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Rats! Foiled Again: A History of Rodent Control Methods Development at the National Wildlife Research Center

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ABSTRACT: The National Wildlife Research Center (NWRC) and its predecessor laboratories have a long history of developing materials and methods for managing rodents and the damage they cause. The NWRC has been influential in exploring, developing, and maintaining legal uses of many traditional field rodenticides such as strychnine and zinc phosphide. Products have been developed for managing rodents in a variety of locales, and for managing a variety of species, from commensal rodents in urban areas, to pocket gophers and mountain beaver in forests, prairie dogs and ground squirrels on rangelands, and nutria and beaver in wetlands. Considerable research has also been conducted on developing methods of managing rodents in underdeveloped countries. Recent efforts by NWRC have focused on development of tools for managing invasive rodents in conservation areas such as island ecosystems and development of alternative, nonlethal control methods.

KEY WORDS: attractants, barriers, damage, history, marking agents, methods, repellents, reproductive inhibitors, rodenticides, rodents, traps, USDA

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INTRODUCTION

The National Wildlife Research Center (NWRC) is the research arm of USDA's Wildlife Services program and is the federal institution devoted to resolving problems caused by the interaction of wild animals and society. The mission of the NWRC is to apply scientific expertise to resolve human-wildlife conflicts while maintaining the quality of the environment shared with wildlife. NWRC develops methods and information to address human-wildlife conflicts related to agriculture, human health and safety, property damage, invasive species, and threatened and endangered species. Efforts to develop methods to manage rodent problems have been an important part of the Center's program. A primary objective of the NWRC has always been to transfer information and technology to user groups, and particularly to the private industry. However, after materials or methods are developed, transferred, used, manufactured, or sold by others, their origination in NWRC's research effort has sometimes been forgotten.

The history of the NWRC reflects a consolidation of many early U.S. Biological Survey programs. Between 1935 and 1938, the Bureau of Biological Survey had a rodent field station in Hilo, Hawaii. In 1940, the Control Methods Laboratory of the Division of Predator and Rodent Control was combined with the Denver Unit of Food Habits Research to become the Denver Wildlife Research Laboratory. At this time, the Biological Survey was transferred from the Department of Agriculture to the Department of the Interior. In the 1950s, research was expanded to include wildlife on public lands, wetland ecology, and migratory birds, and in 1959 the Laboratory was renamed the Denver Wildlife Research Center (DWRC). In the mid-1960s, when a program on pesticide ecology was developed within the Center, research on the effects of rodenticides on non-target wildlife received increased

emphasis. An extensive international research program on control of damage by vertebrate pests began in the late 1960s in cooperation with the Department of State's Agency for International Development (Cadieux 1969). Much of that research focused on reducing the losses to crops and food supplies caused by rodents in developing countries. In late 1985, the Center and its research functions related to wildlife damage management was moved back to the U.S. Department of Agriculture, and research was focused on development and maintenance of methods for the resolution of human-wildlife conflicts.

The NWRC has conducted research on management methods for more than 35 species of injurious and nuisance rodents, ranging from species identification, identification of damage they cause, biology and ecology, control methods and materials, hazard assessment, and management strategies. Throughout its history, the NWRC and its predecessor laboratories have worked closely with numerous partners, including other units within Wildlife Services, universities, other government agencies, non-governmental organizations, foreign agencies, and private companies. Most of the development of the tools, techniques, and materials we discuss has been accomplished in partnership with these other individuals, firms, and agencies.

A particular emphasis of the Center's research through most of its history has been the development of minor use pesticide materials, including those registered mostly for specific field rodent control. Because of improvements in technology and materials, increasingly stringent regulatory requirements for pesticides, and the disappearance of unprofitable or environmentally hazardous compounds from the marketplace, research has been a continuous effort to find better, safer, more effective, and environmentally benign control techniques.

Our goal in this paper is to provide an historical in-

roduction to the contributions of the NWRC in the continuing global battle against rodents that cause economic damage or other problems of public concern. We have cited a considerable amount of accessible rodent control literature published by our colleagues to provide an overview to the history of rodent control research by the NWRC. Many of the early studies, as well as much of the international research conducted by the Center, are reported in unpublished papers – a common practice in the period when the few zoological journals tended to have limited interest in applied research. These papers, as well as published materials, can be found through the NWRC Library's searchable on-line catalog; details of pesticide registrations mentioned are found under NWRC's Technology Registration Unit, both at http://www.aphis.usda.gov/wildlife_damage/nwrc. In recounting the Center's role in the developmental history of rodent control materials and methods, we do not intend to diminish the important research and innovation by our friends and colleagues in other institutions. We cite minimal material published by others, for reasons of volume.

SPECIES IDENTIFICATION

Correct species identification is often the first step in problem resolution because differences in behavior and physiology among rodent species can be important in development of management methods. Particularly in international work in rodent damage control, Center scientists and counterparts collected animals and identified or sought identification by taxonomic experts. Publications documenting this effort and the methodology involved include Barbehenn et al. 1972 (Philippines), Woronecki 1973 (Colombia), Wurster and Atwell 1973 (Philippines), Hirata 1977 (Hawaii), Poché 1980 (Bangladesh), Ahmad et al. 1988 (Pakistan), Elias and Fall 1988 (Latin America), Fiedler 1988a,b (Africa), and Brooks et al. 1992 (Chad). From 1980 to 1986, personnel and facilities of the National Fish and Wildlife Laboratory were incorporated into the DWRC (now NWRC). During this period, biologists at the Center's Gainesville Field Station developed a list of vertebrates of the world; this was the beginning of a project addressing the need for an up-to-date checklist of mammals because of the Convention on International Trade in Endangered Species of Wild Flora and Fauna (CITES). The result of this project and its many collaborators was the publication *Mammal Species of the World* (Honacki et al. 1982). Now in its third edition (Wilson and Reeder 2005), this reference remains the most authoritative sourcebook for determining rodent identification and distribution worldwide.

DAMAGE ASSESSMENT

Regardless of methodology, rodent control is of little value unless it results in a reduction of damage. Much of the Center's rodent research historically and at present has focused on reducing damage to agricultural crops and forests. An important piece of that research program has been developing loss estimation methods for crops and forest protection, stored products, communication cables, and infrastructure protection. Once developed, the methods can be used to determine the overall importance of losses or to evaluate the effectiveness of control programs. More

recent research has focused on assessment of the importance of rodent-borne disease and rodent predation on rare or protected species. Details of loss assessment methods are often included in papers that address the development or evaluation of control methods or unpublished reports or training materials produced for user groups. Important Center publications include Guerro 1971 (rice), Hood et al. 1971 (sugarcane), LaVoie et al. 1971b (rice), West et al. 1975a (rice), Sanchez and Reidinger 1980 (rice), Poché et al. 1981 (rice), Poché et al. 1982 (wheat), Haque et al. 1985 (sugarcane), Ahmed et al. 1986 (deep water rice), Samedy et al. 1986 (corn), Sugihara 1990 (sugarcane), and Tobin et al. 1997a (macadamia). Because of the variability in damage indices, which often greatly underestimated yield loss, investigators developed estimation methods and emphasized actual yield loss for evaluating the effectiveness of control methods, including Fall 1977 (rice), Reidinger and Libay 1980, 1981 (coconut), Fiedler et al. 1982 (coconut), Sultana et al. 1983 (wheat), and Haque et al. 1985 (sugarcane).

POPULATION ASSESSMENT

NWRC scientists have worked on a variety of methods of rodent population or density estimation relying on animal capture (e.g., Libay and Fall 1976, Otis 1980, LeFebvre et al. 1982, Anderson et al. 1983, Benigno et al. 1983, and Matschke et al. 1983) and used the information in to evaluate rodent control methods. However, in many situations changes in population activity indices have provided a more practical way to assess the effectiveness of control methods, particularly in crop fields. Such assessments are easier and have less impact on crop production, damage patterns, or animal behavior. Important papers related to developing or using a variety of such methods include Swink et al. 1972 and West et al. 1972a (damaged rice tillers), West et al. 1972a,b and West et al. 1976 (tracking tiles, trap success), West et al. 1975b (bait consumption and CCTV observation), Kolz and Johnson 1976 (time and frequency of visits), Brooks et al. 1992 (tracking tiles, trap success), Engeman et al. 1997 (closed burrows, trap success), Engeman et al. 1999 and Engeman and Campbell 1999 (open hole method), Engeman 2005, Whisson et al. 2005 (chew cards, monitoring blocks, and track plates), and Arjo et al. 2004 and Engeman and Whisson 2006 (index methods).

RADIOTELEMETRY EQUIPMENT AND TECHNIQUES

During the 1960s and 1970s, large wildlife transmitters were being manufactured by commercial companies but miniature transmitters for use on rodents were not available. To collect information on the movements of small mammals and birds and to evaluate the effect of control applications, NWRC engineers developed specialized expertise in the manufacture of miniature radio transmitters and for uses on marine animals (Dodge and Church 1965, Corner and Pearson 1972, Kolz et al. 1972, 1973). Telemetry has been used by Center scientists for a variety of unique methods development problems (Nass et al. 1971 and research continued to make field applications of telemetry equipment more practical (Kolz and Johnson 1975). Scientists also worked to develop practical radio-

collar attachment mechanisms for mammals and birds. An example of one of the many innovations developed by researchers was development of a radio-collar fastener for a small rodent; previously a collar had to be tuned in the field, on an anesthetized animal, by soldering, but the use of plastic fasteners changed the attachment process to one of a few seconds (Fall et al. 1972). NWRC engineering staff designed, built, and evaluated miniature transmitters for researchers and worked with commercial companies to assure quality materials were available, until the mid-1990s when use of radio transmitters had become a routine part of rodent damage control research. NWRC researchers have continued to evaluate improved methods for transmitter use, recently including use of implantable units for use with subterranean rodents (Witmer and Pipas 1999).

CHEMICAL SCREENING

Between 1943 and 1987, thousands of chemicals were evaluated by the DWRC and the Patuxent Wildlife Research Center (up to 1959) for their potential use in preventing wildlife damage to agriculture, forest resources, packaging materials, and other uses. Various cooperators, including the U.S. Army Chemical Corps' Natick Laboratories for rodenticides, the U.S. Army Quartermaster Corps for repellents, and the U.S. Army Electronics Command for ground-laid wire protectants, as well as a number of chemical or pharmaceutical companies, submitted candidate materials or unidentified compounds for testing. Tigner and Besser (1962) described procedures for evaluating packaging repellents. Tigner and Landstrom (1968) summarized results of some 12,000 chemicals tested as packaging repellents. Kverno (1970) and Lindsey (1977) described the general testing methods involved for determining rodent toxicity and repellent effects. Schafer and Bowles (1985) reported results for nearly 1,000 materials screened for toxic or repellent activity for mice. Engeman et al. (1989) further refined the statistical procedures used in repellent testing. These historical studies led to the development of new chemical management tools, a number of which became commercial products, and now provide valuable information for scientists involved in environmental risk management. The NWRC's "Chemical Effects Database" contains approximately 11,000 published bioassay records and data for over 2,000 chemicals analyzed and evaluated for toxicity to animals and plants, repellency, immobilization, and reproductive inhibition. Much of the information from those studies has been published and the Chemical Effects Database can be accessed on the NWRC web page http://www.aphis.usda.gov/wildlife_damage/nwrc/index.shtml.

RODENTICIDE DEVELOPMENT

For several decades, the DWRC (NWRC) and "rodenticide development" were almost synonymous. Some chemicals from the screening program or from related cooperative work were developed commercially as rodenticides and NWRC scientists were extensively involved in investigations to validate or improve formulations, determine effectiveness on various problem rodent species, describe hazards to non-target species, and develop methods for chemical analysis. Personnel have worked closely with pesticide registration agencies (first the U.S. Depart-

ment of Agriculture, then the Environmental Protection Agency [EPA] after 1970) to develop test methods and registration data. Although NWRC and Wildlife Services personnel have been involved in extensive field testing of these many materials, our focus here is primarily to introduce the methodological studies related to investigations of new materials and the development and maintenance of registrations for prominent rodenticides.

Strychnine Alkaloid: NWRC was instrumental in exploring strychnine (used in pest management for hundreds of years in Europe) as a tool for field rodent management in the U.S. by conducting basic research on toxicity, developing bait formulations, and evaluating efficacy and hazards under laboratory and field conditions. NWRC also worked extensively on minimizing the non-target hazards posed by strychnine, information critical to its continued use (Hegdal and Gatz 1976, Fagerstone et al. 1980, Anthony et al. 1984, Evans et al. 1990, Ramey et al. 2002b). Strychnine is currently registered by APHIS and several private bait formulating companies for use only underground for control of burrowing rodents such as pocket gophers (*Thomomys* spp., *Geomys* spp.), moles, and ground squirrels (*Spermophilus* spp.) to prevent damage to forest seedlings, agricultural crops, and home landscaping.

Red Squill (Drimia [Urginea] maritima): Although the rodenticide red squill was not developed by the NWRC (Crabtree 1947), NWRC scientists were responsible for developing a method to fortify the weak powder available during World War II to produce an acceptable rodenticide (Crabtree et al. 1942, Crabtree 1944). During the 1960s, re-registration was obtained for red squill as a rat toxicant. However, by 1992 all product registrations had been cancelled.

Thallium Sulfate: Thallium sulfate, a toxic heavy metal salt also used overseas, was brought to the U.S. in 1924 by the Bureau of Biological Survey with the help of a German producer (Crabtree 1962). Research showed this compound toxic to rats and rabbits. Following laboratory investigations, thallium compounds were introduced for control of rodents, particularly prairie dogs and ground squirrels, that would not eat strychnine baits. During the 1960s, re-registrations were obtained for thallium sulfate as a field rodent bait. Registrations were maintained into the 1970s when cancelled by EPA. They were, by that date, already being gradually replaced by more selective, effective materials.

Compound 1080 (sodium monofluoroacetate): Compound 1080 was first seriously investigated as a pesticide during World War II, when shortages of strychnine and red squill necessitated the development of other toxicants (Fagerstone et al. 1994). It was initially developed under the NWRC screening program (Crabtree 1945, Kalmbach 1945, Fagerstone and Keirn 2011) with funding endorsed by the U.S. Office of Scientific Research and Development. Following Compound 1080 registration as a rodenticide to control commensal rodents and field rodents, the NWRC had a continuing research role in identifying and minimizing non-target hazards posed by rodenticide uses (Hegdal et al. 1986). U.S. Government rodenticide uses were cancelled in 1972 and all remaining rodenticide uses were cancelled in 1990 because supporting data required

in EPA's reregistration process were not submitted by manufacturers (Fagerstone et al. 1994).

Gophacide (0,0-bis(p-chlorophenyl) acetimidoylphosphoramidothioate): Gophacide (Bayer 38819, DRC-714) was developed as part of the NWRC chemical screening program. Tests began at the Denver Wildlife Research Center in 1961 (Ward et al. 1967, Richens 1967). This organophosphate was found to be effective for controlling pocket gophers, house mice (*Mus musculus*), and rats, and was registered by the U.S. Government in 1969 for pocket gopher control. Gophacide bait was also formulated and marketed by a private firm. That registration was cancelled in 1974.

Zinc Phosphide: Zinc phosphide was first synthesized in 1740 and first used a rodenticide in 1911 in Italy. It was introduced into the U.S. during World War II when it was difficult to obtain other rodenticides from overseas sources. The NWRC has been investigating zinc phosphide as an effective acute field rodenticide since that period and was instrumental in developing many uses for rangelands and agricultural crops, including development of tolerances for use in food crops and development of methods for crop use (Evans 1970, Hilton et al. 1972, Hood 1972, Tietjen 1976a,b, Lefebvre et al. 1985, Matschke et al. 1983, Eisemann et al. 2003). A major focus of zinc phosphide research was on development of techniques for preventing rat damage to agricultural crops and food storage areas (Sugihara et al. 1995, Sugihara 2002). Another focus was to identify non-target hazards and methods to mitigate for those (Johnson and Fagerstone 1994).

NWRC coordinated the reregistration process for both strychnine and zinc phosphide with the EPA in the 1990s, managing the two consortia of commercial registrants that generated funds and data to maintain strychnine and zinc phosphide products held by APHIS, private industry, and state agencies. Without NWRC efforts, these two rodenticides may have been lost as management tools in the U.S. for protecting rangelands, forests and agricultural crops from rodent damage. Zinc phosphide is currently registered by APHIS and private companies for a variety of agricultural and structural pest control uses, as well as for reducing rodent populations at military airports and for protecting human health and safety.

Carbon Monoxide Cartridges: Gas cartridges (ignitable fumigant cartridges placed in rodent burrows) were developed by DWRC, other Wildlife Services collaborators, and several private producers more than 50 years ago. The original Wildlife Services cartridge contained 7 active ingredients; the formulation was changed to two active ingredients during the late 1970s (Savarie et al. 1980, Elias et al. 1983) to facilitate registration by reducing interaction products. APHIS maintains a Gas Cartridge registration for field rodents (Fagerstone et al. 1981, Matschke and Fagerstone 1984, Dolbeer et al. 1991, Hygnstrom and VerCauteren 2000) where they damage rangeland and agricultural crops or carry plague. Several other companies also maintain registrations using similar formulations.

Anticoagulant Rodenticides: The NWRC has not had a role in development of anticoagulants but has conducted research on a number of chronic rodenticides that has allowed their registration and use in managing wildlife conflicts. Early work included investigations of the commer-

cially available anticoagulants warfarin, diphacin, pival, fumarin, PMP, and tomorin in food baits or with soluble formulations in water baits (Crabtree 1950, 1953, 1962; Crabtree and Robison 1952, Robison and Crabtree 1956). Some of this work led to product registrations (for example, pival as a rat and mouse bait), but most were cancelled before 1974. During the 1970s and early 1980s, NWRC personnel in the Philippines tested locally available anticoagulant rodenticides (primarily warfarin, diphacinone, coumachlor, coumatetralyl, and chlorophacinone) and developed sustained baiting method to protect crops on small acreages of rice, coconuts, and corn (Fall 1977, Fiedler et al. 1982, Hoque et al. 1983, Hoque and Reidinger 1980, Reidinger and Libay 1980). Hoque (1979), working with Reidinger, developed procedures for detecting anticoagulant resistance in rodents, were it to emerge as an agricultural problem.

More recently, chlorophacinone, a popular anticoagulant rodenticide, was registered for controlling mountain beavers (*Aplodontia rufa*) using data from the NWRC Olympia Field Station (Arjo et al. 2004), and diphacinone was registered to protect macadamia nuts in Hawaii (Campbell et al. 1998). Chlorophacinone was also registered in Hawaii to protect tropical nut and fruit orchards and to protect corn and soybeans grown for seed, and two conservation methods were developed to deploy diphacinone in bait stations to protect native plants and birds from rodent predation (Pitt et al. 2011a).

NWRC recently obtained EPA registrations for three anticoagulant-based rodenticide products (one diphacinone and two brodifacoum) for eradicating or controlling rodents on islands for conservation purposes (Eisemann and Swift 2006, Witmer et al. 2007b, Pitt et al. 2011a) in collaboration with the U.S. Fish and Wildlife Service and two private rodenticide manufacturers. In addition to efficacy research, multiple studies were required to determine potential nontarget effects of these applications (Swift 1998, Dunlevy et al. 2000, Dunlevy and Campbell 2002, Johnston et al. 2005, Pitt et al. 2005, 2011b). These products, as well as other anticoagulants and zinc phosphide, were used in developing methods for rodent eradication projects by WS and others on numerous islands (Witmer et al. 1998, 2007a, 2010a, 2010c, 2011; Pitt et al. 2011a).

Other Rodenticides: In addition, the Center obtained registered uses of rodenticides introduced in the U.S. by other researchers, including sodium arsenite as porcupine (*Erethizon dorsatum*) bait (Dodge 1959 – all products cancelled by 1992), and pyrinuron (Evans 1980 – all products cancelled by 1987). Work was also conducted on chemicals that were never registered including norbormide (Crabtree et al. 1964), 6-aminonicotinamide (Pank and Matschke 1972, Matschke and Fagerstone 1977), and flupropadine (Savarie et al. 1973). Considerable work was conducted with cholecalciferol, investigating a variety of formulations for different rodent species in both laboratory and field, and developing analytical chemistry methods for assay of bait material (e.g., Tobin et al. 1993, Witmer et al. 1995, and Mauldin et al. 1999).

Recently, NWRC personnel began cooperative studies to identify new rodenticides, some of which is in collaboration with researchers from Australia and New Zealand (Eason et al. 2010). Some of the materials being studied

Table 1. List of patents obtained by NWRC scientists for rodent management techniques (includes radio-telemetry patents).

Patent Number	Date of Application or Patent	Inventors	Title
4,541,199	9/17/1985	R. Reidinger	Method and automated device for applying measured amounts of control liquids to the dorsal fur of rodent pests
4,790,990	12/13/1988	J. R. Mason, M. R. Kare, D. A. DeRovira	Mammalian livestock feed, mammalian livestock feed additive, and methods of using same
4,861,585	8/29/1989	B. G. Galef, J. R. Mason	Enhanced rodent edible with natural attractants
4,888,173	12/19/1989	J. R. Mason, M. Adams	Anthocyanin bird repellents
5,202,638	4/13/1993	A. L. Kolz	Power density measuring apparatus and method
5,460,123	10/24/1995	A. L. Kolz	Electroshock repulsion of waterfowl, aquatic animals, and small mammals
5,464,625	11/7/1995	D. L. Nolte, J. R. Mason, L. Clark	Non-toxic methods of repelling rodents from materials susceptible to rodent consumption
5,877,223	3/2/1999	J. R. Mason, R. A. Dolbeer, G. Preti	Naturally occurring odoriferous animal repellent
7,731,939	5/8/2010	L. A. Miller, J. C. Rhyan	Vaccine compositions and adjuvant

include sodium nitrite and a two-active ingredient rodenticide (cholecalciferol and diphacinone) that may reduce potential non-target hazards.

REPELLENTS

NWRC has a long history of research on exploration and development of rodent repellents for protecting packaging from commensal rodent gnawing (Traub et al. 1950, Welch and Duggan 1952) and controlling agricultural and forestry damage by field rodents (Welch 1954, Besser and Welch 1959, Welch 1967). Information obtained from the chemical screening program at the DWRC proved helpful in early development of three repellents, all of which became commercially available for protecting plants from meadow mice (*Microtus pennsylvanicus*), beaver (*Castor canadensis*), rabbits, and deer (Besser and Welch 1959): trinitrobenzene-aniline (TNBA), zinc dimethyldithiocarbamate cyclohexylamine (ZAC or ziram), and tetramethyl thiuram disulphide (TMTD – as Arasan 42-S). ZAC proved effective in protecting underground cables from pocket gopher damage but is no longer registered. Thiram products are still registered for a variety of rodent species. In the 1950s, the insecticide endrin was developed as a repellent for conifer seed to deter destruction by small mammals; this allowed artificial seeding of conifers in the Pacific Northwest (Spencer 1960, Kverno 1964). Mestranol was another chemical screened by NWRC and registered as a repellent for protection of conifer seeds from consumption by deer mice, *Peromyscus maniculatus* (Lindsey et al. 1974).

Research on repellents was re-emphasized during the 1980s through collaborative research with the Monell Chemical Senses Center. As a result of that collaboration, NWRC researchers received 6 different repellent patents, 2 of which were applicable to rodents (Table 1). One of these patents (5,464,625; Nolte et al. 1995) highlighted the potential repellency of chemicals such as ortho-aceto-

phenone to rodents. Other studies have noted the prairie vole (*Microtus ochrogaster*) repellency of pine-needle oil (Epple et al. 1997) and effects of predator urine and feces on rats (Tobin et al. 1997b).

NWRC personnel have also created additional uses for existing repellents. For example, treating cull Douglas-fir (*Pseudotsuga menziesii*) seedlings with commercially available Big Game Repellent Powder (BGR-P) and placing them in mountain beaver burrows at the time of planting caused conditioned avoidance of untreated seedlings (Campbell et al. 1987, Campbell and Evans 1988), providing a basis for a Special Local Needs Registration of BGR-P for use against mountain beavers. NWRC has been active in testing the addition of bird repellents to rodenticide formulations to reduce risk to seed-eating birds during rodent control efforts (Mason and Epple 1998). Starting in the early 1940s (Kalmbach 1943, Kalmbach and Welch 1946), scientists suggested the addition of colored dyes to rodenticide formulations to prevent consumption by seed-eating birds. Green, blue, and yellow dyes (Pank 1976) or other bird repellents (Mason and Epple 1998) are sometimes used for this purpose. Methyl anthranilate (Patent No. 4,790,990, Mason et al. 1988) was patented as a bird repellent with claims for use to decrease the likelihood of bird poisonings from rodenticide use (Table 1). NWRC also showed that the addition of the bird repellent anthraquinone to rodenticide baits reduced bird consumption (Patent No. 4,888,173, Table 1). Werner et al. (2011) are using these findings to develop formulations that reduce ingestion of zinc phosphide and other rodenticides by non-target wildlife species.

Beginning in the early 1940s, Center researchers investigated ways to prevent damage to buried wire and cables, particularly that caused by the plains pocket gopher (*Geomys bursarius*) (Welch 1943). The search for potentially useful candidate materials was continued during the chemical screening program. In 1966, the Center began

evaluating cable resistance to pocket gopher damage using a standardized laboratory test protocol (Connolly and Landstrom 1969) and continued those evaluations until 1995 (Ramey and McCann 1997). The first studies were conducted at the request of American Telephone and Telegraph Company (Connolly and Landstrom 1969, Connolly and Cogelia 1970). The research focused on the minimum thickness of armor needed to prevent tooth penetration and defined how cable and wire diameters related to damage by gophers, gray squirrels (*Sciurus carolinensis*), and Norway rats (*Rattus norvegicus*). Research included determination of rodent biting pressure, chewing action, and failure modes for cable designs (Cogelia et al. 1976). Thousands of cable samples from many cable companies were submitted over the 29-year period for proprietary testing. Although the proprietary results were not published, many of the parameters for communication-wire protectants such as cable diameter and types of metal casings, as well as above-ground cable guard designs, came out of this research (McCann 1995, Ramey and McCann 1997).

Repellents as gnawing deterrents have also been tested by the Center. A collaboration between the Center and M&T Chemicals, Inc. led to development of a rodent repellent coating (bioMeT12, registration cancelled in 1987) for polyethylene coated telephone cable (Anthony and Tigner 1968, Tigner and Landstrom 1968). The use of paint containing ground glass or sand was developed as a gnawing deterrent for pocket gophers (Welch 1967); a silica sand paint formulation was found effective for beavers (Nolte et al. 2003). The use of shrink-tubing encased repellents was shown highly effective in deterring gnawing responses of rodents on coaxial cables, with a 2% capsaicin oleoresin mixture in a mineral oil eliminating practically all cable penetrations by pocket gophers and rats (Shumake et al. 1999).

REPRODUCTIVE INHIBITORS

With the rapid developments in chemical fertility control for human applications in the 1950s, wildlife applications were suggested (Davis 1961). The Center and a number of research colleagues at other institutions engaged in investigations of materials and applications with several species of mammals (Balser 1964, Howard 1967, Brooks and Bowerman 1969, Kennelly et al. 1970, 1972; Garrison and Johns 1975, Matschke 1977). Problems with the field effectiveness of materials requiring treatments at specific times in mammalian reproductive cycles quickly became clear. That, coupled with recognition that the broad-spectrum hormonal materials available could not meet environmental requirements for pesticide registration, ended most of the Center's research interest in the approach by the late 1970s. Developments in molecular biology and the promise of candidate materials with greater specificity and less dependence on timing of treatments brought renewed interest by the early 1990s. Given the earlier concerns with registration requirements, NWRC regulatory staff and scientists began dialogs with regulatory agency personnel. These discussions had a pivotal role in determining how wildlife contraceptives would be regulated (Fagerstone et al. 2008). Beginning in 1996, an interim understanding was reached between EPA and

FDA that allowed Center research to proceed for several candidate contraceptives using the FDA's regulatory requirements for new animal drug investigations. However, the necessity of field use and the over-riding environmental concerns were finally recognized as incompatible with the FDA's regulatory process, and in 2006, an agreement between the EPA and FDA provided the EPA authority over contraceptives used for wildlife and feral animals (Fagerstone et al. 2008).

Since then, NWRC scientists have researched two wildlife contraceptives for use with locally abundant rodent species. Diazacon (20,25-diazacholesterol dihydrochloride) was first investigated as a cholesterol-lowering drug for humans, but was later developed and registered as the avian contraceptive Ornitrol (Schortemeyer and Beckwith 1970); the registration was cancelled in 1993 due to new data requirements. Research by NWRC scientists began in 1997 to determine the mode of action of Diazacon and to assess its applicability for rodent species. Diazacon is a cholesterol inhibitor that impairs synthesis of reproductive hormones (Yoder et al. 2005, 2011). Nash et al. (2007) found Diazacon effective in limiting reproduction in black-tailed prairie dogs (*Cynomys ludovicianus*) in a field trial. Reproduction was also reduced in laboratory treatments of gray squirrels, an invasive species in Europe that competes with native rodents and causes extensive tree damage (Yoder et al. 2011).

GonaCon™ Immunocontraceptive Vaccine was developed and patented (Patent No. 7,731,939, Table 1) by NWRC scientists (Miller and Rhyan 2010) for use in wildlife species as a single-shot vaccine that stimulates the production of antibodies that bind to GnRH (gonadotropin-releasing hormone), reducing its ability to stimulate the release of estrogen, progesterone, and testosterone (Miller et al. 2004). The vaccine is currently registered by the U.S. Environmental Protection Agency (EPA) for use in adult female white-tailed deer, *Odocoileus virginianus* (Fagerstone et al. 2010) and a registration is pending for wild horses (*Equus caballus*). It also shows potential for effective use with California ground squirrels, *Spermophilus beecheyi* (Nash et al. 2004), Norway rats (Miller et al. 1997), black-tailed prairie dogs (Yoder and Miller 2011), and gray squirrels (Pai et al. 2011).

ATTRACTANTS

For many years NWRC has conducted research to develop attractants or bait enhancers for rodents and to provide methods for assessing their effectiveness (Bullard 1985); attractant research has involved both taste and odor applications (Shumake et al. 1971, 1973; Thompson et al. 1972, Bullard and Shumake 1977, Sterner 1982). Effective attractants can be used to lure rodents to traps, rodenticide bait stations, and detection devices, and to increase uptake of rodenticides, vaccines, or other chemicals. In the 1980s, much of NWRC's attractant research occurred in collaboration with the Monell Chemical Senses Center, where one or more NWRC field employees were based. Galef et al. (1988) and Galef and Mason (1989) demonstrated that carbon disulfide, a chemical emitted in rat breath, served as an attractant to other rats (Patent No. 4,861,585, Table 1), and Shumake et al. (2002) found its use increased rodenticide bait acceptance. Jojola et al.

(2009), applying the concept that semiochemicals produced by one rodent could attract other rodents, found nutria urine, anal gland secretions, and fur extracts of nutria (*Myocastor coypus*) enhanced trap success in Louisiana and Maryland. Witmer et al. (2010b) similarly used an attractive feces/urine mixture to increase trap success for Gambian giant pouched rats (*Cricetomys gambianus*) in the Florida Keys.

Scientists have demonstrated that presentation and placement of baits can over-ride chemical or food attractant effects as long as the bait material is preferred over rodents' normal food. Ward and Hansen (1960) applied the concept to development of the Burrow Builder for pocket gopher control; Tobin and Sugihara (1992) and Tobin et al. (1996, 1997c) developed the approach for selective control of rat damage in macadamia nut orchards. And after extensive investigation of rodent food habits and rodenticide bait development in the Philippines (Tigner 1972), Fall (1982), and colleagues (West et al. 1975b, Sanchez and Reidinger 1980, Fiedler et al. 1982) demonstrated that micro-location placement of rodenticide baits could significantly enhance bait uptake.

MARKING AGENTS

Savarie et al. (1992) noted that of hundreds of materials that evaluated for marking animals, only a few have progressed to common use. The NWRC and predecessors have been instrumental in development of several of these materials. Center scientists have used a number of materials as placebo markers for free-ranging rodents to study rodenticide bait acceptance and exposure of target and non-target animals. Bromocresol green, an acid-base indicator, has been used as a color marker to indicate bait acceptance in rodents within a 24-hour interval (Nass and Hood 1969). Johns and Thompson (1979) proposed the use of Microtaggants (plastic particles with multiple colored layers), as distinct codes for labeling baits. High cost and the need for microscopic examination of Microtaggants led to the development of metallic flake particle markers for determining feeding behavior in field necropsies (Fall and Johns 1988). Tetracycline antibiotics used in human and veterinary medicine are deposited in growing bone and teeth when consumed in bait materials; Crier (1970), following work with coyotes (*Canis latrans*) by Linhart and Kennelly (1967), developed this approach with rodents, and it has been widely used in control methods investigations (Nass et al. 1971, LaVoie et al. 1971a). Similarly, iophenoxic acid was originally used in human medicine as a diagnostic x-ray contrast agent but was used as a wildlife blood marker by NWRC scientists (Larson et al. 1981, Savarie et al. 1992). Many other materials, particularly dyes, such as Rhodamine B (Evans and Griffith 1973) and DuPont oil blue (Ramey et al. 2002a), have been developed for specific uses with rodents. Fagerstone and Johns (1987) used transponders (technique being developed for companion animals) and modified it for use as a permanent identification marker for wildlife. Because marking agents are such a powerful tool for rodent control investigations, NWRC personnel have a continuing strong interest in developing and refining rodent marking strategies.

ANALYTICAL CHEMISTRY METHODS

The value of determining the chemical composition of materials used in rodent control was recognized early in the Center's efforts to develop materials and methods, in part because the chemical screening program involved investigation of unknown chemicals. Before development of promising materials could proceed, chemical characterization was essential (Perry 1970, Okuno and Meeker 1980, Okuno et al. 1982, Johnston et al. 2001). Analytical methods were developed and applied to determine purity of technical materials, concentrations of toxicants in baits, and residues in carcasses of test animals or non-target animals experimentally exposed. Important papers include Johns and Thompson (1979), Kimball and Mishalanie (1993), Johnston et al. (1995), Mauldin et al. (1996), Johnston et al. (1997), Goldade et al. (1998), and Mauldin et al. (1999). As equipment and technology for chemical analyses continued to improve, the need for such information also continued to increase – particularly for pesticide registration and other regulatory purposes related to environmental exposure and human or animal safety (Bullard et al. 1975, Bruggers et al. 1995, Goodall et al. 1998). Increasingly, analytical chemistry techniques have also been applied to other investigations, particularly those involving development of attractants, repellents, and marking agents, and more recently, risk assessments (Johnston et al. 2005, Arjo et al. 2006, Johnston 2007). The Center has developed special expertise in this area and has maintained state-of-the-art laboratories, with chemists now playing a lead role in a number of research areas.

DELIVERY SYSTEMS

Research Center scientists have developed some innovative baiting systems for rodents, many of which are still used. For example, in 1955, E. R. Kalmbach developed and applied for a patent on an orchard mouse (*Microtus* sp.) trail builder. The patent was not granted, but the machine has been used since that time for building artificial trails above ground for applying rodenticides to manage vole populations in orchards and other agricultural areas. In 1960, Center researchers, cooperatively with Colorado State University colleagues, developed a burrow builder to apply rodenticides in artificial burrows for pocket gophers (Ward and Hansen 1960).

Nass et al. (1970) investigated the feasibility of aerial application of bait for control of rat damage to sugarcane and developed methods to assess canopy penetration of several candidate bait carriers. Tietjen and Matschke (1982) found aerial application of prebait material to encourage prairie dog feeding activity, followed by hand-application of surface zinc phosphide bait, to provide effective control and to reduce time, manpower, and expenses associated with then-current technology.

NWRC scientists have worked closely with farmers to develop baiting strategies that are effective for particular crops, such as tree baiting in macadamia nut orchards (Tobin et al. 1994, Tobin et al. 1996, Tobin et al. 1997a) or sustained baiting on small acreages to protect rice crops (Fall 1977, 1982), coconut crops (Fiedler et al. 1982), or corn (Benigno et al. 1976). In Colombia and the Philippines, NWRC researchers developed an innovative method for

increasing bait acceptance by rats in coconut plantations (Elias and Valencia G. 1973, Reidinger and Libay 1980, Fiedler et al. 1982). Crown baiting (where anticoagulant rodenticide bait was placed in the crowns of some palms) provided economical protection from rat damage. NWRC scientists in Olympia, WA developed baiting systems for mountain beaver that take advantage of animals' tendency to carry preferred foods, such as sword fern (*Polystichum munitum*), into burrows (Campbell and Evans 1988). In other baiting research utilizing rodent behavior, a patent was received in 1985 (Patent No. 4,541,199, Table 1) for a method and automated device for applying measured amounts of control liquids (potentially toxicants or aversive conditioning agents) to the dorsal fur of rodent pests (Reidinger 1985).

Witmer et al. (2007a) used elevated bait stations in the roof rat (*Rattus rattus*) eradication on Buck Island, U.S. Virgin Islands. Elevated bait stations were also developed for a rat eradication effort on Cocos Island, Guam (Lujan et al. 2010); the stations were easily accessed by the rats, but excluded land crabs, ants, and other nontarget animals that tended to swamp stations and consume bait. Research has refined bait station designs that minimize access by nontarget animals while maintaining full access by rodents (Pitt et al. 2011c).

BARRIERS, DETERRENTS, AND EXCLUSION

NWRC scientists have long researched physical barriers and other nonlethal means to protect trees from mammal damage. A technique to protect Douglas-fir seedlings from wildlife damage (Vexar[®] seedling protector) was developed and marketed in cooperation with DuPont, Inc. Vexar[®] plastic seedling protectors were originally developed for reducing feeding injuries to Douglas-fir by lagomorphs and big game animals (Campbell 1969, Campbell and Evans 1975). Subsequently, more rigid tubing was developed and found to be effective for protecting roots of seedlings from pocket gopher damage (Anthony et al. 1978). Rigid mesh tubes have been a widely used barrier device for pocket gopher, deer, elk (*Cervus elaphas*), rabbit, and mountain beaver browsing. Center scientists have a long history of research on aquatic rodents such as beaver and nutria and the damage they cause. With the increasing beaver populations throughout the U.S., NWRC scientists have focused on reducing beaver damage. Kolz and Johnson (1997) developed a nonlethal electroshocking repellent device controlled by an infrared motion sensor that was activated by proximity of a warm-blooded animal; the device was patented (Patent No. 5,460,123, Table 1) but never developed commercially (Kolz 1995). Nonlethal electric fencing designed by Shumake et al. (1979), demonstrated impressive yield increases in Philippine rice field plots. Ahmed and Fiedler (2002), found use of a nonlethal electric fence design modified by Reidinger et al. (1985) to be effective. More recently, Nolte et al. (2003) found beaver-proof fencing a feasible approach for reducing damage to 3- to 8-inch fresh test logs on small, targeted areas. NWRC researchers have developed methods for evaluation of repellent-treated multi-layer cloth tarps or fabric barriers containing metal fibers for protecting commodities or excluding rats and mice. Methods have included laboratory procedures with tarps covering bags

of shelled corn (Tigner 1966) or with blocked holes in a barrier wall or holes into a food box (Witmer and Burke 2008). Tigner (1966) also developed field procedures using bags of corn exposed in warehouses or farm buildings. A rat-resistant artificial nest box for cavity-nesting birds was designed, tested, and used to enhance nesting success for the small Kauai thrush (*Myadestes palmeri*), an endangered bird endemic to the island of Kauai, HI. The bird's distribution and abundance are limited by availability of suitable nesting sites, and roof rats frequently cause mortality and nest failure. Ground-based rodent control was ineffective, and the method appeared to provide a solution (Pitt et al. 2011b); additional designs easier to deploy and more attractive to birds are being evaluated.

HABITAT MANAGEMENT

NWRC researchers developed a method of pocket gopher control that was a by-product of range improvement programs in the West. Keith et al. (1959) noted that 2,4-D treatment not only controlled annual and perennial forbs, but also reduced pocket gopher populations. In a 7-year follow-up study, 2,4-D treatment applied on rangeland to reduce forb abundance reduced northern pocket gopher (*Thomomys talpoides*) populations by 80% to 90% (Tietjen et al. 1967) and caused a shift in prairie dog diet (Fagerstone et al. 1977). Engeman and Witmer (2000) evaluated the effectiveness of habitat management methods to reduce pocket gopher damage to reforestation and wove the approaches into an integrated pest management (IPM) strategy. Witmer (2011) identified land use practices (livestock grazing, soybean and corn production) that resulted in lower rodent abundance around airports to lower raptor strikes related to birds searching for prey.

NWRC researchers have used habitat management approaches in agricultural crops to minimize the use and increase the efficacy of rodenticides. In sugarcane, effective habitat management methods and cultural practices have included modifying adjacent habitats to reduce area rat populations, weed control, incorporation of rat-resistant characteristics (harder rind, larger stalks, upright growth habit) into crop breeding programs, and earlier harvesting (Sugihara et al. 1977, Sugihara 1990). Habitat management was also successful in reducing rodent damage to macadamia nut orchards. Techniques developed to reduce rodent damage included the removal of vegetation or debris from adjacent areas, elimination of rock piles, and clearing of thick vegetation, and pruning debris from interior aisles (Sugihara 2002). Habitat management methods have also been developed to reduce the prevalence of rodents at airports, ultimately reducing the risk of aircraft strikes with raptors hunting rodents (Washburn and Seamans 2007).

CAPTURE AND HANDLING TOOLS

Many types of rodent handling devices and traps have been developed or improved, often in the course of other projects. Halvorson (1972) reported on an improved design of a handling cone for red squirrels (*Tamiasciurus hudsonicus*) that was flexible, easy to use, and see-through. Caudill and Gaddis (1973) developed a device for handling or transferring wild rodents in laboratory situations. Fall (1974) found that dim red light could be used for non-

disruptive handling or transfer of several rodent species in laboratory or field; the technique was particularly useful in minimizing behavioral disturbance associated with moving animals in laboratory experiments. Gaddis and Shumake (1982) developed a humane shipping container for moving rats from remote field locations to the Denver laboratories. Witmer et al. (1999) devised a live-capture trap for pocket gophers that is still used in the Pacific Northwest. Witmer et al. (2008) also designed a large, multiple-capture cage trap for nutria. NWRC researchers have also tested various types of commercial traps to identify ones most effective in capturing target rodents in various studies (Pipas et al. 2000).

DISCUSSION

For nearly 75 years, NWRC researchers and their predecessors have developed many materials, methods, and tools that have been used or are currently used by wildlife managers to manage rodent damage. But throughout the world, rodents continue to cause billions of dollars of damage to crops and commodities and to present threats to human health and safety. The loss of materials and methods used to manage rodent damage and the continuing need for new approaches is not a new problem, but one that should be anticipated by scientists and policy makers. This loss occurs for many reasons related to changes in agricultural practices, market uncertainty or market volume, regulatory changes, environmental changes, or human health concerns as more information is developed. An emphasis on rodent research is a continuing need that is well-recognized by NWRC scientists and administrators, and it will continue to be an important part of the Center's research program.

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