

    Salt marsh harvest mouse (*Reithrodontomys raviventris*)

    San Joaquin kit fox (*Vulpes macrotis mutica*)

    Silver rice rat (*Oryzomys palustris natator*)

    Southeastern beach mouse (*Peromyscus polionotus niveiventris*)

    Stephen's kangaroo rat (*Dipodomys stephensi*)

    Tipton kangaroo rat (*Dipodomys nitratoides nitratoides*)

    Utah prairie dog (*Cynomys parvidens*)

Birds:

    Atwater's prairie chicken (*Tympanuchus cupido attwateri*)

    Audubon's crested caracara (*Polyborus plancus audubonii*)

    Hawaiian coot (*Fulica americana alai*)

    Hawaiian crow (*Corvus hawaiiensis*)

    Hawaiian duck (*Anas wyvilliana*)

    Hawaiian hawk (*Buteo solitarius*)

    Mariana crow (*Corvus kubaryi*)

    Mississippi sandhill crane (*Grus canadensis pulla*)

    Nene [Hawaiian goose] (*Branta (=Nesochen) sandvicensis*)

    Puerto Rican plain pigeon (*Columba inornata wetmorei*)

    San Clemente loggerhead shrike (*Lanius ludovicianus mearnsi*)

    San Clemente sage sparrow (*Amphispiza belli clementeae*)

    Whooping crane (*Grus americana*)

    Yellow-shouldered blackbird (*Agelaius xanthomus*)

Reptiles:

Species addressed in the Biological Opinion[a]:

Puerto Rican boa (*Epicrates inornatus*)

Virgin Island tree boa (*Epicrates monensis granti*)

Eastern indigo snake (*Drymarchon corais couperi*)

[a] scientific names are from the U.S. Fish and Wildlife Service's *Endangered and Threatened Wildlife and Plants*, 50 CFR 17.11 and 17.12, current as of December 31, 1998