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Chapter 11 An International Perspective on the Regulation of Rodenticides

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1 Introduction

In the late 1940s, anticoagulant active ingredients were introduced into the global rodenticide market. They were rapidly favored over existing rodenticides, such as red squill, zinc phosphide, strychnine and inorganic compounds, because they were comparatively inexpensive and did not appear to have any unpalatable taste, odor or cause any immediate post-ingestive reaction that could lead to bait shyness in rodents (Wardrop and Keeling 2008). The number of products registered in the United States (US) under Section 3 of the Federal Fungicide, Insecticide and Rodenticide Act (FIFRA), which was passed in 1947 and was the first US law to require product registration, illustrates the rapid dominance of anticoagulants in the US rodenticide market (Fig. 11.1). It is striking that the number of anticoagulant-based rodenticide products (ARs) registered under FIFRA was more than two times greater than the other categories of rodenticide active ingredients 40 years after the enactment of FIFRA. The greatest number of rodenticide products registered in a single year under Section 3 of FIFRA (750) was in 1985, and ARs accounted for 547 (73%) of

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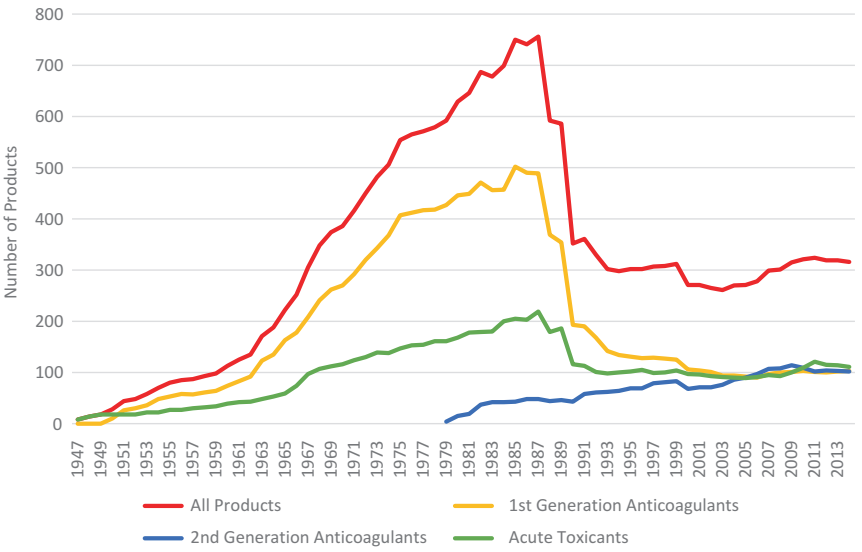

Fig. 11.1 Number of rodenticide products registered in the US since passage of the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) in 1947. Data presented is only for rodenticide products registered under FIFRA Section 3 and does not include aluminum or magnesium phosphide, gas cartridges thallium sulfate, or white phosphorous (NPIRS 2014)

those products. Similar data for international markets is difficult to collate, but it is expected that this rapid rise in popularity was paralleled around the world.

The evolution of pesticide regulations throughout the world followed many different paths. In some countries, including the US and Australia (AUS), the path to current regulatory paradigms appears to have been built on expanding the scope of legislation originally enacted to protect consumers from fraudulent products, but has since evolved to include multiple layers of human health and environmental protections demanded by an increasingly vocal public. US pesticide regulations are based on two principal acts, however, multiple human health and safety, and environmental laws also influence the conditions under which a product will be approved and ultimately used. Like in the US and AUS, New Zealand's (NZ) road to regulation appears to have been based on a single pesticide law. However, they appear to have attempted to combine multiple and sometimes conflicting regulations aimed at human and environmental protection into one umbrella act, which now governs the use of all hazardous substances, including rodenticides. The most dramatic change in international pesticide regulation is currently being undertaken in the European Union (EU), where a massive attempt is being made to consolidate pesticide regulation across individual European Member States into one harmonized set of regulations, agreed upon by all members. This consolidation approach to pesticide regulation may someday be undertaken on a global scale. However, the difficulties currently being encountered within the EU from this harmonization effort do not bode well for future larger scale adoption on any foreseeable time scale. One common thread

throughout the international pesticide regulatory environments is that pesticide laws appear to be based on a risk-benefit paradigm, and if products have significant economic (not necessarily just for manufacturers) and social benefit, products can be approved for use despite other potential or known risks. To achieve this result, regulators may impose restrictions on use, typically identified on the product label, that mitigate the potential hazards a product presents.

The development of pesticide regulation can have a dramatic impact on the availability and use of products. Legislation on a national scale sets the standards for all subsequent regulatory activities, and these broad laws can have a major impact on product availability. Another influence, perhaps equally impactful, can be the interpretation of the intent of legislation by regulators charged with enforcing federal and sometimes state regulations. The rules, guidelines and processes enacted by the regulatory authorities significantly influence the types of products allowed on the market, the speed and cost of registering products, and the motivation of private industry to seek safer uses of ARs or new rodenticide formulations.

Inferences can be drawn as to the impact of regulations by examining the number of products being brought into or removed from the market. Trends in product registrations in the US illustrate major shifts in product availability (NPIRS 2014). Some of these shifts appear to be directly the result of significant regulatory change. For example, the rodenticide product availability in the US grew rapidly between 1950 and 1990 (Fig. 11.1). However, beginning in 1989, the number of rodenticide products in the US market began plummeting from the high of 750, to the roughly 300 products on the market today. What happened in the US in the late 1980s that caused this dramatic decrease in product availability?

This chapter examines the historical influences that shaped the current regulatory environment around rodenticides in US, NZ, EU, and AUS. It compares and contrasts how products are registered, what forces shaped regulatory decisions, and speculates on the future trends in product availability for rodent control over the next 25 years. As you will see throughout this chapter, product availability throughout the world has been influenced greatly by increased scientific understanding of rodenticides' impact on humans and the environment, and the associated increased societal demands for safer products and more stringent regulation.

2 Anticoagulant Rodenticde Regulation in the United States

2.1 Legislative Actions

The earliest pesticide legislation in the US was the Insecticide Act of 1910 (P.L. 61–152, 36 Stat. 331), which was enacted primarily to protect consumers from fraudulent products. Today, there are numerous US federal laws that regulate the use of pesticides, however, two Acts form the primary framework for pesticide regulation, the Federal Food, Drug and Cosmetic Act (FFDCA), originally enacted in

1938 [P.L. 75–717, 52 Stat 1040], and the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) of 1947 [P.L. 80–104, 61 Stat. 163]. FIFRA ushered in landmark changes to pesticide regulation, two of the most significant being a requirement for standardized label language and that all products be registered with the US Department of Agriculture (USDA) prior to interstate or international shipment. These two actions established the foundation of today's regulatory environment by centralizing regulatory review under one agency and providing consumers a means to identify the manufacturer and purity of the product they were purchasing. Since that time, these laws have been amended numerous times and new laws have been enacted to keep pace with cultural changes and increased scientific understanding of pesticide chemistry. They now include regulatory considerations for protecting human health and providing safety from direct and indirect exposure, special protections for children, limits on the amount of residues allowed in food, and a wide variety of environmental protections.

Prior to the 1970s, pesticides were regulated by the USDA, and the general tenor of the regulations favored agribusiness (Carson 1962). However, an increasing segment of US society considered pesticides to be under-regulated. There was growing fear that FIFRA and the FFDCA failed to provide adequate guidance on the proper use of pesticide products, and that insufficient data were required of manufacturers to support product registrations (Carson 1962). Consequently, many felt it was impossible for regulators to assess the potential human and environmental risks associated with pesticide use. Arguably the foremost publication that galvanized public sentiment against what was perceived to be an over-promoted and under-regulated pesticide industry was Rachael Carson's 'Silent Spring' (Carson 1962). Silent Spring served as a rallying call for splintered concern over unknown pesticide impacts and spurred private citizens and public interest groups to mount political pressure for pesticide reform (Bosso 1988). The first Earth Day in the US occurred in 1969. In 1970, President Richard Nixon established the US Environmental Protection Agency (US EPA, 35FR 15623, 84 Stat. 2086) and at the same time, transferred regulatory oversight of pesticides from the USDA to the US EPA.

Two major legislative actions occurred in 1972, the Congress amended the predecessor to the Endangered Species Act (P.L. 93–205, December 28, 1987, 87 Stat. 903) to define imminent hazard to include situations involving unreasonable hazard due to the survival of a threatened or endangered species, including pesticides and Congress amended FIFRA with the passage of the Federal Environmental Pesticide Control Act (FEPCA, P.L. 92–516, October 21, 1972, 86 Stat. 973). The FEPCA included four actions that significantly impacted the use of pesticides. First, it required a systematic review of pesticide labels and supporting data for all products registered with the US EPA. Second, it established the risk standard of 'unreasonable adverse effects' defined it as '*any unreasonable risk to man or the environment, taking into account the economic, social, and environmental costs and benefits of the use of a pesticide.*' Third, the Act mandated that, in addition to US EPA evaluating the risk to human health and the environment posed by pesticide product, US EPA must also consider the benefits of continued use, primarily economic benefits. Finally, the Act also established a dual classification system for pesticide products,

General Use and Restricted Use. General Use products were those found to be safe when used according to label directions and could be sold to general consumers. Restricted Use products are those found to have a higher potential for risk when used according to label directions, and would only be available to trained certified applicators.

US EPA faced a daunting task under the FEPCA. At the time the law was passed, US EPA oversaw product registrations that included hundreds of active ingredients and thousands of end-use-products and associated degradates. The US EPA was required to implement all aspects of the FEPCA for all existing and new products within 4 years of passage. By the mid-1970s, EPA began releasing 'Registration Standards' which summarized the available data supporting a product registration and, if necessary, required additional data be submitted. These data were used to conduct human health and environmental assessments to assess the potential risk when pesticide products were used in accordance with label directions. When label directions were assumed to lead to unreasonable adverse effect(s), product use was restricted by modifying label language and/or additional data was required to further understand the potential risk. Registration Standards for rodenticide products began to be issued in 1981 for the first active ingredient, warfarin.

The next major revision to US pesticide laws came in the form of amendments to FIFRA in 1988 (P.L. 100–532, October 25, 1988, 102 Stat. 2655). These changes were prompted in part because of the slow progress US EPA was making in product reviews under the FEPCA. The principal changes to FIFRA were the standardization of chemical review methods and concurrent implementing process in which registrants were required to identify and commit to submitting missing or additional data required by EPA. This process culminated in US EPA's comprehensive examination of product label language and data submitted in support of continued product registration or 're-registration,' and issuance of Registration Eligibility Decisions (REDs). With renewed emphasis on the speed and comprehensiveness of regulatory review, the US EPA required registrants to submit thousands of missing or invalid studies on pesticide active ingredients, degradates, and end-use products. Because of the significant financial investment required to keep products on the market and pressure on US EPA to restrict or eliminate the use of the most hazardous products, the number of pesticide registrations began to decline. As observed by the product registration trend lines in Fig. 11.1, the 1988 amendments to FIFRA had significant impacts on the availability of all rodenticide products. At the peak of the US rodenticide market in 1985, 750 rodenticide products were registered with the US EPA. By 1994, the number of rodenticide products had plummeted to about one-half of that number.

The dramatic decline in product registrations was not primarily due to US EPA's determination that the products were too hazardous to be registered. Rather, most products were voluntarily or passively cancelled because registrants declined to pay the registration fees or cost necessary to maintain the registration (Jacobs 1992). According to Jacobs (1992), between 1989 and 1991, 52% of all pesticide products (not limited to rodenticides) registered under FIFRA Section 3 were cancelled due to registrant's failure to pay the increased annual registration maintenance fees imple-

mented by the 1988 amendments to FIFRA. While Jacobs (1992) does assign a dollar value to the cost associated with the 1986 US EPA Data Call-In and 1988 amendments to FIFRA, it is speculated that this increased cost to keep low value pesticides on the market contributed to a dramatic increase in product cancellations.

While there have been other amendments to FIFRA and the FFDCA since 1988, the legislation that most significantly impacted human health and safety issues related to pesticide use was the Food Quality Protection Act (FQPA) of 1996 (P.L. 104–170, August 3, 1996), which amended the FFDCA and FIFRA. FQPA regulations covered all pesticides, including rodenticides, but because there are few rodenticide food or feed uses, the impact was not as large as on conventional agricultural pesticides.

2.2 Legislation Implementation Actions

Laws passed by the US Congress form the regulatory framework for pesticide markets and those laws can have wide ranging impacts. However, in many instances, the implementation processes established by regulatory authorities, or judicial interpretation of the laws or implementation processes, can have an even more dramatic impact of the availability and use of pesticide products. A perfect example of this can be observed by examining the regulatory history of strychnine-based products. Insights into the future of ARs can be drawn from this case study.

Strychnine: A case study in the non-legislative impacts on product availability in the US

In 1947, the year FIFRA was enacted and product registrations were required, strychnine-based products accounted for 85% of all rodenticide products registered with the USDA. Today they account for less than 10% of the US rodenticide market (Fig. 11.2). The demise of strychnine can be attributed to increased competition from other rodenticide active ingredients, including the introduction of ARs, but also to mounting evidence of significant negative impacts on non-target species, sustained vocal public opposition to continued use, and the response of regulatory and non-regulatory bodies.

A growing concern for non-target hazards posed by above-ground uses prompted President Richard M. Nixon to issue an Executive Order (Executive Order 11643) prohibiting the use of all toxicants, including strychnine, for controlling predatory mammals and birds on federal lands or in federal programs. By 1976, US EPA's technical review of the supporting data and consideration of input of concerned parties resulted in a determination that strychnine presented unacceptable risk to applicators and non-target species, and they issued a notice on the Rebuttable Presumption Against Registration (RPAR) against all outdoor, above-ground uses of strychnine products (41 FR 52810, December 1, 1976). By 1983, US EPA published a notice of its intent to restrict all strychnine products to a maximum concentration of 0.5%, and to cancel registration of strychnine for above-ground use against most target species, including prairie dogs and meadow mice (48 FR 48523, October 19, 1983).

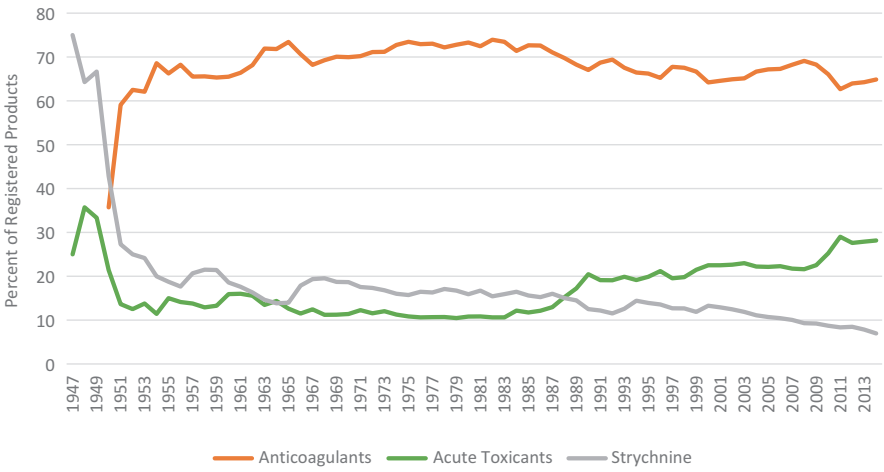

Fig. 11.2 Percent of rodenticide products registered under FIFRA that contain strychnine, other acute toxicants, and anticoagulant active ingredients since 1947 (NPIRS 2014)

Following EPA's 1983 announcement, a series of judicial challenges were filed on behalf of agricultural and environmental interests, including among others the Wyoming Department of Agriculture, Defenders of Wildlife, and Sierra Club (Wade 1985; Defenders of Wildlife 1988). In 1988, the US Circuit Court in Minnesota issued an injunction against all above-ground uses of strychnine to protect non-target species (Defenders of Wildlife 1988). To this date, US EPA has not approached the US Circuit Court with proposals to modify the injunction against above-ground uses of strychnine, and all current uses of strychnine products are limited to below-ground applications to manage pocket gophers.

Most recently, in December 2009, the State FIFRA Research and Evaluation Group (SFIREG), a group composed of representatives from State pesticide regulatory authorities, petitioned US EPA to reclassify all strychnine products as Restricted Use products (US EPA 2009). At the time of writing this chapter, all of the responses to US EPA's request for comments supported the petitioner's request, but the US EPA has not publically acted on this petition. However, US EPA has recently begun another review, 'Registration Review,' and published a final work plan in June 2016 (US EPA, 2016b). It is possible US EPA is withholding any action on this petition until they complete their re-evaluation in 2021.

The legislative regulatory path of strychnine was not unlike all other pesticides regulated by the US EPA under FIFRA and the FFDCA. The decrease in the market share of strychnine products from 1988 to 1996 (Fig. 11.2) can be linked to the 1988 injunction levied by the US District Court in Minnesota against above-ground uses to control rodents, but also to the impact of the legislatively-required periodic review of pesticide products and associated data requirements. The regulatory history of strychnine may serve as a harbinger of the future of ARs. Second generation anticoagulant rodenticides (SGARs) have not been proposed for cancellation by the

US EPA. However, mounting evidence of non-target impacts and the constant public pressure against their continued use may ultimately lead to a shrinking role for them in the future rodenticide market.

2.3 Regulatory Implementation Actions on Anticoagulant Rodenticides

In 1947, US EPA began an aggregate risk and benefit analysis of common AR products in the 1990s. They published their analysis in the Registration Eligibility Decision (RED), Rodenticide Cluster (US EPA 1998). US EPA concluded that all uses of brodifacoum, bromethalin (*not an AR*), and bromadiolone were eligible for registration. Chlorophacinone and diphacinone and its sodium salt, were also suitable for registration, with the exception of some field uses. Pival was ineligible for re-registration because the registrant failed to respond to the Agency's Data Call-in Notice.

For products remaining on the market, US EPA began a two-phase approach to mitigating environmental and human health impacts. Phase One included short-term mitigation measures such as classification of all tracking powders and field use products as Restricted Use Pesticides, the addition of an indicator dye (later abandoned), new labeling requirements designed to clarify proper placement in and around buildings, and registrants were required to submit annual summaries of accidental poisonings compiled by the American Association of Poison Control Centers. Phase Two was aimed at longer-term risk mitigation measures primarily focused on prompting the rodenticide industry to develop safer application technologies.

While these proposed mitigation measures were playing out between US EPA and industry, US EPA began an in-depth environmental risk assessment of nine active ingredients used in rodenticide products and published their findings in 2004 (Erickson and Urban 2004). This risk assessment advanced US EPA's standard stochastic risk assessment methods to include probabilistic risk assessment techniques. They identified that products containing brodifacoum, difethialone, and zinc phosphide presented the greatest overall hazard to birds and non-target wildlife. In addition, baits formulated with loose grains presented the highest ecological hazard.

In 2008, EPA published a final decision on risk mitigation measures for rodenticide products intended to reduce the potential of accidental exposure in children, companion animals, and environmental risk (Table 11.1, US EPA 2008). The rodenticide industry was given 3 years to comply. Most product manufacturers responded by voluntarily cancelling less profitable products and changing other product formulations and use patterns to comply with the new guidelines. The few registrants who initially challenged US EPA's authority to implement these measures finally complied in 2014 (US EPA 2014). The impact of these mitigation measures can be observed in the slight drop in the number of products containing SGARs beginning

Table 11.1 Rodenticide risk mitigation measures enacted by US EPA (US EPA 2008)

To reduce risk to children	To reduce risk to non-target birds and Mammals
All "consumer size" rodenticide bait products must be sold packaged together with a ready-to-use (prebaited) bait station. Only the active ingredients chlorophacinone, diphacinone, warfarin, bromethalin, cholecalciferol, and zinc phosphide were allowed in consumer sized baits. New bait station design and testing standards were developed and a 4 tier suite of bait stations were identified.	Minimum package size requirements in order to minimize the availability of second-generation anticoagulant products on the general consumer market. Second-generation bait products must be sold in packages that contain ≥8 pounds of bait for products that are labeled for use only inside of and within 50 ft of agricultural buildings and not for use in and around the home. For products intended for use by professional applicators, the minimum permissible amount of bait per package is 16 pounds.
Bait stations may be (1) non-refillable (disposable, one-time use stations), or (2) refillable (sold with bait refills). Consumer size bait stations was limited to a total of 1 pound of bait (initial load and refill combined). Bait refills must be sold with a bait station.	Use site restrictions on products containing brodifacoum, difethialone, difenacoum, or bromadialone. Products containing at least 8 but not more than 16 pounds of bait may only be used in and around (within 50 ft) of agricultural buildings (e.g., barns, hen houses), and bear the statement "Do not use this product in homes or other human residences.'
Meal, treated whole-grain, pelleted, and liquid forms of bait were prohibited except in agricultural sites. Bait blocks were the only form of bait approved for consumer size products.	Sale and distribution restrictions on products containing brodifacoum, difethialone, difenacoum, or bromadialone such that they can only be sold or distributed in agricultural stores or to Pest Control Operators.
Below ground uses were excluded from bait station and bait block requirements.	Bait station required for outdoor above-ground placements of second generation anticoagulants. Tamper resistant bait stations are required if the placement is within reach of pets, domestic animals, non-target wildlife, or children under 6 years of age.

in 2008, and a slight increase in the number of registrations of products containing acute toxicants (Fig. 11.3).

In the US, State governments have the right under FIFRA to enact rules and regulations that further restrict the use of pesticide products within their State. California exercised that right in 2014 in an effort to address a state-wide problem of wildlife exposure and poisoning from products containing SGARs. Assembly Bill No. 2657 prohibits the use of brodifacoum, bromadiolone, difenacoum, and difethialone in 'wildlife habitat areas', including state parks, state wildlife management areas, or state conservancy areas. In 2016, Assembly Bill 2596, a far more sweeping prohibition on the use of rodenticides, was introduced into the California Legislature. If passed as proposed, the California Natural Predator Protection Act of 2016 (proposed name) would read as follows *'…the use of any pesticide that contains one or more of the following anticoagulants is prohibited in this state: brodifacoum, bromadiolone, chlorophacinone, cholecalciferol* (not an AR)*, difenacoum, difethialone,*

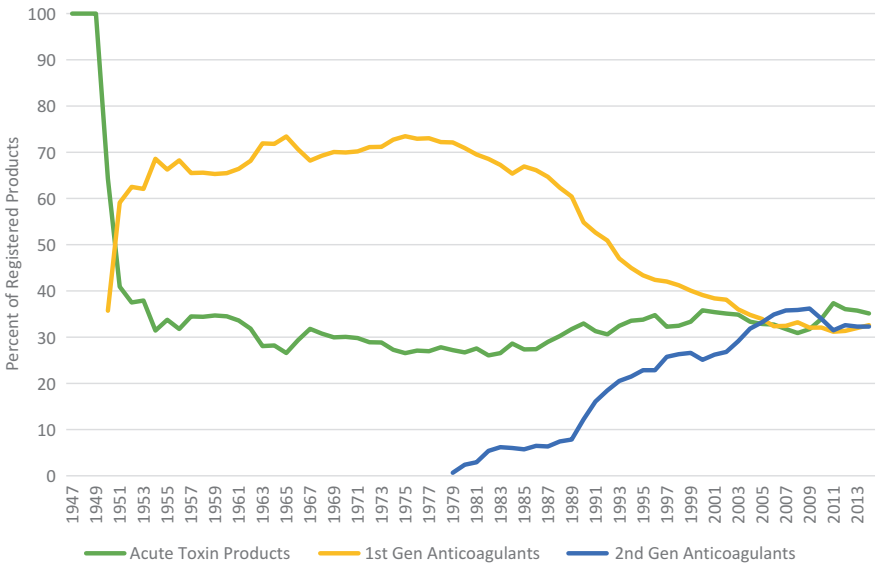

Fig. 11.3 Percent of rodenticide products registered under FIFRA that contain acute active ingredients and 1st and 2nd generation anticoagulant active ingredients since 1947 (NPIRS 2014)

diphacinone, warfarin.' Both California bills exempt agricultural uses of ARs from the prohibitions.

In 2016, US EPA announced their efforts to develop a new web-based system, Bulletins Live 2, which will provide pesticide applicators with guidance on whether the proposed pesticide use is prohibited spatially or temporally because of potential risk to threatened and endangered species (T&E) (US EPA 2016a). Working in conjunction with the U.S. Fish and Wildlife Service, Endangered Species Office, this system will have the benefit of providing species range maps at the township level, perhaps allowing applications in counties where they might have been previously prohibited because previous maps were based on county-level species occurrence. This system might also further to restrict pesticide applications because the ability to respond to changes in known species ranges is much quicker than the old system requiring T&E species prohibitions listed on individual labels. Despite EPA's current efforts, the benefits of this system on a wide-scale will not be realized for years into the future. There are only a limited number of bulletins currently available on the EPA website (https://www.epa.gov/endangered-species/endangered-species-protection-bulletins).

3 Anticoagulant Rodenticide Regulation in New Zealand

3.1 The Agricultural Compounds and Veterinary Medicine Act 1997

Currently, seven AR compounds are registered in NZ as the active ingredient in formulations classed as 'vertebrate toxic agents' (VTAs). A VTA is a subset of 'agricultural compounds' as defined under the Agricultural Compounds and Veterinary Medicines (ACVM) Act 1997 (Public Act 1997 No. 87). The Approvals and ACVM Group sits within the Ministry for Primary Industries and is responsible for developing, implementing and confirming compliance to the NZ approval processes under the ACVM Act, alongside other legislation and amendments. The purpose of the ACVM Act is to prevent or manage risks associated with the use of VTAs, including risks in trade of agricultural produce, public health, animal welfare and agricultural security. In addition, the Act is to ensure that there are no breaches in domestic food residue standards and that there is provision of sufficient consumer information about the VTA products.

Formulations of VTAs are generally trade name products used to kill, control, or limit the viability of vertebrate pests. All VTAs imported, manufactured, sold or used in NZ must be authorized under the ACVM Act and Regulations, under one of three types of authorization: (i) registration of a specific trade name product under section 21 of the ACVM Act, which is essentially an approval to promote, advertise, or sell a VTA, (ii) provisional registration to undertake research to obtain information to determine whether a VTA should be registered, and (iii) approval in special circumstances to allow conditional VTA use without registration or provisional registration.

The New Zealand Ministry for Primary Industries (MPI) is responsible for registration of VTAs, which undergo a technical appraisal and risk assessment of their quality, humaneness (relating to animal welfare) and efficacy. During registration, MPI determines which of three categories apply to a VTA: (i) unrestricted sale and unrestricted use, (ii) restricted sale and unrestricted use, or (iii) restricted sale and restricted use. Unrestricted sale and use VTA products (over-the-counter or OTC) have no restriction on their sale, no expectation of trace-back through the wholesale or retail trade, and no notification or signage requirements around their use. They may be promoted in ways to ensure that potential users are properly informed about the products and used within the conditions of registration. Generally this category includes poisons used in small quantities for domestic, non-commercial pest control and includes a range of first generation AR (FGAR) and SGAR actives. Table 11.2 summarizes the number of products containing ARs as the active agent currently registered in NZ, which includes both restricted and unrestricted products.

The 'restricted sale, unrestricted use' VTA product category requires additional instruction or advice (over and above the label information) at the point-of-sale to ensure that they are used appropriately, which may also entail additional recording of distribution or sales. This group includes some products used for commercial pest

Table 11.2 Anticoagulant compounds that are active agents in currently-registered vertebrate toxic agent formulations, available as products in NZ as of 2016 (MPI 2016).

Anticoagulant Active Ingredient		Number of products	First year a product was registered	Most recent year a product was registered
Brodifacoum	SGAR[a]	20	1996	2016
Bromadiolone	SGAR	6	1981	2013
Coumatetralyl	SGAR	3	1980	1999
Difethialone	SGAR	3	2013	2014
Diphacinone	FGAR[b]	8	1984	2015
Flocoumafen	SGAR	1	2003	2003
Pindone	FGAR	4	1992	2001
TOTAL		45		

aSecond Generation Anticoagulant
bFirst Generation Anticoagulant

control that can be sold only by persons approved by the ACVM Group. They may be required to maintain records of sale, particularly if it is considered necessary to have a trace-back capability. Users purchasing such products do not have to be approved. 'Restricted sale and use' VTA products have conditions on both sellers and users, whereby both parties need to be approved by the ACVM Group. Restricted sale and use VTA trade name products must not be promoted or advertised.

3.2 The Hazardous Substances and New Organisms Act 2001

The development of the Hazardous Substances and New Organisms Act 1996 (the HSNO Act) began in 1988 when the Interagency Co-ordinating Committee on Pollution and Hazardous Substances recommended that a new legislative framework for controlling hazardous substances be developed. Previously, chemical and biological products in NZ were regulated under a range of legislation (Thompson 1973). Each piece of legislation was directed towards a particular product type or aspect of its use, e.g. the Pesticides Act 1979, the Animal Remedies Act 1967, the Toxic Substances Act 1979, the Explosives Act 1957, the Plants Act 1970, and the Dangerous Goods Act 1974. One critique was that these statutes were often inconsistent and required implementation by a range of agencies with different regulatory missions (Allen and Clark 2006). In order to implement a more streamlined, better-practice approach to managing hazardous substances, a "One Act, One Authority" model was agreed upon. The HSNO Act consolidated existing legislation, and the Ministry for the Environment was charged with administering the legislation with support from the newly formed Environmental Risk Management Authority NZ and its operational agency (ERMA NZ). This agency was disestablished on June 30, 2011, and its functions were incorporated into the NZ Environmental Protection Agency (NZ EPA).

The HSNO Act reformed the way that hazardous substances are dealt with in NZ. As part of the consolidation process, all existing hazardous substances were transferred from the multiple-legislation regime. In 1997, the NZ Pesticide Board was still operational (Eason et al. 1997) and considering criteria for reassessment of VTAs registered before 1980 (e.g., sodium fluoroacetate, cyanide, phosphorus, pindone). After a series of transitional provisions to allow for the continued manufacture and importation of products that were legally used in NZ before commencement of new legislation, the HSNO Act came into full effect on July 2, 2001. The HSNO Act aims to prevent, mitigate or otherwise manage the adverse effects that hazardous substances and new organisms pose to the health and safety of people and environmental health, by managing the substances throughout their life cycle (i.e., in respect to manufacture, importation, sale, use and disposal in NZ). A product requires approval under the HSNO Act if it is a substance with one or more hazardous properties that exceeds a prescribed threshold. The definition of substance in this legislation is broad and covers mixtures of chemical and biological compounds such as household detergents, industrial reagents, and agricultural compounds – including ARs and their formulations in bait.

For a substance without a pre-existing approval, the HSNO Act places the onus on the manufacturer or importer to provide sufficient data describing the hazardous properties of their product. It is on this information that a determination is based, as to whether or not a product is hazardous and therefore, requires approval. Once a product is approved, any manufacturer or importer may rely on that approval; an exception to this general rule is where the product is also an innovative agricultural compound or medicine, and this could include some anticoagulant VTAs. Although applicants may identify information submitted in support of an approval application as being confidential, situations may arise where this information can be released to the public.

Section 140 of the HSNO Act provides for regulations to be made to support the implementation of the Act. The most relevant regulations are general sets of regulations that outline the skills and knowledge required to hold office under the HSNO Act, and regulations that classify hazardous substances and set out control mechanisms that must be applied when dealing with these. Other sets of regulations relate to the information requirements that must be used (i.e., labelling, packaging, signage, advertising, documentation and tracking requirements).

Section 78 of the HSNO Act enables the Environmental Protection Agency New Zealand (EPA NZ, previously ERMA) to issue, amend, approve, or revoke an approved code of practice (ACOP) regarding the control of a hazardous substance. This section also gives EPA NZ the ability to approve codes of practice developed by other people if it considers these to be acceptable.

Section 79 of the Act sets out the consultation and notification process that must be undertaken as part of the approval process whereby a HSNO ACOP provides a mechanism to assist people to achieve compliance with the controls set out in the legislation. In the case of ARs, a code of practice has been developed for the broadcast application of a particular formulation of brodifacoum bait for rodent eradication (Anonymous 2006).

3.3 Anticoagulant Rodenticide Use in New Zealand

As of June 1972, there were 1126 fully registered and 180 provisionally registered products containing agricultural chemicals, of which 11 were classified as rodenticides (Thompson 1973). Warfarin was historically used in NZ for rodent control, with at least two commercial bait formulations registered by the Pesticides Board, but these registrations apparently lapsed in June 2000.

There is no formal reporting information publically available regarding the annual retail sales and quantities of some ARs used for commensal rodent control. Therefore, it is difficult to determine the overall and proportional uses for commensal control by (i) the general public who purchase ARs through various retail outlets, (ii) owners or managers of businesses where there is a formal regulatory mandate for rodent control, or (iii) professional pest control companies that are contracted by private individuals or businesses to undertake rodent control in and around buildings.

All currently-registered ARs in NZ (Table 11.2) target *Rattus norvegicus*, *R. rattus*, *R. exulans* and/or *Mus musculus*, however, brodifacoum formulations are currently also used for brushtail possum (*Trichosurus vulpecula*) management, and pindone formulations for possum and rabbit (*Oryctolagus cuniculus*) management. Neither chlorophacinone nor difenacoum appears to have yet been registered in NZ. In contrast to the USA and EU, there have not been any recent significant changes to the ways in which ARs are registered or regulated in NZ. However, perhaps in response to increased restriction and decreased markets for SGAR products in other places, in the last 4–5 years, there has been a marked flurry of new registrations (Fig. 11.4), such that there are now more products containing SGARs than ever before 'on the books' in NZ .

There are two broad use patterns for ARs in NZ: the control of rodents (rats and/or mice) living commensally with human habitation ("commensal control") and field application for management of populations of targeted pests (rodents, possums, rabbits). Commensal control is where bait is applied in and around buildings or structures that can harbor rodents including residential households, farm buildings, factories, warehouses, commercial food handling premises, and on boats. The use of over-the-counter ARs, alongside trapping, are probably the most commonly used method for commensal rodent control in NZ, and a variety of bait formulations containing SGARs are widely retailed to general public.

The second broad use pattern of ARs is for 'field control' of pest animals. ARs are generally not applied for arable crop protection in NZ, however, a globally distinctive use pattern covers control of pest animals living in situations removed from human habitation ("field control"), which can include bush/pasture margins, forested areas, dune/coastal areas, conservation estate and offshore islands. Almost exclusively, these aim to protect biodiversity values from the impacts of rats, and other introduced mammals, as predators or competitors of native NZ fauna and flora. They are also to manage possum populations as wildlife vectors of bovine tuberculosis. Perhaps the most notable NZ field use pattern is aerial broadcast

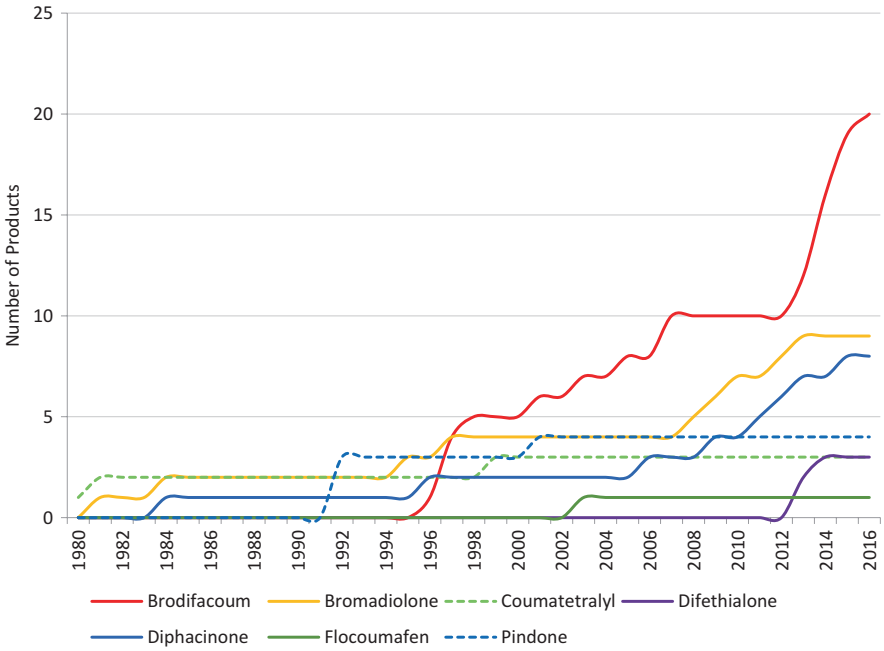

Fig. 11.4 Numbers of currently registered vertebrate toxic agents in New Zealand containing anticoagulants as actives, showing which year these products were first registered. Does not show discontinued or deregistered vertebrate pesticides (MPI 2016)

application of brodifacoum for control of rodents on non-stocked offshore islands or mainland areas enclosed by an effective pest-proof fence. This usage is strictly limited to the Department of Conservation and authorised persons, subject to a formal Code of Practice (Anonymous 2006). While this is not a frequent use, applications can be on a very large scale to facilitate the eradication of rodents from offshore islands where reinvasion can be prevented (Fisher et al. 2011).

4 Regulation of Anticoagulant Rodenticides in the European Union

Anticoagulant rodenticides are widely used in the EU for rodent pest management. The sale and use of ARs in the EU is regulated under two different legal instruments. Those applied to growing crops are known as 'pesticides' and are subject to regulation under the Plant Protection Products Directive (European Council 1991), and the subsequent implementing Regulation (European Council 2009). Those applied for all other uses, considered to be biocides, are regulated under different legislation, the Biocidal Products Directive, and known as the BPD (European Community 1988). Having two different regulatory procedures for the same

substances necessitated a clear dividing line between them to prevent duplication of effort. After considerable consultation and deliberation, the European Commission (the Commission) made this dividing line the 'field gate'. In other words, if ARs are used to protect any crop 'in field', whether the crop is actually growing or stored (e.g., clamps of root vegetables), such uses are considered to be pesticides for crop protection. Any ARs applied beyond the field, and such uses are extremely varied but include the storage of processed agricultural produce within farm buildings, are considered biocides (European Commission 2005, 2015).

Applications of ARs in Europe for plant protection are relatively few. There are several reasons for this. Firstly, rodent pest pressure in European agricultural is somewhat limited, although of course, rodent pest damage to a range of agricultural and forestry crops is well-documented, especially in southern European countries with warmer climates (Buckle and Pelz 2015). The second and probably more important reason for the restricted use of ARs in European crop protection is that mitigation measures are largely unavailable to prevent environmental impacts in these uses (see Chap. 12). The balance between risk and benefit is therefore tilted significantly against such applications when product authorisations are considered by regulators. Hence, by far the greatest quantities of ARs are applied in the EU as biocides to protect human and animal health. The remainder of this section will deal mainly with regulation of such uses.

4.1 The Biocidal Products Directive and Regulation

Until the development and implementation of the EU's BPD (European Community 1998), the regulation of ARs in Europe was conducted through a series of national statutes and other country-specific legal regulatory instruments. In some countries, such as the UK where the Control of Pesticides Regulation (1986) (COPR) as amended (1997) was in force (Health and Safety Executive 2016), anticoagulants were fully regulated according to strict UK national requirements. In other European countries, Germany for instance, there was little or no formal regulation of rodenticides. This situation underwent fundamental change with the introduction of the BPD, and with the subsequent implementing Regulation, the Biocidal Products Regulation (BPR) (European Union 2012). This regulation encompasses ARs, and a wide range of other common biocides such as insecticides, disinfectants, wood preservatives, and anti-fouling agents, as well as less some less widely-used chemicals, such as embalming fluids, metal-working fluid preservatives, piscicides, and others (Knight and Cook 2002).

One of the principal objectives of the EU is to promote free flow of products and services between Member States (MSs), without the imposition of unnecessary regulatory barriers. Clearly, in terms of the movement and use of ARs across Europe, this requires a common framework of regulation of use practices, product registrations (termed authorisations in the EU) and product labelling. The BPD was developed to provide this framework for chemical biocides. The main, and highly

laudable, regulatory principle of the BPD was to implement the highest possible standards of protection of human health and the environment (European Community 1998). This is explicit in the eighth of the 'whereas' clauses that conventionally precede all EU Directives, as follows:

> *Whereas it is necessary, when biocidal products are being authorised, to make sure that, when properly used for the purpose intended, they are sufficiently effective and have no unacceptable effect on the target organisms such as resistance or unacceptable tolerance, and, in the case of vertebrate animals, unnecessary suffering and pain, and have, in the light of current scientific and technical knowledge, no unacceptable effect on the environment and, in particular, on human or animal health;*

It is apparent from other chapters in this book that all of the issues raised in this clause, including resistance, humaneness, and non-target impacts, are relevant considerations in the regulation of the ARs in Europe and elsewhere.

The aims of the European regulators who framed this Directive are supported by everybody, including country authorities, manufacturers, and users, but the vast cost of delivering them has been almost exclusively borne by the industry that develops and puts ARs and other biocides onto the European market (Buckle 2002). These costs (see Adams 2005) have had a stifling effect on research and innovation, because funds which would have supported new product development have been diverted for two decades into projects aimed at keeping old ones on the market. A key benefit of the BPD/BPR presented to industry, and one keenly sought by the Commission, was reduced regulatory costs resulting from harmonized regulation across the EU. In other words, similar (or even the same) products having the same use patterns and risks, being regulated in a similar way among all EU countries. This benefit has remained almost entirely unrealized because of a failure to agree common regulatory principles affecting ARs among the Member States of the EU (see examples below).

4.2 Operation of the Biocidal Products Directive

The Commission, the executive body of the European Parliament and Union, is the agency which proposed legislation for regulating biocides and is now charged with implementing decisions of the Parliament in respect of the BPR. However, as with many other European regulatory schemes, implementation 'on the ground' is multilayered and another organization, the European Chemicals Agency (ECHA), manages the technical, scientific and administrative aspects of implementation. It does this by providing guidance to, and in consultation with, MS regulatory authorities, which are called 'Competent Authorities' (CAs). This European system of regulation of biocides was preceded by the implementation of a system with similar aims for the regulation of crop protection chemicals. Therefore, in many respects, the operation of the BPD/BPR is similar to the operation of the Plant Protection Products Directive (PPPD)/Plant Protection Products Regulation (PPPR) which preceded it.

Regulatory permission to place a biocidal product on the market in the EU is conducted in two stages. In the first, the properties of active substances and the risks of their applications are assessed. This is done by the presentation to the Commission, by a manufacturer of an active substance, of a dossier of studies that addresses a required list of chemical, toxicological, and environmental 'end points', which are set out at Annex II of the BPR (European Union 2012). The method of dossier submission is via an electronic portal operated through the ECHA website called the Register for Biocidal Products (R4BP), now in its third version R4BP3.

The initial assessment of the dossier is conducted by the CA of a Member State nominated by ECHA – the evaluating Member State (eMS or eCA). The eMS completes a draft Assessment Report and publishes its conclusions within a year, which, after a permitted 30-day period for comment by the applicant, is submitted to the ECHA Biocidal Products Committee (BPC) for peer review. This review provides a 270-day period for comment and amendment of the eMS's draft Assessment Report and its conclusions by the CAs of all other EU Member States. The final Assessment Report is completed by the Biocidal Products committee (BPC) of ECHA and an opinion submitted to the Commission for a decision on the approval of the active substance. The cost of these procedures, borne by the applicant, vary depending on the nature and scope of the dossier and the cost to the manufacturer of the services provided by the eMS, but are in the range €100 k to €500 k (~US $113,000 to $565,4000) to per active substance, with additional fees payable to ECHA (European Union 2013). This process results in the addition of the active substance to the Commission's list of approved active substances.

Article 5 of the BPR makes provision for active substances to be refused approval if they possess one or more of the properties listed in it as 'exclusion criteria'. This is the case for the ARs, because they are considered to be both toxic to reproduction and are named potential PBTs (persistent, bio-accumulative, and toxic). However, provisions exists for the derogation of exclusion if "*the active substance is essential to prevent or control a serious danger to human health, animal health or the environment*" or "*not approving the active substance would have a disproportionate negative impact on society when compared with the risk to human health, animal health or the environment arising from the use of the substance*." One or both of these derogations are considered to apply to ARs, and they have been approved for use throughout the EU. Nevertheless, when such derogations are invoked, active substances to which they are applied are named 'candidates for substitution'. These are then approved only for 5 years (instead of the usual ten) and are subject to a review process every 5 years, which involves a public consultation. The public consultation on ARs conducted by ECHA at the first renewal of these active substances (i.e., 5 years after first approval) has just closed at time of writing. The consultation is carried out to determine whether equally effective and safer alternatives to the candidates for substitution have become available. As there are none, ECHA has come to the conclusion that all AR active substance approvals will be renewed for a further 5 years.

A second and different regulatory procedure is applied to the assessment of products containing approved active substances – with further substantial fees in the

region of €100 k (~US $113,000) per biocidal product payable to MS bodies that conduct assessments. If an applicant wishes to sell a product in only one MS, an application for authorization of the product is made to the MS in question. Once again, a dossier of studies elucidating product chemistry, toxicology, and environmental effect is submitted via R4BP3. The assessment must be completed by the MS CA within 1 year. A further provision for 'candidates for substitution' is applied at this point, the procedure of 'comparative assessment' (see Article 28 of the BPR). In the case of applications for the authorization of products containing active substances that are candidates for substitution, the MS CA must conduct an assessment to determine "*If there is already an authorised product, which is sufficiently effective, presents no other significant economic or practical disadvantages and does not affect the occurrence of resistance in the target organism, the new product will be restricted or prohibited*." Once again, these provisions, of course, apply to ARs. Comparative assessment (European Commission 2016a) is a new and as yet, untested regulatory procedure, and there is much uncertainty about how it is to be implemented by the Commission and MSs. It seems to be a global regulatory 'first', wherein a product is considered by regulators to be both effective and safe, and with a full supporting dossier of regulatory studies obtained by a manufacturer at considerable cost, is denied access to the market because an assessment is made that an alternative is equally effective and safer. Both of these concepts are notoriously difficult to quantify with precision, and the provision for comparative assessment seems ripe for legal challenge.

Application for product authorization in only one EU MS is rare. This is because it is an important purpose of the BPR is to expedite movement of products throughout the EU and to harmonize the regulation of ARs among MSs, thereby, reducing costs for manufacturers and users. The procedure of 'mutual recognition' is intended to facilitate this process. In this mechanism, an initial application is made to a single MS, called the reference Member State (rMS), which conducts an initial assessment of the submitted product regulatory dossier. When the rMS has granted an authorization, the applicant notifies the CAs of all other MSs (called concerned Member States, cMS) where authorizations are required. These cMSs must either grant or deny authorization within 5 months, without the need for any detailed examination of the product dossier. If one or more cMS is not prepared to issue authorization under mutual recognition, the dossier is referred for decision to an ECHA coordination group, comprised of representatives of MS CAs, which must reach a decision within 60 days. If this fails, the final arbiter is the Commission.

In practice, it is rare indeed for any of these required time-scales to be achieved by the Commission and MS CAs. It is equally rare for a cMS to issue an authorization by mutual recognition without recourse to the original product dossier and more detailed consideration of the product in question in the context of national priorities. Therefore, once again, a key purpose of the BPR is not achieved. Indeed, far from resulting in harmonized product use patterns and product labels across the EU, the implementation of the BPR seems to have crystalized the different regulatory approaches, and concerns, among the countries involved. No attempt will be

made here to summarize the status of AR regulation in each EU MS because these are highly varied and constantly changing, but here are a few examples:

- In some countries, particularly in Germany, Holland, Belgium and Scandinavian MSs, second-generation anticoagulants cannot be sold to and used by amateurs (see Chap. 12 for definitions of user groups) – even in the small packs that have been previously available to them for decades. (A similar restriction has been recently been imposed on amateur in the US by the US EPA.) In others, particularly in the UK and countries of southern Europe, such products remain available to amateurs because these MSs consider that effective rodenticides must be available to the public to protect their health and well-being. Products, pests, and use patterns are identical, but regulatory approaches of the MS CAs differ completely when weighing the balance between public health and environmental risk.
- Products containing bromadiolone have been removed from the market in the Netherlands after the publication of a report that resistance to this active substance occurs in some parts of the country (Meerburg et al. 2014). However, a survey of anticoagulant resistance among house mice in Germany (Pelz et al. 2012) has found resistance to the first-generation anticoagulants in 24 out of 25 sites examined. In spite of this conclusive evidence of widespread resistance, the German CA has introduced a regulatory scheme in which only the widely-resisted FGARs are to be made available to amateurs for mouse control.
- Because of the widespread resistance in UK Norway rats to difenacoum and bromadiolone (Buckle 2013), the CA (the Health and Safety Executive) has just removed a 30-year-old ban on the use of resistance-breaking products based on brodifacoum and flocoumafen outside buildings; thus, permitting them to be used for the first time for the control of rat infestations. However, the regulatory authorities of several Nordic countries are now introducing just such a ban on the use of these products outdoors.
- The most common pattern of use of all ARs in the EU is "in and around buildings," and there is a sensible definition of this pattern of use provided by the EC (European Commission 2009), which permits AR application wherever rats infesting buildings are found to live, both indoors and out. However, this has not prevented MSs from ignoring this definition and introducing their own. For example, in Spain, AR application 'around' a building is permitted only up to 2 m from the walls of the building. Thus, control action cannot be taken at the site of infestations and, instead, practitioners are permitted to apply bait only within 2 m of the facility to which they are trying to prevent rodent ingress.

The European Commission attempted to reassert harmony into this disparity by employing a group of EU government and academic experts to assess and report on effective and proportionate risk mitigation measures for ARs (Berny et al. 2014). However, there is little sign that this initiative has had any effect on the differing regulatory perspectives of the EU MS CAs to the ARs.

The processes of implementation of the BPR are described in more detail on the website of ECHA (http://echa.europa.eu/). There is also a particularly useful series

of web-pages at the website of the UK CA, the Health and Safety Executive (http://www.hse.gov.uk/biocides/index.htm).

4.3 Consequences of the BPD/BPR and Streamlining

There is little doubt that the implementation of the BPD and BPR has placed a massive strain on the regulatory resources of the European MSs. Staff members of MS CAs have to take on an additional workload and travel to cover European responsibilities in addition to ongoing national duties. However, an initial lack of resources within the CAs of many (if not all) EU MSs, only now slowly being remedied, has resulted in implementation time-tables for the BPD, and latterly the BPR, being set back on numerous occasions. The time-table for BPR implementation is now running about 10 years behind that originally envisaged.

Two novel procedures have been implemented to streamline the process and to save the resources of regulators and manufacturers alike. The first is a process called 'Union Authorisation' (UA). This is now intended to provide an element of harmonization that has not been delivered by the process of mutual recognition. To achieve a UA, an applicant must again engage first with an rMS designated by ECHA. However, the procedure of mutual recognition (i.e., national recognition of the rMS authorization by other MSs) is replaced by Union-wide authorization granted by ECHA and the European Commission. The mechanism used by ECHA for granting UAs is through the BPC and similar to the one applied for active substances (see above). This approach is generally welcomed by manufacturers, although national CAs are wary of it, as they lose the power to determine what biocides are used in their territories.

A second attempt at streamlining is provided by the 'Biocidal Product Family' (BPF) concept. In this, a manufacturer submits a dossier of information and obtains an authorization for a 'frame formulation'. This is a generalized formulation containing a series of specified components, which may itself never be sold. Several, or indeed many products, can then be put on the market under the initial authorization as long as data is provided to show any variations from the frame formulation meet specified narrow guidelines with respect to any differences, and present risks that are lower than those of the frame formulation itself. Once again, this innovation is welcomed by manufacturers but it remains to be seen if its implementation by MS CAs will meet its objectives of reducing regulatory workload and providing enhanced protection of human health and the environment.

A series of studies of the impacts of these regulatory instruments on the availability of biocidal products and on product innovation has been carried out both by the Commission and by industry. The most recent, conducted by the International Association for Soaps, Detergents and Maintenance Products (A.I.S.E.) and the European Biocidal Products Forum of the Confederation of European Chemical Manufacturers (Cefic), has shown that a predicted 25% of all existing biocidal products will leave the market in the coming years (AISE/EBPF 2015).

Although it is impossible to quantify, the effect of these regulations on industry innovation has been considerable. Budgets that would have been committed to the development of novel active substances and new biocidal products have instead been spent to keep existing products on the market (AISE/EBPF 2015). The stated objectives of the BPD/BPR are laudable, namely the harmonization of biocidal product authorization across the countries of the EU and, thereby, the enhanced protection of human health and the environment. However, 17 years after the publication of the BPD, and with vast resources of time and money already expended, it is can be said, with reasonable confidence, that these objectives are far from being fully achieved.

4.4 Decision of the ECHA Risk Assessment Committee on ARs

A recent decision made by ECHA's Risk Assessment Committee (RAC) looks set to alter radically the regulatory landscape for ARs in the EU. RAC has decided to classify all ARs as "toxic to reproduction" (European Commission 2016b). This decision has been made on the basis that all ARs are analogous to warfarin, a known teratogen, and in spite the fact that toxicological studies on all other ARs show little evidence of teratology. Nevertheless, a Specific Concentration Limit (SCL) has been set at 30 ppm for all AR active substances, and products containing them at greater concentrations must carry an appropriate label statement. EU regulation prevents any products so labelled from being sold to, and used by, amateurs and, at first, this was thought to be the main regulatory effect. However, further consideration has found that some professionals may not wish to use these products, and their customers may not want them deployed on their premises, especially where there is general public access. It seems likely, therefore, that there will be a shift from 50 ppm to <30 ppm concentration in many SGAR products, with possible effects on product efficacy and resistance development. Effective FGAR products are implausible with active ingredient concentrations <30 ppm, and the place of this group of substances in the EU rodenticides market seems increasingly tenuous.

4.5 The Plant Protection Products Directive and Regulation

The general statement that rodent depredations of growing crops in the EU are seldom of great financial consequence is undoubtedly true (Buckle and Pelz 2015), although this is no consolation to those farmers and growers who occasionally do, indeed, sustain severe damage to their valuable crops and produce. In particular, damage to grassland and fodder in some parts of eastern France and Switzerland may be catastrophic during the periodic cyclical fluctuations of some vole species. Severe damage is also reported in young forestry plantations in the countries of Fennoscandia and in fruit orchards across continental Europe. There are also

cyclical outbreaks of damage by voles to fruit, cereal and fodder crops across Europe, from Portugal in the west to the countries of the former Yugoslavia in the east.

The use of rodenticides for crop protection, however, brings risks in addition to those presented by rodenticides used as biocides. In particular, when ARs are applied for the protection of broad-acre, orchard and forestry crops, risks to wildlife and the wider environment, particularly potential contamination of soil and water, are of special concern. This is because crop protection application methods do not confine rodenticides to protected bait stations and rodenticide baits that are not consumed by target rodents cannot easily be retrieved (see Chaps. 2 and 12). Furthermore, it is axiomatic that populations of a wide range of wildlife species are likely to be greater in areas of agriculture and horticulture than in urban and suburban environments. Consequently, the suite of regulatory chemistry, toxicology and environmental studies required to quantify the risks for AR applications for crop protection is proportionately increased. This additional regulatory burden, as well as our current knowledge of the risks of the ARs (the subject of this book), has resulted in fewer applications of rodenticide active substance approvals, and product authorizations, under the PPPD/PPPR. Indeed, among ARs the only active substances approved for use in plant protection in the EU are chlorophacinone, difenacoum, and bromadiolone. We must presume that it was an active decision by manufacturers not to pursue crop protection authorizations of the three most potent ARs, brodifacoum, difethialone, and flocoumafen.

The processes of active substance approval and product authorization for rodenticides through the PPPR are similar to those already described for the BPR and will not be further discussed. However, the MS CAs that assess crop protection AR uses are often different to those employed for biocides. For the former, MS departments and ministries of agriculture usually provide CA representation, whereas for biocides, representatives generally come from ministries of health.

4.6 Possible Effects of 'Brexit'

At the time of writing, little is known of the precise nature of the cessation of membership of the EU by the UK ('Brexit') and how it will be implemented. What follows is, therefore, speculative. However, Brexit seems unlikely to have a profound effect on the way that ARs are regulated in the UK. Obviously, UK manufacturers wishing to export rodenticide products into the EU will remain bound by its rules. Classification, labelling and packaging is overseen the ECHA Risk Assessment Committee (RAC) and, while no longer bound to do so, the UK Competent Authority for biocides (HSE) would have to have very firm scientific grounds to deviate significantly from decisions made by that body. In terms of the more practical aspects of AR use, such as who may use these products and where they may be applied, there has been such disagreement among EU Member States (see above) that the principle of harmonization, fundamental to the EU policy of free movement of

goods, has been partially set aside in the case of products containing the ARs. HSE is therefore likely to continue its current regulatory policies on the sale and use of ARs in the UK for the foreseeable future.

5 Regulation of Anticoagulant Rodenticides in Australia

5.1 Rodenticides: Past

The evolution of rodenticide regulation in Australia is not unlike what occurred in the US since the 1940's with initial and current legislation enacted to ensure agricultural-focused uses were effective and safe for consumers. In Australia, all rodenticides, irrespective of use pattern, are considered agricultural chemicals as defined in the AgVet Code, which is a schedule to the Agricultural and Veterinary Chemicals Code Act 1994 (www.comlaw.gov.au/Series/C2004A04723"\t"_blank"). Pre-1950, rodenticides were non-selective acute poisons like strychnine, arsenic, phosphorous, and thallium sulphate. After the second-world-war, sodium monofluroacetate, organochlorines, and organophosphates were also approved for agricultural crop protection (Ryan and Jones 1972). From 1970 to 1980, the reactive emergency-use of acutely toxic chemicals were without exception permitted, coordinated and managed by state government agencies and gradually fewer of these classes of chemicals were used for the manufacture of poison laced grain until only strychnine remained. Just as in the US, during the 1980s, progressive restrictions around pesticide use increased. By 1996, emergency use of strychnine as an in-crop rodenticide ceased altogether. This coincided with the approval of zinc phosphide as a rodenticide and a commercially manufactured ready-to-use laced grain product in 1997. Zinc phosphide remains, to this day, the only approved rodenticide active for in-crop or in-field agricultural applications not requiring bait stations, but it is not approved for commensal rodent control. Coumatetralyl (SGAR) has limited in-field uses for sugarcane, macadamias and pineapples, in bait stations.

The availability of ARs for commensal rodent control around homes and other built environs and infrastructure resulted in this class of rodenticides rapidly overtaking the use of acute poisons on a volume basis. Their original and currently approved use patterns made them readily accessible to the general public, and over time this has increased the risk of human exposure and non-target hazards, which has led to a commensurate increase in federal and state/territory government legislation and regulation aimed at mitigating human exposure risks and to a lesser extent environmental toxicity risks.

Legislation and regulation controlling the approval and use of pesticides in Australia was up until 1993 enacted and set by six independent states and two territories. This legislative and regulatory duplication exists because each state was formed as and remained a partly self-governing British colony up until 1901, after which they agreed to Federate and become states of a single nation, Australia.

During federation, Australia's national constitution and federal government were adopted, and the power conferred to the Commonwealth federal government did not extend to the approval of what chemicals could be used, nor how chemicals could be used in the states and territories.

5.2 Rodenticides: Contemporary Times

Almost 100 years later, Australia's state and territory governments identified the need to improve the registration process and labelling of agricultural and veterinary chemicals with a view to (1) achieving national uniformity in the registration and approval of chemical supply and use, and (2) establishing a mechanism for systematically reviewing chemicals authorized for sale and use under existing state and territory-based registration schemes.

As a result, in 1991 the Commonwealth, states and territories agreed to establish the National Registration Scheme (NRS) for agricultural and veterinary chemicals. The creation of the NRS was enabled through the Agricultural and Veterinary Chemicals Act 1988 (www.legislation.gov.au/Details/C2004A03684) and sought to place under one national umbrella the assessment and registration of all Agvet chemical products. The NRS was operated by the National Registration Authority (NRA) created in 1993 under the Agricultural and Veterinary Chemicals (Administration) Act 1992 (http://www.austlii.edu.au/au/legis/cth/consol_act/aavca1992511/) as an independent statutory authority. The NRA was responsible for the implementation of the Agvet Codes that are schedules to the Agricultural and Veterinary Chemicals Code Act 1994. These detailed the provisions allowing the NRA to evaluate, approve/register and review active constituents and agricultural and veterinary chemical products (and their associated labels); to issue permits and to license the manufacture of veterinary chemical products. It also contains provisions for controls to regulate the supply of chemical products; and provisions ensuring compliance with, and for the enforcement of, the code. Although the national regulator was and is responsible for chemical and product approvals, their legislative reach extended only to the point of sale of pesticide products. Once rodenticide products were in the hands of end-users, which depending on scheduling may require supply via Australian state or territory agency employees, it was the responsibility of the state/territory governments to ensure compliance to the control of use regulations in each state/territory. This is arguably to the detriment of product effectiveness given the control of use regulations are not consistent between Australian states and territories, which is a situation mirrored in the US and between EU member states.

The Australian regulatory authority changed its name in 2003 to the Australian Pesticides and Veterinary Medicines Authority (APVMA). The reasoning for the name change was two-fold: firstly, it was inconsistent with international nomenclature practised by other international chemical regulators within the Organization for Economic Cooperation and Development (OECD), which sets the international

Table 11.3 Scheduling of rodenticide products according to the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) (Gill 2016)

Schedule 5.	Caution – Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.
Schedule 6.	Poison – Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label.
Schedule 7.	Dangerous Poison – Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.

standards and benchmarks for chemicals management, and secondly, and somewhat humorously, a survey in 1998/99 highlighted the acronym was often confused with the National Rifle Association in the US.

The APVMA was now, like the US EPA, responsible for all agricultural chemical active ingredient and product approvals, which currently number, 2687 and 8446 respectively. Of the 8446 approved products, 166 are rodenticides (all classes), 135 are SGARs, 13 are FGARs and 18 are others (e.g., zinc phosphide, alphachloralose, cholecalciferol (Table 11.3) . From the inception of the Australian regulator to the present day, the approval process for new products or labels standardizes all chemical assessments, labelling and packaging by requiring a consistent package of data and taking into account proposed product use as stated on the label.

In addition, the application assessment process involves allocating a 'Schedule' to a new agricultural chemicals and products based on their overall hazard, taking into account information about their toxicology, environmental toxicity and proposed use. Scheduling of chemicals and products is the responsibility of the Australian Committee for Chemicals Scheduling (ACCS) who use the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) (www.legislation.gov.au/Details/F2016L00849), which takes its legislative imprimatur from the Therapeutic Goods Act 1989. There are 10 Schedules that are applied to all agricultural and veterinary chemicals and products. Acutely toxic rodenticides (e.g., zinc phosphide baits and fumigant products) have all been allocated a Schedule 7. SGARs and FGARs are in the main allocated a Schedule 6, but there are nine products containing either warfarin or coumatetralyl that have been allocated to Schedule 5 (Table 11.4) .

As occurs in the EU and the US, the APVMA has powers under sections 31 to 34 of the Agricultural and Veterinary Chemicals Code Act 1994 to conduct reviews of registered chemicals. In broad terms, these powers include the authority to reconsider the approvals of active constituents and the registration of products and their labels, and to require registrants to provide information that may not have been required for the assessment of original product registrations.

In February 2016, the active constituents: brodifacoum, bromadiolone, difenacoum, difethialone, and flocoumafen were placed on a priority list for reconsideration.

Table 11.4 Rodenticide active ingredients and number of rodenticide products currently by the APVMA in Australia

Active constituent		Number of Approved Products
Brodifacoum	SGAR[a]	62
Bromadiolone	SGAR	33
Coumatetralyl	SGAR	6
Difenacoum	SGAR	37
Difethialone	SGAR	10
Diphacinone	FGAR[b]	1
Flocoumafen	SGAR	5
Warfarin	FGAR	6
Total		160

[a]Second Generation Anticoagulant Rodenticide
[b]First Generation Anticoagulant Rodenticide

Scoping of the reconsideration is to commence in December 2016, with the reconsideration to commence at a later date taking into account relevant, new scientific information available since their original approvals with the following facts taken into account in the prioritization decision:

- These chemicals persist in organs of poisoned rodents and present a risk to non-target animals that feed on poisoned animals or carcasses.
- Use of products in domestic premises, animal production facilities and food production facilities is currently allowed. This presents potential risks to humans, pets and wildlife through accidental poisoning. Around 1400 human exposure incidents to rodent baits are reported to Poisons Information Centres annually.
- Products are not intended for use in crops or the field, though some labels make it difficult to discern this.
- Use of liquid formulations are a concern because they are not designed for use in bait stations.

Fortunately, the registration reconsideration process does take into account the downside risks and in this case the APVMA has pragmatically identified that removing SGARs carries with it the risk that less effective anticoagulants will be the only option for controlling rodents in commensal situations. The registration reconsideration process that began in February 2016 for these SGARs is not yet complete, so the implications for SGAR regulation in Australia remains to be seen.

6 Conclusion

Rodents inflict damage to growing crops, grasslands, orchards, and fodder (Buckle and Pelz 2015); foodstuffs by direct consumption and contamination during storage, production, transport and sale; physical damage to property, installations and belongings; and perhaps of greatest importance, the transmission of diseases to

humans and domesticated animals (see Chap. 1). Rodenticides, by design, are lethally toxic, and in most situations this toxicity pathway is not unique to rodents. Consequently, their use presents a risk to humans and the environment and measures must be taken to lessen the potential risk. Traditionally, and perhaps as it should be, that responsibility falls to government entities. Government officials, in turn, use the most basic available tool to them: enacting regulations and implementation procedures. Like most product-driven markets, regulations typically impose manufacturing and labeling standards on manufacturers, but regulations and risk mitigation measures are also aimed at the end-user of the products. Ultimately, proper use, stewardship, and training on the safe use of pesticide products are the responsibility of the end-user.

This chapter has presented four examples on the development of pesticide regulation in international markets. In each example, the country or collection of countries (EU) followed their own unique path toward current regulatory paradigms, but ended at essentially the same point, a focus on product performance, and safety to humans and the environment. In all four regulatory environments, AR use is still allowed, but they are under increasing scrutiny as a result of growing public concern and regulatory response to that concern, some of which is justified. However, the conclusions international regulators are making on the risk and benefits of continued product use and the disparate policies they are adopting, have created an international regulatory environment that is difficult and costly for product manufactures to navigate. Harmonization of world pesticide regulation standards would serve to rectify this disparity, but agreement may be extremely difficult, as is being witnessed by the EU harmonization effort.

As was observed in the case of strychnine in the US, the disappearance of products did not occur overnight as a result of a sweeping legislative actions. It took 40 years of study, growing public concern, an executive-level ban on the product, a series of judicial reviews, and the US EPA's unwillingness to challenge judicial decisions, to arrive to the situation today where strychnine is a minor player in the rodenticide market. It is the opinion of the authors that ARs, especially SGARs, are experiencing similar regulatory paths. Restrictions on AR use throughout the world are not being driven by high level congressional, parliamentary actions, or executive level actions, but are succumbing to the effects of regulatory implementation and associated risk mitigation measures enacted by well-intentioned regulators.

In many cases, risk mitigation measures are justified for continued use ARs (see Chap. 12). As pointed out in other chapters of this book, there is a significant body of evidence that many wildlife taxa are exposed to ARs, in particular SGARs, almost wherever they are used. Certainly, there is also evidence that some wildlife have been killed by ARs. That knowledge alone might be justification enough to severely restrict their use or even ban them. However, no significant advances in rodenticide chemistry have been made since the introduction of SGARs and cholecalcifereol more than 30 years ago. The risks and benefits of the old chemistries we rely on are becoming better understood and it goes without saying that all products come with their own unique set of issues. Forcing a shift from ARs to other chemistries is simply substituting one set of risks for another.

As is usually the case, more information is needed properly to evaluate the risks and benefits of continued AR use. Early research focused heavily on acute effects of exposure to rodenticide baits and residues in tissues of poisoned animals. Recent research trends are focused on sub-lethal exposure scenarios and the impact of low-level, potentially non-lethal levels of residues in the tissues of exposed animals (see Chap. 3). This is an area that deserves a more in depth understanding. However, it should also be balanced with an equal understanding of what sub-lethal exposure actually means in relation to the health of individual animals and their possible impact on the ability of species to maintain viable populations. The same can be said for understanding the risks of other exposure scenarios such as repeat exposures and exposure to multiple ARs either concurrently or over time.

A systematic study is warranted of pesticide regulations and the associated success or failure rate of those regulations on meeting their intended objectives. As pointed out above, changes in product availability provides the opportunity to observe the direct impact of regulations. This measure alone is not adequate if one tries to draw conclusions on the real impact on protection of human or environmental protection. For example, as the use of one product decreases and the use of another increases, questions arise around what new risks have been realized or benefits have been given up. In reality, funding for this type of research is extremely limited. Government regulators are typically inadequately funded and there is little incentive for industry to conduct this research. It is essential however, that regulators take informed and balanced positions, and do not act precipitately, in the absence of concrete information. Application of unreasonable risk mitigation could result in the loss of valuable products, potentially resulting in unacceptable levels of loss to food supplies and increased risk of negative impacts to human health and safety.

It is apparent that the number of years AR products will be available for operational rodent management is limited. Such is the life of any pesticide product. Whether it is a growing understanding of a product's unanticipated consequences, target pests developing resistance to chemistries, growing public concern, or over-regulation, a pesticide product's days are numbered beginning the day it is first registered. In the case of rodenticides, you only need to look at strychnine, red squill, and arsenic-based products to observe the life of a pesticide. In many instances, this obsolescence is warranted. As presented above, the perception of the risk and benefit of SGARs varies among governments. The availability of SGARs is likely shorter in the US than other countries. What will be the next in line in the evolution of rodenticides? Perhaps it will be simple reformulation of existing active ingredients. Will that meet future rodenticide needs into the twenty second century? The future more than likely lies in the development of new active ingredients, biological agents and novel technologies that have a higher degree of target species specificity. However, the costs necessary to bring a new active ingredient to market are extremely high and the time-frames very long. Risk of failure, low market potential and short product life, only lessens the desire or ability of a private manufacture to invest in such an endeavor.

One thing is certain, the quest for new rodent management techniques, including rodenticides, will be never-ending. Adequate scientific understanding of the risks and benefits accompanying new technologies will lag behind product development and as a result, regulations will be reactionary as regulators address the impacts of new technologies. Perhaps, as is currently being attempted in the EU, governments will work out harmonized international regulatory standards and systems, thereby reducing the costs and time required to bring new safer, more effective technologies to market.

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