REDUCING RODENTICIDE HAZARDS TO HUMANS AND WILDLIFE: THE NEED FOR USE REGULATIONS

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Abstract: Rodenticide use poses significant exposure risks for children and poisoning risks for native wild birds and mammals in the United States. Poison Control Center reports document 15,000 calls annually identifying household rat poison ingestion, with 88% of cases for children under age six. Wildlife poisonings from ingestion of baits or treated grain may occur whenever birds or mammals have access to the products. This is especially true for broadcast baits and treated grain used above ground in agricultural settings, or when baits are distributed around structures or outside waste containers. Secondary poisoning of predators and scavengers occurs when target rodents are moribund or die above ground in locations accessible to predatory birds or mammals. Secondary poisoning risks appear to be highest for the "second generation" anticoagulant rodenticides, because rodents consume them in super-lethal doses in multiple feedings during the 4-6 days required for these poisons to kill the target rodents. These anticoagulants persist for long periods in tissues of scavengers and predators, increasing the risk of adverse effects from subsequent feedings on poisoned rodents. The risk of both human and wildlife poisonings can be greatly reduced by packaging rodenticides in bait stations and restricting the use of second generation products to licensed pest control operators.

Key words: anticoagulant rodenticides, brodifacoum, bromadiolone, chlorophacinone, diphacinone, rodent, secondary toxicity, strychnine, warfarin, zinc phosphide

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INTRODUCTION

Commensal rodents present public health and disease risks to human populations, living in almost every urban and rural region. Rodents also damage stored crops and structures resulting in economic loss and contamination of stored grains. Control of these populations is necessary, and effective rodenticide baits and treated grains have been developed with a variety of different mechanisms of action.

Because these toxicants are designed for mammalian rodents, rather than insects or plant pests, the chemicals are also toxic to humans, other mammals, and birds. The high availability of over-the-counter rodenticide products to children has resulted in many reported incidents to poison control centers, and the high toxicity to other vertebrates has resulted in both primary poisoning of non-target mammals and birds ingesting baits or treated grain, as well as secondary poisoning of carnivorous scavenging mammals and birds.

The poisoning of non-target animals and humans has been a major concern of the US Environmental Protection Agency (EPA), which initiated regulatory review of nine rodenticides in 1998, resulting in a comprehensive risk assessment and mitigation plan by the EPA in 2007 in an

effort to minimize the exposure to non-targets, including children.

RODENTICIDES CURRENTLY ON THE CONSUMER MARKET

The EPA currently has ten rodenticide active ingredients registered for use in the US. The products available are three "first generation" anticoagulants (warfarin, chlorophacinone, and diphacinone), three "second-generation" anticoagulants (brodifacoum, difethialone, bromadiolone), and four non-anticoagulant compounds (zinc phosphide, bromethalin, strychnine and cholecalciferol). The rodenticides are predominantly used to control commensal rats and mice in and around buildings and other urban areas. All are available as consumer products "over-the-counter", sold without restrictions, although the more concentrated formulations of several are "restricted use" and available only to licensed pest control operators. Some products (zinc phosphide, strychnine, chlorophacinone and diphacinone) also have registrations for outdoor and agricultural uses against rodent and small mammalian pests. Additionally, brodifacoum and diphacinone have important island conservation uses on lands managed by the US Fish and Wildlife Service, US National Park Service, and other agencies.

Anticoagulant Rodenticides

Warfarin was patented by the Wisconsin Alumni Research Foundation in 1945 after a series of coumarin compounds were isolated and synthesized by university researchers (Stahmann et al. 1941). Warfarin and other anticoagulants act by disrupting blood clotting through inhibition of vitamin K synthesis. The inhibition and depletion of clotting factors takes several days, and intoxicated animals usually die 4-8 days after ingestion of baits. The "first generation" anticoagulant rodenticides (FGAR) registered in the US include warfarin, and the indanedione derivatives chlorophacinone and diphacinone. These have been marketed for the past 50 years. Rodent resistance to warfarin occurred in many areas in the 1960s and a group of highly toxic derivatives were developed as alternatives for the first generation anticoagulants. Brodifacoum was described by Hadler and Shadbolt (1975) and termed a "superwarfarin" or "second generation" anticoagulant rodenticide (SGAR). Other SGARs registered in the US include difenacoum, difethialone and bromodialone. They all are derivatives of coumarin, and act by the same mode of action as FGARs. The SGARs are more toxic, and formulated in bait blocks at concentrations of 0.025 to 0.005% active ingredient, and are generally lethal to rodents after a single feeding. Since the mechanism of action is similar for both first and second generation anticoagulants, the time to death for intoxicated target animals is very similar (5-7 days), even though only a single feeding is required for the SGARs to be lethal.

Non-anticoagulant Rodenticides

The four non-anticoagulant rodenticides currently registered in the US include a variety of chemicals with diverse modes of action. Two are neurotoxins: strychnine and bromethelin. Strychnine causes excitation of all parts of the nervous system by blocking inhibitory neurons resulting in convulsions. Bromethalin is a disruptor of energy metabolism with central nervous system effects that also causes convulsions and paralysis. Zinc phosphide has been registered as a rodenticide since the 1940s, and liberates highly toxic phosphine gas in the gut of exposed animals which adversely and rapidly affects major organ systems. Vitamin D_3, cholecalciferol, is registered as a rodenticide, and when fed in large amounts, disrupts normal calcium

metabolism, resulting in calcium mobilization and deposition in many tissues and, ultimately, kidney failure.

RISK OF FIRST AND SECOND GENERATION ANTICOAGULANT RODENTICIDES TO NON-TARGET ANIMALS

Laboratory studies conducted EPA protocols for anticoagulants with first generation (chlorophacinone, diphacinone, warfarin) and second generation (bromodialone, brodifacoum, and difethialone) ingredients have shown that all compounds are greater than 90% effective, and time to death was very similar for all compounds tested, with median times to death of 4.5-6 days (Erickson and Urban, 2004).

Because time to death is similar, the more acutely toxic second generation compounds have a greater potential to overload target animals during successive feedings, and they pose a significantly greater secondary toxicity hazard to raptors and mammalian scavengers.

The potential for target rodents accumulating super-lethal levels of SGARs was reported to EPA by the producer (ICI Americas, Inc., Goldsboro, NC) and reported in Erickson and Urban (2004). Brodifacoum (Talon™, 50ppm) was fed to captive Norway rats (*Rattus norvegicus*) and monitored for consumption. Rats were given bait alone or as a choice with untreated food, and fed until death, which averaged 6.5 days. Rats fed only bait as food consumed an average of 80 lethal doses before death, and rats given the choice of baits and untreated food ingested an average of 40 lethal doses before death.

In EPA's comparative assessment of rodenticides (Erickson and Urban 2004) this issue was specifically addressed, and the data indicate a substantially reduced risk from first generation anticoagulants compared to SGARs. A review of 17 studies, including all three first generation anticoagulants (warfarin, diphacinone and chlorophacinone), showed little mortality from secondary exposure to many species of predatory birds. Mortality ranged from 0 to 9%. In eight chlorophacinone studies with 9 species of raptors, there was no mortality from consuming laboratory poisoned rodents. There was a 9% mortality in three diphacinone studies with five different species of birds, and in four warfarin studies, there was also a 9% mortality. For most studies, adverse effects such as prolonged clotting time were observed in some surviving individuals. There were no observed sublethal effects in surviving birds exposed to warfarin.

In contrast to the relatively low mortality with first generation anticoagulants, EPA review of SGAR studies demonstrated high mortality for predatory birds and mammals fed carcasses of brodifacoum-poisoned rodents. In eleven studies, an average of 63% of exposed predatory or scavenging birds died following ingestion of poisoned prey. About 33% of survivors showed signs of toxicity. In five studies with bromadiolone, however, mortality occurred in 8% of birds exposed to poisoned prey.

These reviews indicate that SGARs, especially brodifacoum, pose significant secondary risks to wild birds and mammals whenever target rodents are accessible outdoors.

EXPOSURES TO CHILDREN AND NON-TARGET ANIMALS

Human Exposures

The American Association of Poison Control Centers (PCC) collects and reports data from human exposure cases reported by telephone to the network of poison control centers throughout the USA. In 2005, more

than 2.4 million calls were reported to PCC of which 15,120 were reports of ingestion of anticoagulant rodenticides, and 13,366 were reports for children under 6 years of age. Of that total, 4,590 cases were treated in medical facilities, and 307 cases had symptoms indicative of anticoagulant rodenticide exposure. However, 4,951 cases exhibited no clinical symptoms. These figures are indicative of several things: 1) rodenticides in households are accessible to young children and apparently ingested relatively frequently; 2) mothers finding young children with rodent baits are highly concerned, and call the local PCC, regardless of whether the child exhibits symptoms or not; and 3) ingestion of rat poison is rarely fatal to children, although hundreds of cases per year cause demonstrable symptoms. Treatment with an injectable vitamin K antidote is usually sufficient to counteract any potential long-term effects.

The number of calls to PCC indicate that there is a problem with packaging of rodent baits, and improved packaging is needed to prevent access to poison baits by young children. Pets also may ingest household rodenticides, and packaging in tamper resistant bait stations would prevent inadvertent exposure.

Wildlife Exposures

The EPA comparative risk assessment on nine rodenticides (Erickson and Urban 2004) documents more than 300 cases of non-target bird and mammal mortality associated with legal use of rodenticides in the US. The risk assessment estimates this is a small fraction of the actual number of cases, because of under reporting by the public as well as difficulty in finding poisoned birds and mammals and associating them with a rodenticide incident that may have occurred a week previously at some distance from the location where the non-target animal was found. The report uses the incident information to evaluate which chemicals are most frequently involved in non-target kills, and has developed assessments as to which chemicals are responsible and the relative risks posed by rodenticides on the market. The report concluded that brodifacoum and difethialone stand out as the two rodenticides posing the greatest overall risk to birds and non-target mammals, followed by bromadiolone and diphacinone. Zinc phosphide also ranked high for overall risk, because of high primary risk, especially to birds.

American Bird Conservancy (ABC) has also compiled pesticide poisoning cases affecting wild birds, and the data are available on the web at URL http://www.abcbirds.org/aims/. The ABC's Avian Incident Monitoring System (AIMS, ABC 2005) database, developed collaboratively with the EPA, documents 2,575 avian pesticide incidents, and includes cases of pesticide misuse and abuse in addition to legal uses. AIMS lists 309 incidents involving rodenticides, in which a specific rodenticide was identified as the probable cause of death. In 208 of these cases, chemical residues of the rodenticide active ingredient were present in sufficient quantity to be certain of the cause of death. Residues of the specific rodenticide were detected in an additional 53 cases, but at insufficient levels to be certain of the cause of death. AIMS data indicate that approximately 15% of all identified wild bird poisonings are the result of primary or secondary poisonings by rodenticides.

Brodifacoum and bromadiolone were responsible for the highest proportion of secondary rodenticide poisoning cases, as indicated from residue analysis of carcasses. The raptors killed in the highest numbers were red-tailed hawks (*Buteo jamaicensis*), great horned owls (*Bubo virginianus*), bald

eagles (*Haliaeetus albicilla*), and golden eagle (*Aquila chrysaetos*). Table 1 compares the number of incidents in the AIMS database for the seven rodenticides reported and presents the numbers of birds exposed. The greatest number of cases is for brodifacoum, and the high number of strychnine incidents reflects many illegal poisoning incidents not reported in the EPA data.

Table 1. Rodenticide incidents reported in the American Bird Conservancy's Avian Incident Monitoring System database, 1968-2005.

Pesticide	# Incidents	# Birds Killed	# Birds Sub-lethally Affected
Brodifacoum	150	242	17
Strychnine	91	1967	4
Zinc phosphide	29	599	
Bromadiolone	21	66	1
Warfarin	8	9	1
Diphacinone	6	9	
Chlorophacinone	2	9	1
Total number of cases or birds	309	2901	24

The increased risks from SGAR have been confirmed with field data from California, Canada, France, and the United Kingdom, which all indicate significant secondary toxicity risks to predatory birds, and mammals. (Mineau and Shore 2006).

The Pesticides Investigation Unit of the California Department of Fish and Game has documented exposure to endangered San Joaquin kit foxes (*Vulpes macrotis*), bobcats (*Lynx rufus*), and mountain lions (*Puma concolor*), from second generation anticoagulants during the past ten years. Liver tissue from 32 dead kit foxes was analyzed for rodenticide residues and anticoagulant rodenticide was detected in the liver of 84% of the foxes (Erickson and Urban 2004). Brodifacoum was detected in 27 individuals. Several of the foxes had residue levels above 0.5ppm, and most had greater than 0.2ppm. This is below the experimentally determined lethal level (Schitoskey 1975) but indicates that these endangered foxes are frequently exposed to rodenticides, most probably through consuming moribund or dead rodents that have died outside buildings. The detection of brodifacoum and other SGARs in carcasses of mountain lions and bobcats in suburban and rural areas of Californa (Riley 2006) also indicate wide availability of SGARs either in bait placed outdoors or in carcasses of poisoned rodents accessible to these wild cats. The residue levels in liver of most of the mountain lions and bobcats have been below lethal levels, but still indicate wide availability and exposure to SGARs marketed for household use.

Zinc phosphide and strychnine have been responsible for many incidents in the AIMS database. Both are available as consumer products, although some strychnine products are classified as restricted use. Zinc phosphide is responsible for the poisoning of grain-eating birds and mammals when treated grain is broadcast or made accessible above ground. Wild turkeys (*Meleagris gallopavo*) have been the

most frequently poisoned birds (ABC 2005). There is little danger of secondary toxicity with zinc phosphide, because the phosphine gas liberated in the stomach of intoxicated animals is oxidized quickly, and generally not available to scavengers. (IPCS 1989). The exception to this appears to be mammalian scavengers that consume poisoned rodents containing a lethal quantity of undigested zinc phosphide poison grain (Erickson and Urban 2004).

Strychnine has been responsible for many wildlife poisoning incidents, frequently arising from deliberate misuse of the poison used to kill scavengers or predators by dosing sheep carcasses or raw meat in the field. The AIMS database includes 91 incidents involving 63 species of birds and 26 poisoning incidents of bald and golden eagles. The labels for both strychnine and zinc phosphide specify below ground uses only, but the documented poisoning incidents demonstrate that consumers may not follow label instructions, resulting in non-target poisoning incidents.

THE NEED TO LIMIT USES OF SECOND GENERATION ANTI-COAGULANT RODENTICIDES

The SGARs were developed in response to the genetic resistance to warfarin in rats (*Rattus* spp.) in some geographic locations (Hadler and Shadbolt 1975). These chemicals have proven highly effective against commensal rodents and are used widely around the world. Rodents have not developed resistance to SGARs, and there has been no need to develop replacements. Uncontrolled consumer use, however, has led to widespread wildlife exposure, and exposure to some endangered species, such as the San Joaquin kit fox.

The American Bird Conservancy believes that restrictions must be placed on the availability and use of these highly toxic SGARs. Limiting the availability of SGARs by making them restricted use pesticides will eliminate inappropriate uses by consumers, reduce child and pet poisonings, and reduce wildlife poisonings. Consumers should be able to obtain adequate rodent control with FGARs, and because the first generation rodenticides do not pose the elevated hazards of secondary poisoning to predatory and scavenging mammals and birds, possible consumer misuse will be less injurious to wildlife.

Reducing Human and Wildlife Exposure

Primary poisoning incidents with rodenticides appear to arise from consumer product "place packs" and bait blocks distributed both indoors and outdoors in a manner that makes them available to children, pets and non-target wildlife. The majority of primary exposures could be avoided if all consumer products were sold only in tamper resistant bait stations. Cost analysis by the Biological and Economic Analysis Division of EPA (Chiri et al. 2006) indicates that inexpensive bait stations can be marketed at a minimal increase in cost, and the overall savings in poisoning incidents justifies the minimal added expense. For situations where rodenticides may be accessible to large dogs, more robust bait stations should be made available, but will add additional cost. Secondary toxicity arising from scavengers and predatory birds eating moribund or dead rodents will also be reduced if the SGAR are removed from the consumer market.

There appears to be little justification for allowing the availability of highly toxic SGARs to remain on the consumer market. The efficacy of first generation rodenticides is high, bait shyness and genetic resistance is generally low, and if either of these conditions were to arise in any specific geographic location, licensed pest control operators could be contracted to manage the problem. The high toxicity of the SGARs,

and their efficacy make them ideal back-up products to have available when needed, but their potential for misuse and non-target poisoning is justification to remove them from the consumer market. Secondary poisonings of wildlife would also be reduced if the restricted use SGARs were limited to indoor use only.

EPA Mitigation Plan

In January 2007, the EPA announced a draft mitigation plan for rodenticide use and availability, after a prolonged review of rodenticide use patterns and risks (US EPA 2007). The plan also addressed an August 2005 US Federal District Court decision requiring the agency to adopt safety measures to protect children from inadvertent exposure to household rat poisons. The draft mitigation plan proposes to make brodifacoum, difethialone and bromodialone restricted use pesticides, available only to registered pest control operators. The plan further proposes to require all over-the-counter rodenticides to be sold only in tamper resistant, pre-loaded bait stations. In an effort to reduce wildlife exposures, the EPA further proposes to require all outdoor above ground uses of SGARs to also be in approved bait stations.

CONCLUSIONS

Current EPA pesticide regulations permit over-the-counter sales of all rodenticides in easy to open packaging accessible to children and pets, resulting in thousands of unintended exposures annually. Many of the products are sold as treated grain, making these products a hazard for granivorous wild birds and mammals. The unrestricted wide availability of second generation anticoagulant rodenticides has resulted in secondary poisonings of predatory and scavenging birds and mammals in both suburban and rural areas of the US.

American Bird Conservancy believes the mitigation measures proposed by the EPA will significantly reduce secondary poisonings of raptors and predatory mammals. The packaging requirements for pre-loaded tamper resistant bait stations will also reduce the approximately 15,000 child poisonings documented each year by Poison Control Centers.

The direct poisoning of wild birds by zinc phosphide, strychnine and chlorophacinone grain baits has not been addressed by EPA, and the American Bird Conservancy believes the continuing use of grain baits above ground in agricultural settings will be responsible for direct poisoning of many protected birds each year. We recommend the use of bait stations to prevent poisoning of wild turkeys and even deer (*Odocoileus* spp.) who find access to poison grain. The American Bird Conservancy also recommends curtailment of the special local needs (FIFRA Section 24(c)) use of grain baits in western states for prairie dog (*Cynomys* spp.) control, unless better education and enforcement to eliminate illegal practices are conducted.

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