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Concerns Regarding Proposed Restrictions in the Use of Second-Generation Anticoagulant Rodenticides for Commensal Rodent Control

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Abstract: The development of second-generation anticoagulant rodenticides for commensal rodent control arose from the need to overcome genetic resistance to earlier anticoagulants, to improve efficacy, and to reduce hazard over older acute rodenticide materials. Over the past three decades, the second-generation anticoagulant products have become the principal commensal rodenticides used in the U.S. and elsewhere. During this long usage, individual cases of human and nontarget wildlife exposure have been documented, and the significance has been debated. Following a lengthy re-registration and review process, the U.S. Environmental Protection Agency in January 2007 proposed restrictions on the use of second-generation anticoagulant rodenticides for commensal rodent control. The proposed restrictions would shift emphasis to other rodenticides, including those with inherent problems that were the basis for developing second-generation anticoagulants. Reduced efficacy, prolonged public exposure to rodents, limitations in bait formulations and placements, increased genetic resistance, and greater application rates (exposure) are anticipated if these restrictions are adopted. Various nontarget concerns will remain with alternative products and use patterns by professional users and consumers, including use of products without specific antidotes. These impacts would occur amidst increasing rodent problems in many U.S. municipalities with declining management resources and aging infrastructure. Alternative measures should include use of human taste deterrents in baits and revised label statements to limit the use of all commensal rodenticide from sensitive areas, including placement along fence lines, and bordering natural habitats.

Key Words: anticoagulant rodenticides, brodifacoum, bromadiolone, bromethalin, commensal rodents, efficacy, nontarget species, secondary poisoning, warfarin, wildlife hazards

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INTRODUCTION

Pest rodents cause extensive economic damage and risk to public health (Kaukeinen et al. 2000). The environmental impacts and economic costs in the U.S. have been estimated at $19 billion per year, far more than any other invasive animal species (Pimentel et al. 2000). As a primary control technique, rodenticides constitute about 60% to 80% of control purchases to manage these harmful species, with the remainder primarily for traps (USEPA 2006). Homeowners purchase about 40 to 50 million containers or placements of rodenticides yearly (Kaukeinen et al. 2000).

The characteristics of an ideal rodenticide are given in Table 1. The anticoagulants, as first developed in the 1940s with warfarin, have most closely met these characteristics and were significant improvements over less efficacious and more hazardous materials that previously were available (arsenic, strychnine, zinc phosphide, thallium sulfate, etc). However, the advent of genetic resistance to warfarin in the U.S. (Jackson and Kaukeinen 1972) resulted in control failures. Federally-funded studies of rodents from 30 states found warfarin resistance at significant levels in Norway rats (*Rattus norvegicus*) in 45 localities, house mice (*Mus musculus*) at 14 localities, and roof rats (*Rattus rattus*) at 4 localities (Jackson et al. 1985). This led to the development of more potent anticoagulants that would still retain the many advantages of the earlier anticoagulants: antidote, low doses, and delayed effect, while giving greater efficacy against warfarin-resistant rats and mice. In 1979, the first registration of a second-generation rodenticide product occurred in the U.S. with brodifacoum rodenticide; other similar materials followed (Table 2). The resulting so-called 'second-generation' anticoagulants (SGARs) provided greater efficacy than the first-generation anticoagulant rodenticides (FGARs) (Kaukeinen and Rampaud 1986). In particular, they were more effective against house mice, controlled rodents resistant to warfarin and other older anticoagulants, and were effective in limited feedings, which was helpful in controlling sporadically-feeding commensal rodents as well as limiting the duration that baits had to be exposed to achieve control (Kaukeinen et al. 2000). During the past three decades, the SGARs have been used to control commensal rats and mice in and around structures by homeowners, business personnel, and pest management professionals (PMPs). Issues of anticoagulant resistance and poor mouse control faded with the use of these advanced products.

Table 1. Characteristics of the ideal rodenticide.

Efficacious in small amounts	Non-cumulative
Palatable in baits	No plant uptake
Selective	Stable in baits
Low human hazard	Antidotable
No resistance	Registerable
Slow-Acting	Economical
Painless/humane	

Initial registration of the SGARs followed the submission of extensive data to the U.S. Environmental Pro-

Table 2. Second-generation anticoagulant rodenticides.

Compound	Date of Discovery	Discovering Company	Date of U.S. Introduction	Global Tradename Examples	Principal Manufacturers
brodifacoum	1975	Ward Blenkisop	1979	Talon/Klerat Final	Syngenta Bell Labs
difenacoum	1975	Ward Blenkisop	2007	Ratak	Sorex Woodstream
bromadiolone	1968	Lipha	1980	Maki Contrac	Lipha Bell Labs
flocoumafen	1984	Shell	Not Introduced	Storm/Strategem	Cyanamid
difethialone	1986	Lipha	1994	Generation Rodilon	Lipha Bayer

tection Agency (EPA), including on impacts to nontarget species. These data and subsequent submissions provided for use in and around structures for the control of Norway rats, roof rats, and house mice. The rodenticide products containing SGARs were assigned a 'Caution' Signal Word by EPA, and this lower-hazard classification allowed retail sales to homeowners and others without an applicator's license. To maintain the registration for commensal rodents, including brodifacoum use outdoors around agricultural buildings, extensive toxicological and other data were submitted, including environmental studies of barn owls (*Tyto alba*) around brodifacoum-treated farmsteads (Hegdal and Blaskiewicz 1984). Besides their global adoption for commensal rodent control, the SGARs found value in controlling rodents on islands for protection of nesting seabirds and other indigenous fauna. Registrations for SGAR products to control agricultural rodent pests in the U.S. were not pursued, based upon initial evaluations noting potential hazards (e.g., Merson et al. 1984, Hegdal and Colvin 1988). However, some non-U.S. uses against agricultural rodent species were undertaken (Kaukeinen and Rampaud 1986), and some overseas uses were extended to non-rodent pests in forests and other environments (e.g., Eason et al. 1996).

ENVIRONMENTAL CONCERNS

Concerns by individuals, groups, and EPA over possible effects of SGARs to nontarget species have been reviewed previously (Kaukeinen et al. 2000, Silberhorn et al. 2000). Anticoagulants accumulate in the liver, where they can be detected by analytical techniques. Interestingly, the limit of detection of the SGARs, and brodifacoum in particular, was commonly 0.05 ppm in research published in the 1980s, (e.g., Hegdal and Blaskiewicz 1984). By 2003, for brodifacoum and bromadiolone, it was 0.003 ppm (Stone et al. 2003), while for FGARs the methodology cited had detection limits 3 to 15 times less sensitive. This difference in detection limits may contribute to the greater number of 'SGAR-positive' samples without elucidating the role that this apparent contamination plays in the health of wildlife populations.

Nontarget carcasses were analyzed for anticoagulant residues by state employees in California and New York. Among the limited data cited in resultant publications (Hosea 2000, Stone et al. 1999), anticoagulant residues were found in about 60% to 80% in samples of 38 to 55 carcasses. A later paper (Stone et al. 2003) found anticoagulant residues in 49% of 265 raptor carcasses collected in New York. The EPA (USEPA 2007) cites their EIIS (Ecological Incidents Information System) database as containing information on these and additional unpublished incidents totaling some 400 cases of one or more rodenticides detected in carcasses of birds and nontarget mammals. These limited findings over a decade (upon which the greatest EPA concern appears based) compare to a national use during the same period of an estimated 160 million pounds of anticoagulant rodenticide bait used by professionals and approximately 70 million pounds of anticoagulant bait product used by consumers (calculations based upon data in Kaukeinen et al. 2000). It is arguable that the greater incidence of SGARs in the analyzed carcasses also is a function of market share, recognizing that the SGARs represent the majority of products sold to both consumer and professional users. It is undeterminable if these wildlife contamination findings arose from labeled product use, misuse or abuse, or use by consumers, farmers, or PMPs.

Increased attention to the SGARs and their consumer (homeowner uses) occurred during the re-registration and re-evaluation processes. Besides possible risks to wildlife, concern also was expressed by EPA regarding exposure of these rodenticides to children. The inclusion of a human taste deterrent in rodenticides, as described by Kaukeinen and Buckle (1992) was a positive step to help preclude ingestion of rodenticides by children. Bittering agents were added by some rodenticide manufacturers to all or part of their product line. Although the EPA initially sought to mandate the inclusion of a bittering agent (and an indicator dye) in all rodenticide products to reduce risks to children, EPA rescinded these requirements in 2001 (USEPA 2007); thus not all products today have a human taste deterrent or warning color. This action seems contrary to EPA's expressed concern about children.

As a result of a mandatory reassessment of older pesticides as required by federal statute (USEPA 1988), the EPA issued a Reregistration eligibility Decision (RED) document (USEPA 2003). This initiative included the anticoagulants, as well as the acute products zinc phosphide, cholecalciferol, and bromethalin (Table 3). Following public comment and the review of additional submitted information, EPA released a Revised Comparative Ecological Risk Assessment (RCA) for these nine rodenticides in September 2004 (USEPA 2004). EPA subsequently published the 'Proposed Risk Mitigation Decision for Nine

Table 3. Rodenticides subject to EPA Re-registration Eligibility Decision.

Anticoagulants	Non-Anticoagulants
Warfarin	Bromethalin
Diphacinone	Cholecalciferol
Chlorophacinone	Zinc Phosphide
Bromadiolone	
Difethialone	
Brodifacoum	

Rodenticides' in 72 Fed. Reg. 1992 of January 17, 2007 (USEPA 2007). During the period 1999-2007, besides the public release of written documents by federal staff (EPA, FWS, and others) on nontarget concerns, numerous participants provided opinions and information in meetings, testimony, and extensive submissions. This included state regulatory and environmental agencies, stakeholder groups, a rodenticide registrants' taskforce, individual registrants, and members of the public.

Since many meetings and communications were private, and the EPA does not publically respond to all inquiries or submissions, it is difficult to determine the basis for EPA's subsequent decisions. Low-level anticoagulant contamination in nontarget animals was accepted but its significance argued. Registrants were reluctant to support speculative and complex studies beyond the basic requirements under FIFRA in support of decades-old, off-patent chemistry. This was particularly true in the absence of compelling evidence that restricting SGARs was necessary for human health or preventing wildlife hazard. Regulators cited lack of data to determine which use patterns of rodenticides were contributing to nontarget wildlife exposure, and to understand whether the contamination seen in the small samples available was deleterious. They sought information on determining where poisoned commensal rodents go to die (critical to the question of whether an 'indoor use only' restriction would have value) and were cautious in accepting any proposed alternate label language or user education programs. Without a clear cause/effect understanding, regulators favored SGAR restrictions and increased use of FGARs and acute rodenticides, apparently in hope that some wildlife effects and human exposure would be curtailed.

EPA PROPOSED MITIGATION

The mitigation measures proposed by EPA (USEPA 2007) are:

1. To minimize children's exposure to rodenticide products used in homes, EPA would require that all rodenticide bait products available for sale to consumers be marketed only in tamper-resistant bait stations with solid bait blocks.
2. To mitigate ecological risks, EPA would classify all bait products containing the active ingredients brodifacoum, bromadiolone, and difethialone as restricted use pesticides, available for purchase and use only by trained, certified pesticide applicators or persons under their direct supervision.
3. For all rodenticides under review, EPA would require that labels provide clearer direction on rodenticide use while minimizing potential exposure to children, wildlife, and pets.

This paper challenges the basis of these EPA proposals and considers their impact on the future of rodent control by both professional and retail users. A final decision by EPA is pending and has not been issued as of March 2008.

Bait Station Use

The EPA in its Proposed Risk Mitigation Decision (PRMD) notice (USEPA 2007) is seeking to require that above-ground uses of all retail rodenticides be within tamper-resistant bait stations, and all formulations for such uses be bait blocks (as compared to pellets, grain baits, or place packs). Current labels on retail rodenticides direct users to apply the bait in locations inaccessible to children, or in tamper-resistant bait stations. However, EPA has concluded that these instructions are not sufficiently effective and that more stringent requirements are needed. Stations may also be mandated with some products for professional users. The EPA has stated: "Refillable tamper-resistant bait stations (baited with bait blocks) would be required for outdoor above-ground placements of second-generation anticoagulant baits used by PCOs and other certified operators" (USEPA 2006).

The EPA acknowledges that their review of the American Association of Poison Control Centers (AAPCC) data of yearly rodenticide exposures to children shows only a small number experiencing medical symptoms or suffering adverse health effects, but states there is "emotional toll and unacceptably high social costs" (USEPA 2007). The use of bait stations is also proposed to reduce hazard to household pets.

Bait Station Limitations

EPA proposes that unlicensed users only have access to rodenticide block baits inside bait stations, such as for use in and around dwellings. Normal infestations of rats and mice include burrows, and burrow baiting is one of the most effective and least hazardous methods for rat control. The inability to place bait in rodent burrows will impede control. Work by Quy et al. (1996) noted that even less-palatable rodenticide formulations could control local rat infestations if placed in burrows, while the same baits in above-ground containers were not readily consumed when alternate food was available. They determined that the method of bait application was one of the most important factors in whether or not treatment was successful.

The stakeholder group assembled by EPA in 1999 to review issues, including mandatory use of bait stations, rejected the requirement that all products be sold in tamper-resistant bait stations (Silberhorn et al. 2000). The stakeholders group consisted of 25 members including governmental agencies such as the Centers for Disease Control, the Consumer Product Safety Commission, and others. Consumers have very limited experience in using rodenticide bait stations and will experience control limitations in attempting to use these new products. Station use will result in delayed control, which will be less acceptable when quick control is needed when rats

and mice are inside a dwelling and posing a risk to residents. Rodents, especially rats, exhibit neophobia that can keep them from entering bait stations, even when placed near well-travelled areas. The delay to enter can extend to weeks, based on replicated studies (Kaukeinen 1987) that showed the extent of delay was related to the degree of tamper-resistant features such as inner baffles. Delays with mice are more related to placement than to station design, with poor placement causing significant delays (Morris and Kaukeinen 1988).

Mixed infestations of rats and mice can be present in residential situations. The use of mouse-sized stations in a rat infestation can result in stations gnawed open by rats to reach bait. This event usually exposes bait and leads to loss of the station's tamper-resistant characteristics. The cost of bait stations for rats in the U.S. professional market is currently from about $7 to $15 each, in multiple quantities, sold without bait. It is expected that any consumer-use stations sized for rats, individually sold and filled with bait, may sell for about $20 each, making even one station prohibitively expensive to most consumer purchasers, especially in economically disadvantaged areas. The EPA (Jacobs 2000) published an opinion that the tamper-resistant station option for consumers was less viable for rats than for mice. The proposed bait stations with block bait for consumers would be of the 'tamper-resistant' variety but might not require fastening down per published design criteria (USEPA 1983) and labeled use patterns by PMPs. This reduction of the tamper-resistant standard, in recognition that it would not be desirable to nail, screw or glue bait stations to floors and other interior household surfaces, would seem to jeopardize the original intent of secure stations, allowing them to be dislodged and manipulated by children or pets.

No design criteria for consumer bait stations have yet been released by EPA to accompany the PRMD. Tamper-resistant bait stations as used by PMPs are made by manufacturers in a variety of sizes and designs, principally in rigid plastic, but are sold empty (typically in case quantities with minimal packaging). Because prefilled stations require efficacy testing, child and dog resistance testing, and registration (Jacobs 1990), there are no known current examples of such station products sold to consumers that can be used around children and pets. The empty stations currently marketed to PMPs may not be suitable for consumer use because they are designed for industrial applications with different criteria for size, strength, and serviceability.

Proper design of bait stations can be critical to their performance in controlling pest rodents. Mice prefer larger stations (Volfova and Stejskai 2003), but many retail manufacturers will undoubtedly feel compelled to keep mouse stations as small as possible to conserve "shelf space" (which is at a premium and competitively allocated in retail stores) and to reduce costs; this could further limit their effectiveness. Corrigan and Collins (2004) noted that a difference in height of stations could affect entry and feeding by mice by 15%-18%. Such differences can be significant with baits requiring multiple feedings (i.e., FGARs).

Retail manufacturers previously have explored consumers' responses to stations and voluntarily introduced several prebaited mouse station products, including those with tamper-resistant features. When sold adjacent to simpler and cheaper packaging, none of these attempts (American Cyanamid Combat™ station, Sherman Tackle station™, d-CON® Mouse-Killing Station) have met with sufficient consumer acceptance that allowed for sustained sales (Kaukeinen 1994, Jacobs 2000). Currently, prefilled mouse stations that are not tamper-resistant are sold by the Motomco and the Atlantic Past and Glue companies as retail products, but these are not tamper-resistant designs and labels clearly state to "keep out of reach of children." It is not known if they would meet all or any of the EPA's ultimate criteria for consumer stations.

There is no information that establishes that consumers can successfully place, bait, inspect, monitor, clean, and service bait stations as needed to ensure they are effective in use, even if the stations are placed in optimum protected active areas. PMPs normally have policies of changing bait on a monthly basis to keep it fresh and to remove moldy or decayed baits. Refillable tamper-resistant stations typically have locking mechanisms and require special keys to open. The EPA proposal contains ambiguity but seems to propose that consumer stations may be sold with additional bait blocks to allow for refilling (which seems to necessitate a 'refill pack'). If stations can be opened for refilling, then bait can become contaminated, infested with arthropods, or exposed to nontarget animals, if care is not taken. If disposable station designs are produced, then there may be limited ability to assess the condition of the bait or need for replacement of the unit.

Because of increased costs associated with bait stations, consumers may not purchase enough stations to achieve control, particularly if the active ingredients are FGARs and thus require more bait use due to low efficacy. The thigmotrophic and nocturnal behavior of commensal rodents lead them to orient movement to dark, hidden areas where station placement is difficult but essential. Utility passageways commonly are used by mice within structures, including at high, hard-to-reach, and narrow locations non-conducive to bait station placement. Thus, requiring use of bait stations creates a situation whereby consumers no longer can financially or physically match the distribution of mouse infestations within a structure or the methods needed to control mice. While EPA believes that professionals can better use second-generation products if called upon by householders, many PMP companies have a policy to not place rodenticide bait inside homes, due to liability reasons, privacy concerns, and the impracticality of gaining regular access for servicing.

Wax Block Formulations

In terms of hazard reduction, the EPA's stated preference for wax blocks is based on the argument that they can be better held within bait stations and will reduce spillage over other formulation types such as pellets. However, wax block formulations that contain whole grain or portions of grain stimulate rats and mice to gnaw the block apart to consume the grain particles, leaving toxicant-containing particles loose that can fall out of stations and be exposed to nontarget animals. Formulations containing whole grain also can swell with moisture and break apart. There are no EPA requirements of manufacturers to avoid

inclusion of whole grain particles in wax block formulations versus finely-ground grain ingredients. Paraffin formulations may also delay absorption of the active ingredient in the pest after bait ingestion, and allow more active ingredient to pass through the body and be excreted in feces, which could present increased environmental risk.

The size difference of wax blocks versus other formulations is also of concern regarding nontarget species. Wax block products currently on the market are generally at least 20 grams (¾ ounce) in size, versus pellets that are typically only a fraction of a gram each in weight. Relocation of a single block from the point of placement presents a more serious exposure and nontarget issue than a few pellets. Blocks more closely resemble candy and other food, and are much easier for a small child or pet to pick up and place in their mouth than a small pellet or bit of seed or meal bait. If bait stations are to be refilled by consumers, the block refills will be unprotected from the time packaging is opened until blocks are secured inside a station (assuming the blocks are not used in an exposed manner).

Wax-block baits were developed for use in outdoor, moist situations such as sewers, drains, and burrows. Typically these formulations require from 20% to 40% wax to maintain sufficient weatherability and hold grain ingredients together. Putting weatherable wax sewer and drain-type bait inside a protective bait station and building is not a logical match of product to application. Paraffin wax is not inherently palatable to pest rodents and can result in less efficacious baits. Rodent infestations develop because of an availability of food materials in the area, and block baits may not perform well when alternative foods exist.

Because wax has no intrinsic taste or palatability to pest rodents, it acts to mask or dilute food content and related flavors, sweeteners, and odors. While SGAR actives work reasonably well in wax-block baits, given their single-feed properties, the FGARs will perform poorly in comparison, because of low palatability combined with the need for repeated feedings to ingest a lethal dose. The wax content of block formulations complicates the addition of many formulation ingredients, as well as making analytical results (e.g., quality control) far more difficult in recovering active or additives (such as bittering agents, insecticides or mold inhibitors). Few block products have ever been marketed that contain zinc phosphide, cholecalciferol, or bromethalin. Most active rodenticide ingredients besides anticoagulants are not amenable to incorporation in wax formulations; acute products may not be stable in the high-temperature processes that produce wax block products or may be rendered inefficacious.

Restricted Use Classification

In an attempt to mitigate ecological risks, EPA would classify all bait products containing the active ingredients brodifacoum, bromadiolone, and difethialone as restricted use pesticides, available for purchase and use only by trained, certified pesticide applicators or persons under their direct supervision. These SGAR products currently are assigned to a general use category after registrants provided extensive toxicological, environmental, and other data. Normally, classification as a Restricted Use Product (RUP) status occurs when initial data indicate that the dermal, oral, or inhalation toxicity with key indicator species is expected to cause injury or death with small amounts that could be encountered in a limited exposure. Other triggers include fetotoxicity (adverse effects on the fetus), mutagenicity (genetic changes in an organism), oncogenicity (causing tumors), teratogenicity (causing birth defects), or materials judged likely to lead to problems of food, crop, or water contamination. The SGARs have not been demonstrated to fall into any of these categories during 30 years of use.

There are few RUP products currently sold in the PMP arena, principally only some termiticides and fumigants. The use of RUPs requires additional work, expense, and liability for certified applicators in terms of purchase, storage, transport, handling, use, reporting, and disposal. RUPs must be stored by PMP companies in a room that is structurally separated from working or living areas. A change to RUP status may change the reportable quantity and limit shipping by some common carriers. It may also complicate emergency planning, notification, and response. Many states require each RUP applicator to be personally certified, rather than working under the supervision of a licensed applicator as for general use pesticides. This will prevent many PMP companies with hundreds of technicians commonly working under a supervisor's certification, such as Orkin, from effectively conducting rodent control with SGAR products (F. Meek, Orkin, pers. commun. 2007). Many customers and sites are not expected to allow use of RUP products, particularly inside buildings.

Limitations of First-Generation Anticoagulant Rodenticides

The FGARs have limited efficacy to commensal rats and mice. In a review of available published data, Greaves (1985) questioned the suitability of warfarin as a rodenticide against 8 species of rodents, including the roof rat and house mouse. House mice have a naturally low susceptibility to not only warfarin, but to other FGARs such as diphacinone (Prescott 1996). This means that consumers using FGARs per the EPA proposal would have to make more bait placements and use more rodenticide to achieve control, in comparison to SGARs with higher efficacy and single feeding capability. As a result, the amount of bait used and duration of potential exposure to nontarget animals and children would be greater, especially if genetic resistance was present. Concurrently, because of lower efficacy and bait station use, the period of human exposure to public health risks from rodents would likely be extended.

The EPA has argued that because FGARs presumably pose less risk to wildlife, they are more appropriate for use by consumers. No adequate field evaluations have been conducted to examine the hazards to predators and scavengers from the use of FGARs, and published analyses of wildlife carcasses recoveries do not use methodology that is as sensitive as that used for SGARs, possibly masking FGA-positive samples. The fact that studies (for example, Hosea 2000) have found examples of both first- and second-generation anticoagulant residues in wildlife suggests that some wildlife exposures (whether from labeled or off-

Table 4. Tests of warfarin-resistant rats and mice with warfarin and brodifacoum baits.

Test No *	Formulation	Resistant Strain	Test Period	Mortality	
				males	females
GB01-05-R022	250 ppm Warfarin	House mouse	21 days	4/5	0/5
GB01-05-R023	250 ppm Warfarin	Norway rat	6 days	3/5	1/5
GB01-05-R024	50 ppm Brodifacoum	House mouse	2 days	5/5	5/5
GB01-05-R025	50 ppm Brodifacoum	Norway rat	2 days	5/5	5/5

*Reading University (UK), Rodent Lab Test results from 2005; see Kaukeinen and Prescott (2006).

label use) have occurred, even though these products are far less used at present for commensal rodent control (but are common products for control of agricultural rodent pests). As the market-share of FGARs increases, because of the EPA proposal, proportional increases in wildlife contamination from FGARs are likely to occur.

FGARs have been registered based upon different efficacy requirements than those for the SGARs. The older materials, such as warfarin, chlorophacinone, and diphacinone, typically are tested using protocols exposing the test animals to 15 to 21 days of feeding, and such methods require minimum palatability figures in addition to mortality minimums. This lengthy exposure and the resulting mortality in the laboratory gives a misleading impression of efficacy for such products when compared to what should reasonably be expected in field use, where rodent consumption of baits is limited and sporadic. The SGARs are registered upon passing efficacy testing of only a 24-hour choice exposure, with no minimum palatability required because of the limited intake needed for a lethal feeding.

A theory cited by the EPA in support of continued use of warfarin or other FGARs involves repetitive feeding studies with wild resistant Norway rats in the laboratory and noting some mortality upon no-choice re-exposure to warfarin (Frantz and Madigan 1998). The resulting lab mortality was only 14%-18% for rats from a Chicago resistance site, which would hardly be advantageous if the same results were obtained against field populations. Lab tests with wild-trapped rats from mixed locations found 60% to 83% mortality with re-testing after 1 to 6 months of holding time. There is little practical application of such findings to the field, where rodenticide application cannot be phased or presented without competition from alternative foods. Studies have shown that if field control efforts do not produce at least 90% kill of rats, their numbers can quickly rebuild (Kaukeinen et al. 2000).

FGARs are problematic for use against wild rat and mouse infestations today, given that the resistance-conferring genotype is still widespread. Studies in Chicago involving tests of rats trapped in resistance areas showed that the incidence of warfarin resistance of 67% observed in the 1970s was 85% a decade later, although warfarin was no longer being used (Jackson and Ashton 1992). Studies in Boston with Norway rats captured in utility manholes revealed an incidence of warfarin resistance in feeding tests in 13.6% of one sample, and in 17.8% of another, although no sewer baiting program involving warfarin had been conducted previously (Colvin et al. 1998). Surveys of anticoagulant-resistant rats in England and Wales during 1988-1995 found a high prevalence of resistance to warfarin remaining in several regions after widespread use of other products, but did not find evidence of resistance to brodifacoum (MacNicoll et al. 1996). No resistance has been noted anywhere in the world to the widely used products containing brodifacoum, after more than two decades of continued use (Corrigan 2001).

Recent tests (Kaukeinen and Prescott 2006) revealed that a currently available warfarin rodenticide product in the U.S. achieved an unacceptably low level of mortality with warfarin-resistant rodents, despite the prolonged test periods of 21 days of no-choice feeding for mice and 6 days for rats (Table 4). Mice survived exposures to 15 to 26 times the expected lethal dose, and rats survived from 33 to 55 times their expected lethal dose of warfarin, indicating high levels of resistance that would not be addressed by continued use of FGARs. Against the same strains of resistant rats and mice, a brodifacoum rodenticide product achieved complete mortality against both resistant species in a 2-day test.

Characteristics of Acute Rodenticides

The EPA has proposed that acutely toxic rodenticide products could be used in place of, or in rotation with, anticoagulant rodenticides to avoid further development of anticoagulant resistance. Acute rodenticides are more rapid acting and with profound effects on body systems that can lead to such outcomes as paralysis, heart failure, and kidney failure before death. Faster acting acute rodenticides typically produce bait shyness (feeding avoidance) in sublethally poisoned rodents. This phenomenon has been noted for cholecalciferol (Prescott et al. 1992) and zinc phosphide (Marsh 1987). Quy et al. (1998) found that wild rat populations with high levels of anticoagulant resistance were not effectively controlled with use of calciferol and zinc phosphide baits.

Anticoagulants have been studied in rats through monitoring of nervous system responses, and clinical signs of pain or distress from delayed internal hemorrhage, the primary cause of death, were not shown. Conversely, tests with products causing acute symptoms and paralysis were judged inhumane (Rowsell et al. 1979).

The EPA proposal would shift risks associated with anticoagulant rodenticides to risks associated with alternative products, some of which do not have a specific antidote if consumed by a child or pet. The FGARs and SGARs have an established antidote, vitamin K; they also have a distinctly delayed effect before onset of symptoms which allows for timely treatment of a nontarget animal. Non-anticoagulant rodenticides such as zinc phosphide, cholecalciferol, and bromethalin do not have specific antidotes and are fast acting.

Potential Hazards to Companion Animals

Reports in the U.S. of secondary poisoning to pets from SGARs do not figure in the veterinary literature (Murphy and Gerken 1986, Corrigan 2001), yet dogs and cats represent a far more likely scenario in being exposed to poisoned commensal rodents than wildlife. The toxicity of SGARs to dogs has been variously reported, and the most robust study puts brodifacoum as comparable in toxicity (LD_{50} of 3.56 mg/kg) to the other SGAR products with regard to canines (Godfrey et al. 1981). Diphacinone, a FGA rodenticide which would not be restricted under the EPA's proposal, is as toxic to canines as some SGARs, and cats and dogs are highly susceptible to the effects of the acute rodenticide cholecalciferol, which at 750 ppm is from 15 to 30 times more concentrated than the SGARs (Corrigan 2001).

Bromethalin, an acute rodenticide that would not be restricted under the EPA proposal, is highly toxic to dogs, with the LD_{50} between 2.4-5.6 mg/kg, and cats are even more sensitive (Dunayer 2003). Reports by the National Animal Poison Center of the Humane Society of the U.S. note that bromethalin is now the most common active ingredient involved in poisoning cases of household pets (Khan and Farbman 2005, 2006). This potential for adverse impact to household pets is expected to increase with wider use of bromethalin products.

ALTERNATIVES TO RODENTICIDES

EPA believes that traps and glue boards serve as effective alternatives to SGAR products. As unregulated products, there is currently no labeling required to help direct effective use and to minimize nontarget hazards, particularly for untrained users (consumers). A considerable biohazard exists from exposure to trapped rodents. Traps are not discriminatory and their outdoor use may catch protected and desirable animals, including small birds that may be common around building perimeters and associated landscaping.

Trap shyness is common in rodents. Rats and mice remember near misses or injuries from traps, sticky surfaces, and adhesive odors, thus resulting in trap avoidance (Corrigan 2001). Traps of different types vary greatly in effectiveness. Glue traps commonly are rendered ineffective in a few days from dust and dirt, and are not effective for rats (Corrigan 2001). Corrigan (1998) found that snap traps were about seven times more effective than glue traps in capturing house mice; enclosing glue traps reduced their efficacy further. Glue traps also can have limited utility because of humaneness concerns (Frantz and Padula 1983).

Ultrasonic and electromagnetic devices are sold to consumers, but testing has shown they are ineffective for rodent control (Howard and Marsh 1985). There are no rodent chemosterilants that are commercially available, and sterile rats can still cause property damage and bite children. The polygamous nature of rat populations means that low numbers of fertile males and females can still maintain significant population levels, and thus proposals to use chemosterilants for urban rodent control are unrealistic.

RECOMMENDED FURTHER LABEL REVISIONS

Commensal rodenticide labels (for both consumer and professional products) presently contain precautionary statements, such as: "Caution – may be harmful or fatal if swallowed", "This product is toxic to birds, fish and wildlife", "This product can pose a secondary hazard to birds of prey and mammals", "It is a violation of Federal law to use this product in a manner inconsistent with its labeling", "Do not expose children, pets or other nontarget animals to rodenticides", "To help prevent accidents: Apply bait out of reach of …nontarget wildlife or in tamper-resistant bait stations", "Dispose of unused, spoiled and unconsumed bait", "For use in and around structures", "Do not apply in water", and "Do not broadcast bait". However, these statements do not preclude rodenticide use in many locations that create nontarget risk. The selection of treatment areas on most product labels is limited to locations where rodents will find and consume the bait in and around structures.

Regulators should consider and evaluate the utility of adding further clarifications and specific use restrictions to existing rodenticide product labels. Such clarifications could preclude use of all products and active ingredients in areas that could cause nontarget exposures. Possible statements would include: "Do not apply in landscaped areas away from buildings where nontarget animals may feed on the bait", "Not for use in parks and open areas or edge areas along such open areas", "Not for use in hedges, along streams and creeks, ditch banks, along crops, gardens, or around fruit or nut trees", "Do not bait outdoor compost piles", and "Do not use along fence lines or facility perimeters bordering fields and woodland." These restrictions would eliminate many problem areas where use of any rodenticide could cause wildlife exposure.

Label restrictions to reduce hazard to nontarget animals should equally include products used by consumer (homeowner) and professional users. Although the EPA mitigation proposals suggest that homeowners' application practices are the source of inadvertent exposures to nontarget animals, there is no evidence to support this assumption. PMPs place and maintain a far greater quantity of rodenticides along building perimeters and fence lines, particularly in commercial accounts, and must share the risk of nontarget exposure and the responsibility of reducing hazard. The widely-used practice of sustained baiting along fence lines and building perimeters should be challenged. Such efforts could be replaced by use of non-toxic census bait and traps in bait stations. Limiting areas for rodenticide use for all users and all products seem appropriate.

SUMMARY AND CONCLUSIONS

The urban trend in the U.S. has been toward expansion, more congestion, abundant food establishments, reduced sanitation, aging infrastructure, and economically-depressed neighborhoods. It has become prohibitively expensive for municipalities to address, in any organized fashion, the many factors that contribute to a growing rodent problem in many U.S. cities, a problem that is predicted to progressively worsen during the 21st Century (Colvin and Jackson 1999). The burden will fall on residents to maintain their personal well-being, with whatever tools are at their disposal.

While sanitation and exclusion are useful preventative measures, it is not feasible for individual homeowners to make neighborhood-wide improvements to limit rodent pressures. Surveys have indicated that greater than 50% of homeowners do their own pest control (Kaukeinen 1994). Products containing the SGARs have become the most successful in both the retail and professional markets because of their superior efficacy. PMPs and municipal workers do not normally bait inside

homes, due to liability concerns and access limitations. PMPs are expected to limit their use of SGARs because of RUP product requirements, leading to a further decline in rodent control and more selection for resistance to the FGARs.

Risks from rodenticides must be balanced in view of the well-documented and significant risk to public health and property from rodents. A proposal to reduce risks from rodenticides should not create parallel risks to public health. The proposals by EPA will bring some renewed emphasis on older anticoagulants that were less effective in protecting public health in the 1960s-1970s. Resurgence in using those compounds will lead to efficacy problems because of genetic resistance, the need for multiple feedings for FGARs, and the limitations created by only allowing consumers to use wax-block baits in bait stations. The biological principles of rodent behavior and control, well established over the past 65 years, must be fully considered in any risk management strategy.

Increased national risk to the public health from ineffective rodent control would include risk to children from rodent-borne disease and rat bites, and greater exposure to products without antidotes. Human taste deterrents have been successfully incorporated in rodenticide formulations and offer a positive step in reducing child exposure, yet this approach has not been mandated by EPA. The EPA proposals also will shift nontarget hazards in homes to products/formulations that can have equal or greater risk to companion animals. Similarly, wildlife risk and impact will be shifted to the products that acquire a greater market share, in the absence of changes in use patterns.

It might further be predicted that within the span of two decades, the failures to control commensal rodents by consumers and PMPs alike, and the associated increases in genetic resistance and public health problems (as widely observed 40 years ago) will require a return to second-generation anticoagulant rodenticides.

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