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Final report

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RISK MITIGATION MEASURES FOR ANTICOAGULANT RODENTICIDES AS BIOCIDAL PRODUCTS

FINAL REPORT

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1 EXECUTIVE SUMMARY

Rodent pest control worldwide relies largely on the use of anti-vitamin K anticoagulant rodenticides (ARs). ARs have considerably changed our practice and perspectives for rodent control. The delayed action of these compounds, with mortality occurring several days after bait consumption, makes them particularly effective against neophobic species such as the Norway rat (*Rattus norvegicus*). The intensive use of these compounds has been rapidly followed by the selection of resistant strains in Norway rats, roof rats (*Rattus rattus*) and house mice (*Mus musculus and M. domesticus*). ARs are usually classified as First Generation AR (FGAR) (warfarin, chlorophacinone, coumatetralyl), requiring several days of feeding to be fully active, Second Generation ARs (SGARs) (bromadiolone, difenacoum, brodifacoum, flocoumafen, difethialone), more potent and active after only one day of feeding. Bromadiolone and difenacoum are considered less potent than the other SGARs and resistance to them is described, while there is no evidence of 'practical' resistance on the field to the three other SGARs.

Alternatives to ARs are limited today. Alphachloralose has been registered as a biocidal product against mice only. Cholecalciferol has been recently submitted as an active substance to the EU. Because of its delayed action, it can overcome neophobia, although bait aversion has been demonstrated against Norway rats. Old compounds (zinc phosphide, sodium selenite, bromethalin) all may have some interest but also have major drawbacks (either in terms of efficacy, toxicity to non-target species or lack of antidotes). Methaemoglobin-forming compounds are currently being investigated as rodenticides but usually act too fast to be good rodenticides. ARs are also being reconsidered with modern tools in order to separate their activity and their persistence. With the exception of the above, there is no evidence that chemical alternatives to ARs will be available in the next 5 years, (no results anticipated before 2020).

Because chemical control of rodents relies almost exclusively on ARs, many distinct resistant strains of Norway rats and house mice have been identified. These resistant strains have developed specific genetic traits through a modification of the VKOR enzyme involved in the catalytic recycling of vitamin K and through enhanced metabolism of the active ingredient by means of the induction and over expression of selected CYP450 isoforms. The most widely spread resistance mechanism appears to be related to VKOR alterations and specifically Single Nucleotide Polymorphisms of the VKORC1 gene (resulting from a single mutation in the DNA sequence), at least in rats and mice. A lot of work still needs to be conducted on these mutations to determine precisely the level of resistance conferred by each Single Nucleotid Polymorphism (SNP). Resistant strains have been identified in most western European countries, but information is lacking for most central, eastern and southern parts of Europe. Other countries in the world also have detected mutated strains. Resistance testing can be done either via *in vivo* tests (BCR for instance) or by *in vitro* identification of the mutations. Because of its simplicity and lower cost, the latter appears to be the most promising tool, provided field information is available on the level of resistance associated with each mutation. This technique could be used to monitor AR resistance in all EU countries, with information presented using GIS mapping by dedicated institutions.

Alternatives to chemical rodenticides are limited. Trapping can be effective but is time-consuming. Ultra-sound, repellents and attractants are of limited utility, because rodents readily become habituated. Some interesting areas of research, including pheromones and fertility control, are under investigation, but are unlikely to become commercially available in the near future.

Integrated rodent management and resistance management are important issues and should be considered in all circumstances. Several guidelines (from RRAG, RRAC, ECPR-R) are available which set out resistance management strategies, aimed both at preventing the selection of resistance and the removal of resistant infestations once they are established, although much research remains to be done. Two guiding principles emerge. The first is the requirement to monitor rodent infestations for resistance, in order to identify the type of resistance involved. The second is to use only effective anticoagulant active substances against rodent infestations where resistance has been identified, and to cease using anticoagulant active substances at resistance foci, where they are known to be ineffective against a particular type of resistance.

Non-target poisoning by ARs is commonly described in many species. Human accidental poisoning is benign in most instances and generally requires no further investigation from poison control centres. Medical advice and long-term data can be obtained from human poison control centre databases. Domestic animal poisoning is commonly described and may be severe in many cases. Some countries have public/private reporting of poisoning, but information is poorly accessible. AR exposure in wildlife has been recognised worldwide and in Europe especially. Monitoring schemes and reporting systems exist for several countries and long-term monitoring data can be obtained in some countries. The actual impact of biocidal products versus agricultural ones is difficult to determine, since this information is usually lacking in the databases. Available data suggest that accidental poisoning rarely occurs when products are used correctly. This is an area for further investigation.

In Europe, today, there is no common standard to define a trained Pest Control Operator (PCO) for the application of rodenticides. European pest control trade associations have been working for several years on the definition of a professional standard for their group (guidelines for training, certification and control), which should be made available across Europe in 2014. This is an important step in the process of defining categories of users for the implementation of risk mitigation measures.

Starting in 2009, biocidal products have been placed on the market according to the EU Directive (98/8). Because of their risk to non-target species, several Risk Mitigation Measures (RMMs) have been suggested and applied by Competent Authorities CAs delivering marketing authorisations. As a result, across Europe, a single commercial product may have more than one set of RMMs attached to its marketing authorisation, despite it being registered under the Mutual Recognition procedure. To date, it is extremely difficult to assess the impact of these RMMs on both resistance selection and non-target poisoning, because the monitoring tools have not been developed to satisfy these requirements. Nevertheless, the existing domestic and wildlife monitoring schemes in some member states (MSs) do provide some information on non-target poisoning, both before and after the implementation of the Biocidal Product Directive (and the associated RMMs).

The expert group responsible for this report collected data in the R4BP database to obtain information on the recommendations and RMMs for all AR marketed in the EU, and also asked specifically CAs for their standard set of requirements. Below are listed some of the RMMs which may differ widely between MSs and can be controversial.

- Restrictions of use for amateurs
- Rat control use for PCOs only
- Restriction to indoor use
- Picking up dead rodents and other animals (and disposal of bodies)
- Remove bait at the end of treatments and disposal
- Mandatory use of tamper-resistant bait boxes

- Erection of notices to indicate presence of rodenticides
- Resistance Monitoring

Based on this work and on the experience of other countries (including the US), the expert group developed a set of suggestions and recommendations for common RMMs.

1.1 RMMS to be applied for active substance approval

- For rat control, FGARs and less potent SGARs should always be considered as the first choice. SGARS should only be used against rats, where there is evidence that infestations are resistant.
- For mouse control, SGARs should always be considered as the first choice, as FGARs have low efficacy against House mice. FGARs should only be used against mice where there is evidence that the local strain is susceptible.
- Provided the other RMMs are applied (pack size, bait boxes see below), there is no reason to restrict the use of SGAR for amateurs, especially in order to control House mice populations, which are the number one problem in the amateur sector.
- Pack size should always be limited for amateur use and SGAR should be sold in smaller amounts than FGARs. A precise computation and list of suggestions is provided. Products intended for use by amateurs should be clearly different from products intended for use by professionals and PCOs.
- Amateurs should have the option to use ARs in and around buildings for the control of rat infestations, since there is evidence that rat infestations almost invariably have an outdoor origin (burrows). Any restriction of an active substance, or a biocidal product, to use 'indoors only' is a *de facto* restriction preventing use against most rat infestations.
- Dyes should always be included in the formulations. Using specifically green/blue dyes for ARs which are not absorbed appears as an interesting RMM to monitor both bait uptake (efficacy) and non-target primary exposure.
- Bittering agents should be included in all bait formulations. Denatonium benzoate at 0.01% (10 $mg.kg^{-1}$) is currently the most commonly used bittering agent in bait formulations.
- Baiting area: professionals and trained professionals should conduct surveys prior to application of ARs that consider the extent of the rodent infestation, and the risks posed to humans and non-target species. Information should always be applied on the bait boxes but not in the surrounding area.
- For amateur use, tamper-resistant bait boxes should always be mandatory, with baits securely fixed inside the bait boxes when possible (wax blocks, paste). Loose baits (such as grain and pellets) cannot be excluded, even for amateur use, because of their higher palatability. Using smaller packs and pre-packed bait boxes should reduce the risk of accidental human exposure, and possibly pet exposure.
- For PCOs and professionals, bait can either be presented in tamper-resistant bait boxes, or in open trays that are protected from non-target species using a combination of natural cover, materials located on site and materials brought onto site specifically for that purpose. Infestations are likely to be large, and non-target impact will be minimized by optimizing bait presentation to the rodents, and thus minimizing the duration of the treatment. The utility of tamper resistant bait points will vary from site to site and their use should be left to the discretion of the operator, in the light of the risk assessments conducted at the outset of the treatment.
- Pulsed baiting should be used when SGARs are applied to reduce the quantity of bait applied provided data is available to support the efficacy of this practice with particular active substance and biocidal product.

- Permanent baiting should not be conducted outdoor unless there is a high risk of re-invasion, because it poses a very high risk to non-target species.
- Permanent baiting may be conducted indoors, particularly where there is a regulatory requirement, or where there is a high risk of re-invasion, because it can be managed to pose a low risk to non-target species.
- In the first instance, the duration of outdoor baiting should always be limited to 35 days (5 weeks). Subsequent continued rodent activity could indicate that the rodents are resistant to the rodenticide, or that a significant proportion of the infestation are not being treated, and are continually moving into the treated area.
- Frequency of visits should be left to the discretion of the operator, in the light of the risk assessments conducted at the outset of the treatment. The wide diversity of sites with rodent infestations precludes any strict frequency. However, as a minimum treated sites should be visited once a week.
- All rodent bodies should be disposed of on each visit by the PCO, and clients should be encouraged to dispose of rodent bodies, taking necessary steps to ensure their safety (providing advice on wearing gloves, minimizing contact, and washing hands after disposal). Specific recommendations for disposal of rodent bodies should be specified (avoid the general sentence "according to local regulations"). For clients and other amateurs, sealing the bodies in two separate plastic bags and safe disposal in the garbage can be considered.
- Uneaten bait should always be removed and disposed of at the end of the treatment. Amateurs may dispose of their remaining uneaten baits by sealing it within two plastic bags and safe disposal in the garbage.
- Resistance in rodent populations should be managed by ensuring that only effective ARs are used to control population rodents. For House mice, first generation anticoagulants should be avoided unless there is good evidence that populations can be controlled with a particular active ingredient, and for House mice and Norway rats, resistance surveys involving the sequencing of the VKORC1 gene should be conducted for any population of rodents where physiological resistance is suspected. Where mutations of the VKORC1 gene are detected, subsequent use of ARs should be restricted to the active ingredients currently believed to be efficacious against that particular mutation. Such information should be made widely available across all MSs in a format similar to that of the Rodenticide Resistance Action Group (see RRAG, 2010), and should be regularly updated in the light of results generated across all member states.
- In the long term, mapping of the different VKORC1 mutations across all MSs should also be made available online, to allow predictions to be made for new infestations located within areas that have previously been surveyed.

1.2 RMMs to be set at the stage of product authorization

- Bait boxes should be mandatory for amateur products. Various levels of protection can be obtained with the different bait boxes and it is suggested to develop specific requirements for bait boxes qualification. Different levels of protection are described in the document and levels 2-3 should be considered for amateurs.
- All bait formulations should be available to all user categories, with limited amounts and tamper-resistant bait boxes for amateurs.
- A standardized Summary of Product Characteristics (SPC) template should be completed for all products and readily available to all potential users. It should be the basis for label recommendations. It is strongly suggested to have a common and simplified label across MSs.

- Product manufacturers should provide a list of the information media available for the various user categories. Information leaflets or labels should be provided at this stage.

1.3 General recommendations

- Resistance evaluation should be considered in cases where there is a of lack of efficacy of a rodenticide application, despite good bait consumption. If there is no local information on the presence and nature of the resistant strain, *in vitro* evaluation (genetic testing for VKORC1) should be considered. Based on the mutation detected, appropriate AR application should be considered. If no mutations are detected, *in vivo* evaluation of resistance may be considered. Further research work still needs to be done to determine precisely the impact of each mutation on the susceptibility of rat and mouse strains.
- Resistance monitoring should be considered for all stakeholders including local government agencies. Tissue samples properly identified and GPS-referenced should be submitted to national registries in order to provide accurate mapping of resistance.
- Resistance management is the appropriate use of the most effective AR for a given situation, based on the known mutation and its susceptibility to various ARs. A detailed list of already known mutations and potentially effective ARs is given.
- Non-target poisoning monitoring should be reinforced.
    - Human exposure cases can be dealt with by poison control centres and it is recommended to add phone numbers on the product package for each MS.
    - Domestic animal exposure may also be monitored using poison control centres or dedicated veterinary structures (some MSs have specialized animal poison control centres, colleges of veterinary medicine could be used as reference centres in all MSs).
    - Wildlife exposure monitoring should be considered. Dedicated wildlife pesticide poisoning surveillance systems exist in some MSs. These structures only deal with animals found dead and spontaneously transmitted. Encouraging the development and cooperation between similar organisations across Europe should help provide valuable information on the actual impact of ARs and RMMs. Also, research and epidemiologic surveillance (on wildlife populations) should provide information on the actual impact at the population level for specific species (birds of prey for instance).
- Training is an essential component of appropriate use of ARs.
    - Trained professionals should receive appropriate and certified training, resulting in certified qualification. A European standard is currently being developed and appears as a very promising tool. Detailed recommendations with respect to subjects to be covered are given. Adaptation of existing programs is encouraged.
    - Professionals should also receive appropriate training. Farmers usually receive training in Plant Protection Product application. Rodenticides could be included in such training programs or as separate training sessions, depending on local uses of ARs (some MSs have permitted uses of ARs as Plant Protection Products).
- Provision of information for the general public. It is strongly suggested to develop specific leaflets, boards and video loops for local points of sale. Information should also be provided by stakeholders, but also by CA and the EU on the internet (dedicated websites, QR codes…). A suggestion to deliver ARs only in specialized shops or in shops with specifically trained personnel is made.

- Best practice guidelines already exist in several MSs. A detailed list of these is provided. These documents should be available to all categories of professional users (paper, websites…).
- Support new active substances development. Europe is quite unique in that ARs are almost the only rodenticides available to control rodent infestations. Relying on a single class of compounds is not reasonable and it seems important to have support from research agencies to help companies and public research laboratories to develop the next class of substances (or strategies) for the control of rodent populations.

2 INTRODUCTION

A thorough review of Anticoagulant Rodenticides (AR) and their advantages and drawbacks has been provided as a preliminary report. This report is attached as Annex 1 in the present report.

Comparison of anticoagulants with other rodenticide active ingredients.

According to Brooks (Brooks & Bowerman, 1973), the eleven features of the ideal rodenticide are:

1- The onset of symptoms should be slow to avoid bait shyness

2- It should be lethal in a normal amount of food

3- It should be palatable to rodents

4- It should be inexpensive

5- It should be easily formulated

6- It should be easily degraded in the environment

7- There should be no difference in susceptibility due to variations in age, sex or strain

8- Resistance should not develop

9- There should be no secondary poisoning hazard

10- There should be no danger to man or domestic animals

11- It should be specific to the target species

It could be argued that the ARs meet the first seven features, and it is perhaps the slow onset of symptoms (feature No 1), which set the anticoagulants apart from the acute rodenticides. The ability to achieve complete control of a rodent infestation without the development of conditioned bait aversion revolutionised rodent control.

Basic physiology and metabolism are similar among mammal species. Therefore, it is inherent to effective rodenticides to pose a risk to non-target mammals including humans and domestic animals (features 10/11).

Features 8 and 9 also raise the concerns about the anticoagulants. Unfortunately, the anticoagulants that raise least concern about secondary poisoning, are the ones to which target species are most likely to develop a level of resistance that will have practical implications. For environmental reasons, concerns about secondary poisoning have outweighed the concerns about resistance, leading to the development and spread of resistance across many parts of Europe.

It will be difficult to find a rodenticide that can meet more of the above features than the anticoagulant rodenticides. However, there are the following four additional features that should be added to the above list, that add to the favourable features of anticoagulant rodenticides:

1- Where animals receive a sub-lethal dose of rodenticide they will suffer no long-term detrimental physiological effects. This is of particular importance where there is exposure to humans and non-target species.

2- There is a delay between consumption of a lethal dose and the development of adverse physiological effects, thus allowing medical or veterinary intervention.

3- There is an effective antidote available

4- Action of and symptoms caused by anticoagulants are considered more humane than for many of the acute rodenticides.

As all anticoagulants have the same mode of action (see below), and active ingredients such as warfarin are routinely and widely used in human medicine in the prevention of thrombosis, medical and veterinary treatment of human and non-target poisoning is routine and well established. Sub-lethal effects are unlikely to be significant and can be easily managed.

In contrast the action of the acute rodenticides is rapid, providing very little time for medical or veterinary intervention, available treatments for the different modes of action are not straightforward and there are no antidotes. Furthermore, the actions of the acute rodenticides have significant impacts on the physiology of the recipient, be it target, non-target or human, and the sub-lethal effect will probably have long-term consequences.

The mode of action of anticoagulant rodenticides (ARs).

The only known action of ARs is to block the vitamin K cycle and prevent activation of vitamin K dependent proteins. In contrast to most other rodenticides, ARs are not toxic to the animal's fundamental physiology, but simply bind with a long half-life of elimination to certain enzymes involved in the recycling of vitamin K. This effectively, but temporarily, blocks the enzymatic pathway involved in the recycling of vitamin K, and thus prevents the production of the active form of the vitamin, hydroquinone. This results in the decline in endogenous levels of proteins whose activity is vitamin K dependent.

On the molecular level, there are specific binding sites predominantly located in the liver and pancreas, where ARs bind, and the activation of vitamin K dependent proteins is only compromised after all these specific binding sites become occupied by AR. The active proteins important for the rodenticidal properties of ARs are the blood clotting factors (factors II, VII, IX and X). Prolonged (lethal) exposure to anticoagulant prevents further activation of new proteins, and over time, causes the decline in plasma concentrations of these active factors. When the plasma concentration of one of these factors falls below a critical level, blood can no longer coagulate and a lethal haemorrhage may occur, typically within 3 to 10 days. ARs with a shorter half-life of elimination require repeat feeding on rodenticide bait to achieve a lethal effect, while ARs with a longer half-life of elimination can achieve a lethal effect following a single feed.

There are other vitamin K dependent proteins whose activation will also be affected by anticoagulants, but their biological function is unclear.

The AR warfarin is routinely used as a medical treatment to prevent blood clots and cerebral transient ischaemic attacks; at a rate sufficient to increase coagulation to a level equivalent to an INR (International Normalised Ratio) of between 2 and 4.5. Such long term sub-lethal exposure of AR in humans is reported to have side effects, such as easy bruising and bleeding from mild trauma, but has not been found to result in any long term detrimental effect.

Vitamin K_1 provides the complete antidote for all ARs; and in combination with the delay of at least 3 days from consumption of a lethal dose to death, anticoagulant rodenticides have an extremely good safety record.

The modes of action of other rodenticide active ingredients.

In contrast to the ARs, the majority of other rodenticide active ingredients do have a toxic effect on the animal's physiology. For example:

- Zinc phosphide and aluminium phosphide rely on the generation of phosphine gas, which is reported to cause heart failure and damage to internal organs.
- Sodium fluroacetate (1080) and fluoroacetamide block the tricarboxylic acid cycle, causing convulsions, respiratory failure and / or circulatory failure.
- Calciferol causes hypercalcaemia, osteomalacia, and the calcification of soft tissues, particularly in major arteries and kidneys.
- Bromethalin uncouples oxidative phosphorylation in the cells of the central nervous system, causing tremors, convulsions, prostration and hind limb paralysis.

There is every likelihood that sub-lethal effect of such compounds will have long-term detrimental effects on non-target species including humans. Most of these active ingredients are fast acting (achieving mortality within 24 hours), and none of them has an effective antidote.

The possible exception might be alphachloralose, which is a narcotic with a rapid effect that has been found to be an effective rodenticide against small rodents. Non-target species exposed to this active substance that are kept warm often make a full recovery. Alphachloralose is considered humane in view of its recorded use as a human anaesthetic, although symptoms can have an alarming appearance, including loss of motor coordination and agitated wild or convulsive behaviour before prostration and torpor set in.

3 CRITICAL REVIEW OF EXISTING RMMS AND THEIR IMPACT

3.1 List of products and applied RMMs

A detailed list of authorised products in the EU (as of January 1st, 2014, with only partial inclusion of 2014-registered products) has been put together as an excel spreadsheet. Separate sheets have been used for different active substances. Important information on authorised uses and available RMMs as described in the documents attached to the product authorisation in the R4BP database have been included. This file is available as Annex 2 of the present report.

3.2 List of RMMs applied by MS

MS have been solicited to provide their common set of RMM and strategies for authorisation. All relevant information has been included in a specific spreadsheet, added to the present report as Annex 3.

3.3 Measures or initiatives other than RMMs

As a general rule, several MS are developing programmes to reduce risk by reducing exposure. This is currently the case in MS such as Germany (Germany's National Action Plan on Sustainable Use of Plant Protection Products), the UK (the proposed UK SGAR Stewardship Regime) and France (Ecophyto 2018). Similarly, Integrated Pest Management (IPM) should generally be considered as a cornerstone of rodent control. Chemical control only appears, therefore, as one of the tools available to manage and control rodent populations.

3.4 Critical review of the impact of RMMs

As of today, it is extremely difficult, or even impossible to have a good idea of the qualitative as well as the quantitative impact of existing RMMs applied by MS.

The first reason for this lack of data is related to the recent and progressive delivery of marketing authorisations across the EU, starting in 2009. The existing monitoring systems for non-target poisoning were not adapted to include all appropriate data on animal exposure. Retrospective surveys should be conducted in order to compare data before and after the introduction of biocidal products. Some non-target poisoning data obtained from France and the UK will be included in this part.

The second reason is that most MS do not collect animal data, or this information is not readily available, especially for wildlife. In most instances, only Plant Protection Products are surveyed (see for instance (Berny and Gaillet, 2008) (Sánchez-Barbudo *et al.*, 2012) (Hughes, Sharp *et al.*, 2013).

As will be discussed in section 4.3, resistance monitoring and non-target incident monitoring systems should be developed and harmonised across the EU to collect quantitative data on the actual impacts of AR and the various RMMs applied.

Some important information could be obtained from the online questionnaire available for PCOs and rodenticide manufacturers. A general comment was that MS requirements were quite different and moderately or greatly affected the production and sales of rodenticides for 82% of the manufacturers. This was promised as one of the principal benefits for industry of the Biocidal Products Directive and it has demonstrably not been delivered.

Most companies, either PCO or chemical companies encounter resistance problems with rats and/or mice (>60% of responders).

Similarly, 60 to 80% of responders are contacted for questions regarding either human or animal exposure to rodenticides.

In this part, we will briefly present data collected in the UK and France.

3.4.1 Acute mortality events in domestic and wildlife species

Mortality in wildlife that is believed to be a result of pesticides is investigated in the UK by the Wildlife Incident Investigation Scheme (WIIS).

The UK WIIS Scheme published their results from 1998 to 2007 in a series of detailed annual Reports, while from2008 to date they published their results quarterly in a spreadsheet format with considerably less detail.

The 2007 Report, which was published in December 2008, reported a total of 354 incidents of wildlife mortality. The cause of death was determined in 189 incidents, and of these, 124 incidents were confirmed as being caused by pesticides.

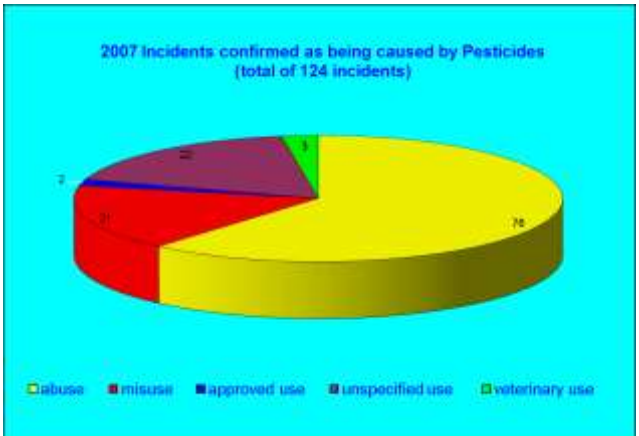


Figure 1: 2007 incidents confirmed as being caused by pesticides (N=124 incidents) in the UK.

Only two of these incidents resulted from the approved use of pesticides (a buzzard found dead near an area where a rodent control operation was being carried out; and a dog that had consumed slug pellets that the dog's owner had put on her flower beds).

Of the remaining 122 cases, 76 were considered abuse, 21 were considered misuse, 3 were considered veterinary use (and outside the scope of the Report), and 22 were considered unspecified use, where the cause could not be assigned to one of the other categories. It is considered most likely that the cases of unspecified use will be a result of abuse, misuse, veterinary use and approved use in proportions similar to that verified above.

An incident is classed as misuse where there is a failure to adhere to the correct practice, and in 2007, 15 of the 21 cases involved rodenticides.

An incident is classed as abuse where there is a deliberate illegal attempt to poison animals using a pesticide or biocide. In 2007, the following 12 cases out of a total of 76 abuse cases involved SGARs, although in a number of these cases, pesticides such as alphachloralose, carbofuran, endrin and mevinphos were the likely active substances abused, and the presence of SGARs were likely the result of the widespread low-level exposure of SGARs in predatory and scavenging wildlife species.

- Buzzard involving bromadiolone, difenacoum and alphachloralose
- Two ravens and a buzzard likely killed by carbofuran, but both brodifacoum and difenacoum were found
- Two buzzards, where carbofuran, bromadiolone and difenacoum were found
- A pheasant involving difenacoum
- An incident involving endrin and difenacoum where two dogs and a buzzard died (endrin being the likely cause of death)
- An incident involving mevinphos, bromadiolone and difenacoum, where two kites, a crow and a rabbit were found

The UK Predatory Bird Monitoring Scheme, which started in the mid 1960's and was instrumental in proving that organochlorine pesticides (like DDT) caused mass declines in species like kestrel and sparrowhawk, is currently monitoring the exposure of SGARs in several predatory bird species. The most recent report entitled "Anticoagulant rodenticides in predatory birds 2011" was published in 2013, and reported the presence of SGARs in barn owls (84% of 58 birds analysed), red kites (94% of 18 birds analysed), and kestrels (100% of 20 birds analysed).

In France, the Toxicology Diagnostic Laboratory of the College of Veterinary Medicine (Lyon, France) is part of a national network of wildlife disease surveillance. As such, it receives suspected poisoning cases from all over the country.

ARs represent one of the most common causes of suspected, as well as confirmed, poisoning incidents. Between 2008 and 2012, the laboratory received 7,088 suspected poisoning cases, 25% of which were suspected AR poisoning incidents. Figure 2 below shows the annual distribution of cases.

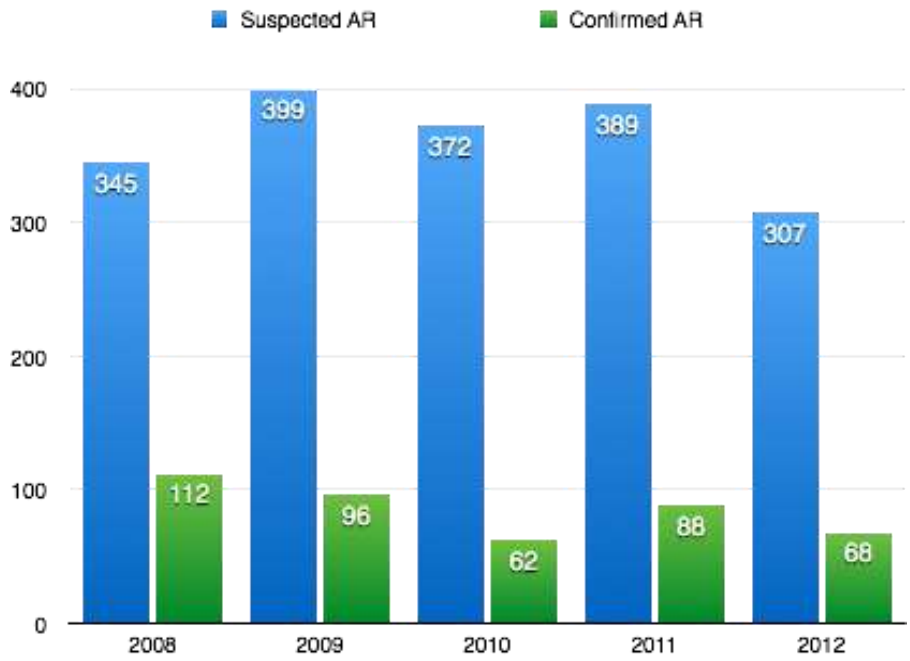


Figure 2: Suspected and confirmed anticoagulant rodenticide poisoning cases in domestic and wild animals received at the College of Veterinary Medicine, Lyon, France

Both domestic and wild animals are received. Figure 3 below presents the proportion of confirmed AR poisoning events in the most common species

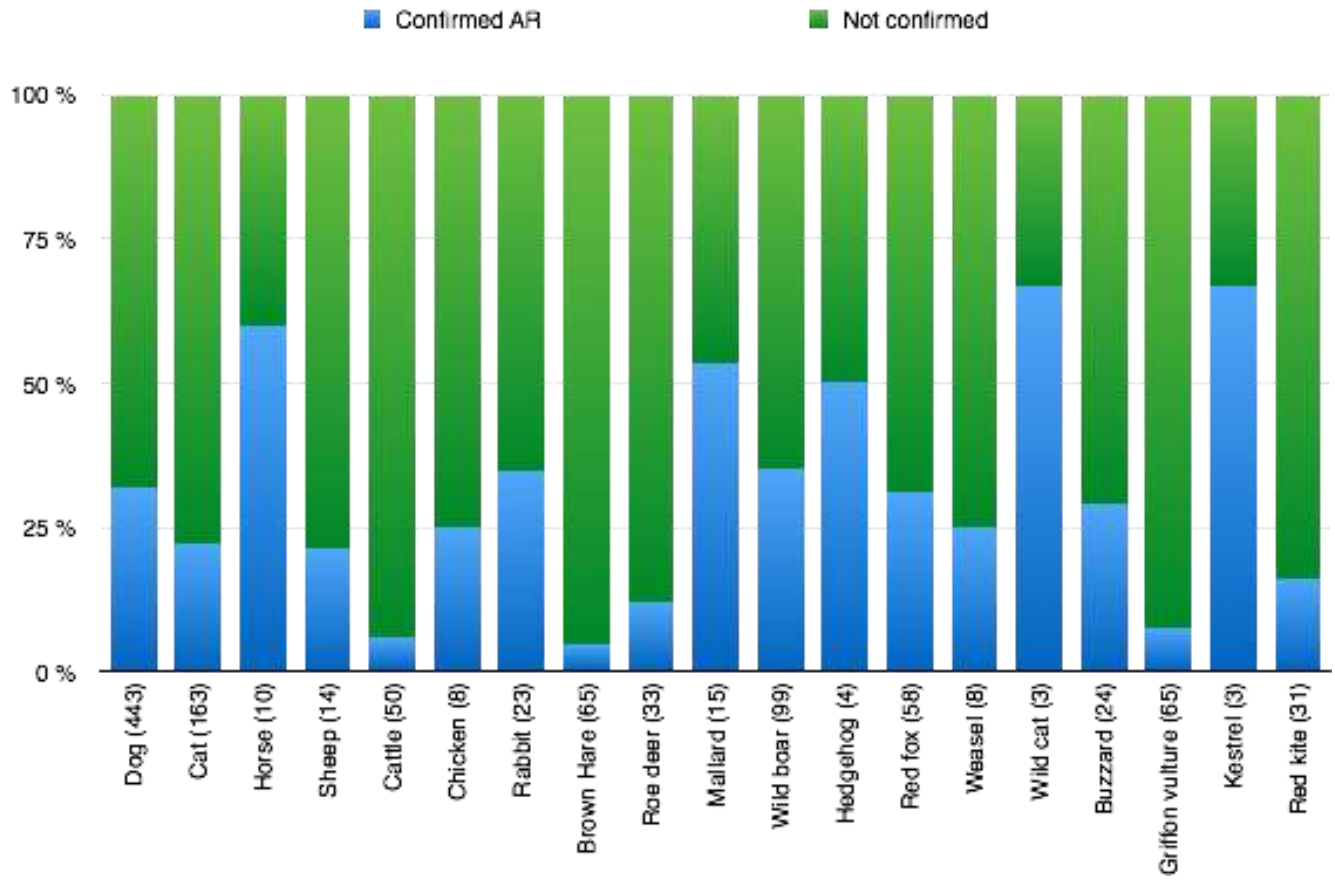


Figure 3 Proportion of confirmed AR (anticoagulant rodenticides) poisoning incidents in domestic and wild species (total number of cases submitted in brackets).

As can be seen in this figure, the proportion of confirmed AR poisoning cases may vary greatly but is usually around 25-30% of the cases submitted for investigation.

Poisoning cases by bromadiolone, chlorophacinone and difenacoum are presented in the table below.

Table 1: confirmed poisoning cases in domestic and wild species most commonly found with AR residues (bromadiolone, chlorophacinone, difenacoum).

Species	Bromadiolone	Chlorophacinone	Difenacoum
Dog	37	76	22
Cat	11	16	8
Sheep	3	0	0
Rabbit	3	4	1
Brown hare	2	0	1
Roe deer	3	1	0
Mallard	2	5	1
Wild boar	32	1	1
Red Fox	17	1	1
Red kite	5	0	0
Griffon vulture	4	0	0
Buzzard	3	1	1
Kestrel	2	0	1

This table confirms that bromadiolone is commonly found in wildlife, while chlorophacinone and difenacoum are primarily responsible for domestic species poisoning. Nevertheless, some incidents are described with these two biocidal products in wildlife.

In Table 2 the detailed number of confirmed cases for each AR is given. It should be remembered that bromadiolone was the only AR approved for use as a Plant Protection Product during the survey period (commonly used against water voles in France, (Berny *et al.*, 1997)).

Table 2: Non-target AR poisoning cases in animals in France between 2008 and 2012 (data : Vetagro Sup, Lyon)

Year	Warfarin	Coumatetralyl	Chlorophacinone	Bromadiolone	Difenacoum	Difethialone	Brodifacoum	Flocoumafen
2008	0	0	37	47	20	0	5	4
2009	0	2	41	32	19	1	1	1
2010	1	3	29	18	8	1	0	0
2011	0	3	31	30	19	3	3	1
2012	1	2	24	38	4	1	3	0

Apart from bromadiolone (commonly used in the fields) all other AR are only used as biocidal products. Chlorophacinone was discontinued for use against water voles in 2007. All accidents recorded in animals could, therefore, be related to biocidal use.

3.4.2 The impact of SGARs on predatory birds at the population level

This widespread contamination of predatory birds is of particular concern, although the organisations reporting these SGAR residue levels often report a very low frequency of incidence where ARs are considered to be the cause of death; and the situation is similar with the data reported by the WIIS. However, both the PBMS and the WIIS raise justified concerns about the potential sub-lethal effects of these residue levels, which they recognise, is largely unknown.

There are significant published data available about UK predatory birds that would suggest that these potential sub-lethal effects are not having an effect at the population level. The British Trust for Ornithology (BTO) conducts periodic surveys of breeding birds in Britain and Ireland, with the three most recent surveys conducted between 1968 and 1972, between 1988 and 1991, and between 2008 and 2011 (Balmer et al, 2013). For the species of raptors known to be exposed to SGARs, there have been some substantial population increases (Table 3)

Table 3: The frequency of residues of one or more SGARs in UK raptor species, breeding distribution and population changes and population estimates. (From Eaton *et al*., 2013)

Species	**% carrying residues of one or more SGAR (n=number examined)**	**% change* in breeding range distribution since 1988-1991**	**2013 Estimated UK breeding population (number of pairs)**	**% change in breeding numbers from Breeding Bird Survey 1995-2011**
Red Kite (*Milvus milvus*)	94 (17)	+728	1,600	+676
	69 (114)			
Barn owl (*Tyto alba*)	84 (49)	+67	4,000	+279
	35 (63)			
Kestrel (*Falco tinnunculus*)	100 (20)	-1	46,000	-30
	41 (22)			
Buzzard (*Buteo buteo*)	44 (479)	+67	57,000-79,000	+80
Tawny owl (*Strix aluco*)	38 (34)	+6	50,000	-18
Sparrowhawk (*Accipiter nisus*)	54 (37)	+7	35,000	0
Peregrine falcon (*Falco peregrinus*)	29 (24)	+39	1,500	-28

* Range changes given are for Britain, Isle of Man and Channel Islands

Overall, the breeding distribution of predatory birds in Britain and Ireland showed a marked increase between the periods 1968-1972 and 2007-2011, with associated increases in several of the exposed species (Table 3). These increases, driven primarily by increases in red kite, common buzzard and barn owl, have occurred during a period from 1975 to date, in which there has been increasingly extensive use of SGARs in the UK. These data do not permit an assertion that exposure to sub-lethal SGAR residues is having no impact on the UK populations of the exposed species, but neither do they permit the assertion that exposure to sub-lethal SGAR residues is having any discernible population effect on the species which carry them.

3.5 Critical review of RMMs in the EU

This report has been structured so that each RMM suggested is discussed in light of what is currently being done (rationale / assumptions / scientific evidence). In other words, all current RMMs are discussed and amended if necessary to suggest appropriate RMMs based on scientific evidence whenever possible or on experts' judgement. Below are listed some examples of divergent RMMs among MS which have, or may have, negative impacts on either efficacy (limited efficacy of rodent management and/or on increased resistance selection) or non-target species exposure to rodenticides.

Restrictions of use are currently applied in several MSs. Very few active ingredients are currently available in the EU besides anticoagulants, and the almost exclusive reliance of chemical control on one class of product is of major concern.

It is suggested to re-consider these restrictions in view of both toxicity and resistance issues. Resistance in Norway rats and House mice is widespread, and will increase when ineffective ARs are used. Where resistance is suspected, the VKORC1 mutation should be determined, unless VKORC1 data are already available for the location of the infestation. ARs should only be used against rodent populations where there is good evidence that they will be effective. Resistance guideline documents should be produced and regularly updated (see RRAG 2010; RRAG 2012[a]), so that the selection of some ARs and restrictions against using other ARs should be based on the VKORC1 mutations of the resistant population.

It is acknowledged that the use of rodenticides poses risks to man, domesticated animals and wildlife; and to minimise those risks, the rodent infestations must be controlled effectively and over the shortest possible period of time.

Any Risk Mitigation Measure would be totally counter-productive if it significantly prolonged the period required to achieve control. Consideration should be given to the following:

- Ensure that the rodenticide used is effective against the pest species, particularly for House mice and for resistant strains of Norway rat.
- Not to use rodenticides where they are unlikely to be effective. This should include infestations located within or near geographical areas where resistance has been verified.
- Ensure that the rodenticide is protected from most non-target species, using any available device and construction, including the use of commercial tamper-resistant bait boxes.
- Ensure that the extent of the infestation has been mapped, and that sufficient bait points are used to ensure rodenticide is available to the whole infestation wherever it is located.
- Set a limited duration for a rodenticide treatment; more frequent site visits would be cost-effective, to monitor control of the rodent infestation, to collect and dispose of rodent

carcasses, to reduce the quantity of bait available to the rodents as control is achieved, and to ensure that bait points remain protected against non-target species.
- Once control is achieved, remove all rodenticide baits and possibly use census bait to monitor for future infestation. Perhaps Industry could develop Census Bait systems that can be inspected regularly by Clients.

Amateur / First generation

There is ample evidence demonstrating the lack of efficacy of first generation products against most strains of mice, irrespective of their VKORC1 sequence (Buckle, 1994, 2012). In Spain, in some parts of Germany and probably elsewhere, it has been demonstrated that the Algerian mouse (*Mus spretus*) hybridised with the House mouse (Song *et al*., 2011) and introduced mutations conferring a high level of resistance to ARs. As a consequence, House mice may not be susceptible to FGARs. Irrespective of that hybridisation, House mice can possess a number of mutations of the VKORC1 gene that is associated with resistance to AR (Pelz *et al*., 2011). It is of concern that some MSs (Germany, Sweden for instance) only allow amateurs to use FGARs to control House mice.

Restrictions on the use of some rodenticides, in particular the SGARs, by amateur users has either been proposed or implemented in some EU regulatory agencies (see Annex 3). The reason for this is frequently stated to be that amateurs are unlikely to follow label instructions and other advice about best practice, and will not use personal protective equipment, where this is necessary.

Among the risks thought to be presented by amateur use, in particular, is exposure of companion animals and wildlife. However, as far as we are aware there is only limited evidence that amateur use is more or less likely to cause exposures to these animals than, say, use by untrained professionals and other user groups.

It is frequently said, but again little quantified data exist, that most amateurs use rodenticides, including SGARs, mainly for the control of house mice in the home – that is indoors. It is also widely accepted that SGAR products are the most effective for such applications and, when applied correctly, pose little risk to the environment.

Therefore, any regulatory decision that removes SGARs from amateur use denies them the most effective intervention for their most important rodent problem. Two fall-back options are available. The first is the use of FGAR products, which are generally considered to be largely ineffective for use against mice. The second is the use of a professional pest control technicians. The cost of the latter solution is likely to be prohibitive to many members of the public. Furthermore, in some areas of the EU there is insufficient geographical coverage by professionals to treat all infestations. Therefore, the denial of use of SGARs by amateurs is likely to result in adverse impacts to public health and hygiene.

The widespread use of FGARs in areas where there is evidence of resistance is unlikely to have any long term effect on the rodents at the population level, will selectively kill the more susceptible animals in a population and will select for resistance. It will also result in live animals with high body loadings of AR, which is a potential risk to predatory and scavenging non-target species (Vein *et al*, 2012).

As explained above, this RMM may result in poor efficacy and increased selection pressure on resistant individuals. It would therefore appear reasonable to consider SGARs as necessary compounds for amateur control of House mice infestations in buildings.

Progressive use of FGAR and SGAR

In some MS, like Denmark, it is suggested to use FGAR as a first step to control rat populations and, if resistance is detected, gradually increase the potency of the AR used (coumatetralyl, chlorophacinone, bromadiolone/difenacoum…). As clearly described in the RRAC-resistance management guideline (www.RRAC), gradually increasing the potency of AR is a good means of slowly selecting resistant strains and leading to the presence of mostly homozygous resistant individuals. For most identified resistant strains, a definite jump in potency / toxicity usually provides excellent results in terms of efficacy with limited or no non-target problems if all safety precautions are taken. A general recommendation would be to use alternative active substances with a different mode of action, as generally recommended with antibiotics for instance, but to date, there are no alternatives to the use of SGARs against Norway rats. Other strategies such as pulsed bating with the more potent SGARs should also be considered when a resistance focus has been identified.

Rat control for PCOs only

Several MS have limited rat control products to professionals or trained professionals only. These limitations may be the result of regulatory decisions (restricted use to PCOs) or consequences of other requirements. For instance, it is sometimes recommended to have AR used only in enclosed areas (see § on indoor use only), although most rat infestations have a major outdoor component.

In most MS, rat control can be carried out by amateurs. It is the experts' opinion that most rodent problems encountered with amateurs concern House mice infestations. It is obvious, however, that Norway rats may be present in urban areas, in sub-urban environments and in private houses surrounded by gardens.

In some countries (Denmark for instance), rodent control is financed by the local Government, but in most countries, it has to be supported by the owner of the infested premises. The basic cost of rat control products is much lower than any PCO intervention, and it is expected that limiting availability of products to control rat infestations may be counterproductive and result in illicit use of products. This situation has already been observed in France with several banned pesticides (http://www.oncfs.gouv.fr/IMG/communique_trafic%20dejoue_produits%20phytopharmaceutiques.pdf).

Recent developments at the 28th Risk Assessment Committee (RAC) Meeting

In March 2014, at its 28th meeting, the Risk Assessment Committee (RAC) for Harmonised Classification and Labelling concluded that all AVKs rodenticides should be classified as toxic for reproduction (R1A - "Known Human Reproductive toxicant" or R1B - "Presumed Human Reproductive toxicant").

As the majority of rodenticide products contain >0.003%, the RAC opinions will result in such products being classified and labelled as a reproductive toxicant. As a product classified as R1A or R1B cannot be made available to the general public in accordance with Article 19(4) of the Biocidal Products Regulation (BPR), these opinions may significantly alter the number of products, in particular FGARs but also bromadiolone and difenacoum containing products, that may be available to the general public to control rodents.

At the current dosage, all FGAR active ingredients would become unavailable for the general public. Should companies seek to reformulate their products to maintain them available for the general public, a concentration below 0.003% would be ineffective for all FGARs against fully susceptible populations of Norway rat and House mice, and the SGARs bromadiolone and difenacoum would be ineffective against resistant strains of both species where they possess certain mutations of the VKORC1 gene.

As the expert team recommend that amateur users should not be provided with rodenticides that are ineffective, or rodenticides that are very likely to select for anticoagulant resistance in populations where the rodents are predominantly susceptible to anticoagulants, and unless bait palatability is significantly improved, reformulated products with concentration below 0.003% of FGARs and of the SGARs bromadiolone and difenacoum would not be efficacious enough and the change in the current authorisations should not be agreed by competent authorities.

The RAC opinions could therefore lead to a greater use by the general public of difethialone, brodifacoum and flocoumafen containing products, as these would be the only products available and efficacious below the 0.003% concentration limit.

In addition, as discussed earlier in the report anticoagulants are essential for effective rodent control in order to protect the health and well-being of humans and animals, prevent the consumption or contamination of stored foodstuffs by rodents, avoid deterioration of facilities, structures and property and remove invasive non-native species posing a threat to vulnerable wildlife. The proportion and the speed of treatment made by the general public are essential to stop the spread of rodent populations within communities. If no suitable alternatives are available to the general public, which have an equivalent efficacy spectrum (i.e. against rats and mice), the restriction to the number of products available to the general public could have serious consequences for public health. Indeed, if rodent control were to become completely reliant on professional operators, this could cause a delay in treatment of household infestations due to cost (if a private pest control operator (PCO) was used) or resources (if government funded PCOs are used), which in turn could result in an increase in the associated risks to public health and society.

Furthermore, although the labelling of products as R1A or R1B does not mean that products cannot be authorised for professional operators, there is a concern that products which carry specific classification and labelling (including toxic by reproduction) could not be used to protect important areas such as food factories, due to restrictions placed on professional operators by individual companies in charge of these sites. Indeed, many organisations that use professional pest control services follow protocols for the choice of products that prevent the use of those classified as toxic to reproduction at their sites (CEPA communication with the expert team).

Therefore, careful consideration is required of the practical consequences for rodent pest control and public health of the RAC opinions on AVKs, as the potential impacts of these opinions could be much wider than their effect of preventing products being used by the general public.

Restriction to indoor use

The use pattern in which baiting is restricted to 'indoors' is not one of the application scenarios proposed by the EUBEES ESD (ECHA). Consequently, we are unaware that any formal risk assessments have been conducted for this application method and the following discussion is based on qualitative assessment and the cited literature sources.

Clearly, a restriction of use of a biocidal product to 'indoors' is likely to provide the most effective mitigation against primary exposure of wildlife because wildlife does not usually frequent areas that might be considered 'indoors', with the possible exception of isolated and uninhabited farm structures, such as barns, stables and animal sheds.

Given the natural behaviour of House mice, which is frequently restricted to the 'indoor' environment (Murphy *et al*., 2005), it is likely that a regulatory mitigation restriction to 'indoor' applications would have no significant impacts on our ability to control House mouse infestations. However, the opposite is true for the control of rats. Throughout the EU, virtually all infestations of Norway rats and of roof rats will include an element of the infestation outdoors.

Indeed, in many circumstances the dominant portion of any rat infestation will be harboured outside the infested building. The inability to bait the full infested area that is imposed by an indoor only restriction will radically adversely impact the ability to exert rapid and effect control of rat infestations.

It is worthy of repeating the statement that an 'indoor' restriction of a rodenticide biocidal product is equivalent to a ban on its use to control Norway rats.

The strategy suggested in NL, for instance, excludes control of rat infestations by amateurs (see previous paragraph). To a lesser extent, FI limits the use of SGAR to indoor use for rats (amateur use), which could result in poor efficacy on resistant strains and increased selection of resistant rodents.

In many situations, the absolute purpose of a rodent pest management strategy is to prevent <u>any indoor incursion</u> of rodents. Such a strategy is intended to prevent any risk of disease transmission to humans, companion animals and farm livestock that may inhabit the buildings, to prevent structural damage to the fabric of the building and to avoid the contamination of the contents of the building with rodent faeces, urine and hair. Therefore, a restriction that only permits baits to be applied in the places where the absence of rodents is an absolute requirement appears to be entirely counter-intuitive.

Furthermore, in order to avoid the risk of possible contamination of foods with rodenticide baits, many food manufactures apply hygiene protocols that prevent the use of particulate rodenticides within factories and other facilities where foods are processed and stored. Obviously, an 'indoor' baiting restriction will prevent the use of any rodenticide anywhere at such facilities because the products would be effectively banned both 'indoors' and 'outdoors'.

Certain second-generation anticoagulants, namely brodifacoum, difethialone and flocoumafen, have been restricted to 'indoors' only use in the UK since their introductions. Surveys of rodenticide use conducted by the UK government (Figure 5) show the effects of this restriction in the very small quantities of the restricted active substance used. This is because of the consequent inability to apply them for the control of Norway rats. This restriction has resulted in three decades of the dominant use in the UK of the two active substances, bromadiolone and difenacoum, that are registered for use against Norway rats. This in turn has resulted in the subsequent spread of Norway rats that are resistant to these two compounds during the prolonged period in which effective resistance-breaking anticoagulants could not be used (Buckle and Prescott, 2013, Buckle, 2012).

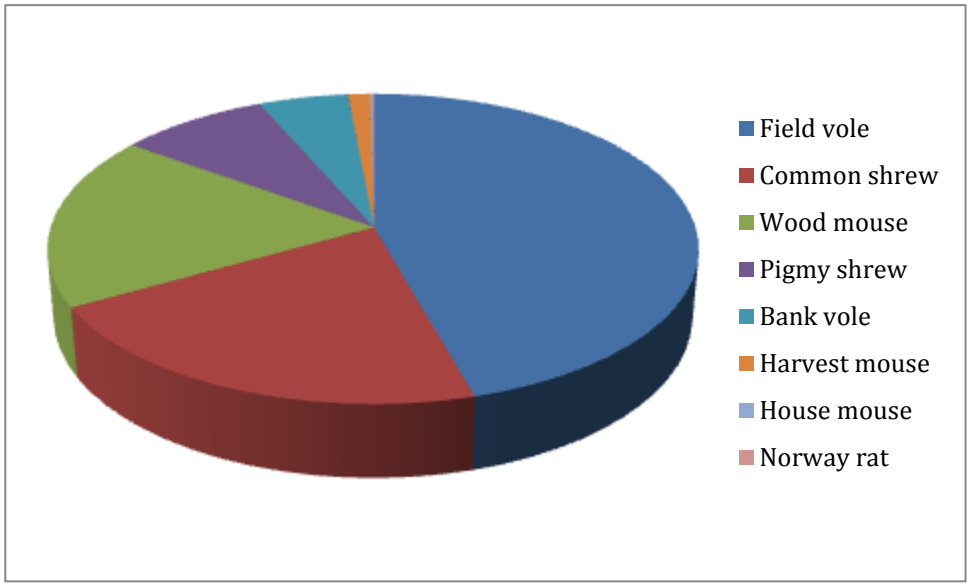
<u>Picking up dead rodents and other animals</u>

This measure is done to avoid secondary poisoning of non-target animals when they consume poisoned target animals or non-target animals. It is clearly a sensible and necessary measure. However, a key point is the requirement for safe disposal of the poisoned carcases according to local waste disposal regulations.

It is worth remembering, however, that the consumption of poisoned target rodents is only one of the sources of wildlife contamination and may not even be the main one. This is demonstrated by the fact that many species of contaminated wildlife (e.g. barn owl and kestrel) do not feed much on target rodents but feed predominantly on non-target small mammals.

Figure 4. The percentage of different prey species in the food of barn owls in the UK. The figures are aggregate data from surveys conducted in the UK during the period 1974 to 1997 and are adjusted for mean prey weight. Note: barn owl diets are very variable and the diets of individual owls may vary considerably from that shown in the figure. Adapted from: Love, A.R., Webbon,

C.E., Glue, D. and Harris, S., 2000, Changes in the food of British Barn Owls (Tyto alba) between 1974 and 1997, Mammal Review 30: 107-129.



Remove bait at the end of treatments and disposal

Users of rodenticide baits often leave them in position at the end of treatments. The usual justification for this is the possibility that rodents may return and the desire to have bait already in place when they do. This practice should be discouraged with all severity for any outdoor uses, unless there is evidence of high risk of re-infestation (based on the on-site risk assessment by PCO) Baits left down are frequently taken by non-target species, especially wild small mammals, and this is the source of wildlife exposure and contamination. It is unjustifiable to deploy a rodenticide bait in the absence of an infestation.

During the course of a treatment, bait consumption would be expected to decline as the rodent infestation is controlled. It is recommended that bait application is reduced at bait stations where there is a decline in bait take, so that during the course of the treatment, the quantity of rodenticide presented to the rodent infestation also declines.

Use of tamper-resistant bait boxes

An imperative mitigation measure in the placement of rodenticide baits is that they should not be deployed in such a way so as to be available for consumption by non-target animals. There are numerous ways to achieve this essential objective and one of them is the use of commercially-available tamper-resistant bait stations.

However, there is good evidence that rodents, in particular Norway rats, are reluctant to enter these bait boxes and to feed on baits within them. Two recent studies have demonstrated the significant negative impacts on bait consumption caused by tamper-resistant bait stations (Buckle and Prescott, 2011; Quy, 2011). The main adverse effects are to:

- delay the onset of consumption of bait by rodents, and
- reduce the quantities of bait consumed

Both of these impacts would be expected to prolong the duration of baiting programmes and, thereby, prolong the risks of non-target exposure to bait. In the survey conducted online, both

PCOs and manufacturers consider this as a major drawback to the use of tamper-resistant bait boxes.

It is difficult to conceive a stronger evolutionary pressure for the development of a trait than one in which animals that enter a device are killed and those that do not enter it survive. Therefore, it is to be anticipated that behavioural resistance to entering bait stations will develop. In the UK, there are several anecdotal reports of such behaviour in house mice. On one farm in Hampshire, Norway rats refused to enter and feed on bait in any of 30 bait boxes on the site for a period of six weeks, although they took bait from numerous other bait points that did not comprise tamper-resistant bait stations (Prescott personal observations).

Therefore, what should be mandatory is the requirement to protect baits from consumption by non-target animals. Practitioners should be permitted to achieve this objective using any available device and construction, including the use of commercial tamper-resistant bait boxes, but the use of the latter should never be mandatory for professional use.

In contrast to Norway rats, mice (*Mus* or *Apodemus*) are less likely to show an aversion to feeding from tamper resistant bait boxes, so their deployment for the control of Norway rats may generate a secondary non-target risk to predatory species that would not normally feed on Norway rats (such as Kestrel and Barn Owl).

Erection of notices to indicate presence of rodenticides

Most (if not all) CAs advise putting up notices to indicate to the public, or warn the public, that rodenticide baits are being used. This should not be mandatory.

- On the one hand, erecting notices that indicate that rodenticides are in use would raise awareness of the potential risk, and in certain circumstances could increase safety.
- However, it would also be likely to increase public interference with the bait points, either from members of the public opposed to such control programmes, or from disruptive members of the public, who would actively vandalize the bait points.
- In both the above instances, there would be a high risk that baits would be made available to non-target species.
- There are many instances where operators would be very keen for their clients' customers not to be aware that there is a pest infestation (e.g. shops, restaurants, hotels, hospitals etc.). Infestations do not indicate poor housekeeping, and it would seem counterproductive for responsible clients to be penalised when they are taking responsible action by controlling their pest problems.

Resistance Monitoring

Only a MS (France) asks for a specific resistance monitoring program from authorization holders of AR productrs. At present, such a request is difficult to fulfil (see Section 4.3.1). Genetic monitoring of VKORC1 resistance is a very useful tool, which has been used to map resistance foci in many MS (see for instance Buckle, 2012; Grandemange *et al*., 2009b; Meerburg, *et al*., 2014; Pelz *et al*., 2005). Future monitoring of resistance in the different target species should be coordinated at EU level and addressed at AS level rather than at product authorisation level. To do so, scientific advice from an independent panel is necessary to provide accurate and up-to-date maps that are available online, that can be used as the basis of a resistance Management Strategy (see Section 4.3.2).

Collaborative strategies between the companies selling products containing a given AS should be drawn up for sampling and monitoring at MS level. These strategies should be designed in consultation with the scientific panel, interested parties (authorisation holders, PCOs, etc.) and CAs, to ensure that the data generated to be made available on-line is both up-to-date and of high quality.

4 RECOMMENDED RMMS

4.1 RMMs to be set as conditions for the active substances approval:

Trained professional users will apply rodenticides for the control of infestations of House mice Roof rats and Norway rats, within commercial and residential properties, in outdoor areas surrounding these premises, and in isolated outdoor areas. When controlling rodents, they can be expected to adhere to the Product Label instructions, and in addition, to use rodenticide products in the light of their training and experience, to minimise any impact on non-target species and humans. If amateur use is restricted to the purchase of small packs, and to the application of bait against mice indoors, these conditions would appear to provide a substantial degree of mitigation against primary exposure of amateur baits to wildlife and also some protection against the contamination of wildlife through the consumption of poisoned House mice.

One of the most frequently proposed mitigation measures for rodenticides is the denial of their availability to amateur users. Many reasons may be given to justify this restriction. These include the assertion that amateurs are either unable or unwilling to read product labels and, therefore, properly to apply mitigation measures recommended on labels. It is also sometimes asserted that poor practice in application of ARs by amateurs promotes the selection of anticoagulant resistance. For example, both of these assertions are made by the German regulatory authority when denying amateur users' access to SGARs (UBA, 2014).

However, we are aware of limited evidence that amateurs are, in fact, less likely to apply rodenticide properly than other user groups, such as professional pest controllers and farmers; both of which almost certainly purchase and apply much larger quantities of rodenticides. Equally, there is no quantifiable evidence that one user group or another is more or less likely to apply ARs in ways that promote the development of resistance. On the contrary, it is readily apparent that the requirement in Germany that the only chemical rodent control interventions available to amateurs are the FGARs will promote the increased spread and severity of resistance, in both House mice and Norway rats. Resistance is already there. It is found in House mice across Germany at many locations and in Norway rats in North-West Germany (Pelz *et al*., 2005, Pelz *et al*., 2012, Esther *et al*., 2014). Amateurs will not be able to manage the species with FGARs because of the occurrence of resistance. They will select resistant individuals when using FGARs. Accumulation of ineffective ARs in resistant individuals could happen. It is doubtful that amateurs will engage PCOs in case of unsuccessful management because of the costs involved.

If amateurs are mainly concerned with control of small infestations few incidents, it is apparently wholly proportionate that amateurs should be restricted to small packs of rodenticide baits that are appropriate for such use (see UK HSE Risk assessment document ref.). See below for detailed proposals.

4.1.1 RMMs related to the user category (trained professionals, professionals and general public):

4.1.1.1 Pack size

Rationale

Assumption

There is a general consensus on the need for appropriate package size to the pattern of use and the duration of treatment. Because the uses and species may vary greatly, it is almost impossible to recommend specific pack sizes for all anticoagulant rodenticides in the EU. It seems quite reasonable, however, to encourage the production of different product sizes, different product lines and/or names, different distribution channels for amateurs and professionals or trained professionals. Therefore, it would be possible to have specific pack size recommendations, as recommended in other countries (Bradbury, 2008). Loose forms of baits such as whole grain and pellets cannot be strictly secured in bait boxes, but they are attractive to rodents and should remain available for amateur use (HSE, 2012), with even more restricted pack sizes. As a consequence, they are usually recommended to maintain good efficacy, and limited pack size should limit the risk of non-target exposure. A major source of exposure lies in the storage of commercial products and availability of large quantities of bait to non-target species. Indeed, there is evidence (from interviews with animal poison control centre specialists) that pets may be exposed by chewing on cardboard bait boxes. As a consequence, in the long term, replacing cardboard boxes by more resistant boxes or even restricting amateur packs to non-refillable bait boxes could be considered.

The following recommendations are based on the following formula:

Pack size = IxDxCxT with

- I: number of individuals to control: 5 for rats, 10 for mice
- D: number of days necessary to reach a lethal dose (5 days for 1st generation, 1 day for SGAR)
- C: daily consumption of one rat (30g or less) or one mouse (10g or less)
- T: avoidance factor (arbitrary set at 1 for wax block and 0.5 for gel, pellets, grain).

Recommendation: Pack size limitation for amateurs

As general recommendations, for most products, the following suggestions can be made for amateurs (Table 4)

Table 4: Suggested maximum pack size for anticoagulant rodenticides for amateur use

Target species	Bait type	Pack size (g) FGAR	Pack size (g) SGAR
Mice only	Grain, pellet	<250	<50
	Wax block	<500	<100
	Paste	<250	<50
	Gel	1 tube (<250g)	1 tube (<50g)
Mice and rats	Grain, pellet	<750	<150
	Wax block	<1,500	<300
	Paste	<750	<150
Norway rats	Grain, pellet	<750	<150
	Wax block	<1,500	<300
	Paste	<750	<150
Black rats	Grain pellet	<750	<150
	Paste	<1,500	<300

It seems important to distinguish clearly products designed for professional use and products for amateur use, at least based on the package size and, if possible, with different names, in order to avoid confusion and erroneous distribution of large amounts of rodenticides to amateurs.

In the long term, replacing cardboard boxes by more resistant boxes or even restricting amateur packs to non-refillable bait boxes could be considered, in order to reduce accidental non-target species exposure, keeping in mind the high economic and environmental cost of such decisions, as well as the potential risk of decreasing the number of bait points, thereby reducing efficacy.

Benefits

- Reduced amount available and potential primary non-target accidental exposure
- Reduced risk of accidental exposure to humans

Limitations

- Revision of current products with respect to recommended pack size / material
- Economic and environmental cost
- Limitation of baiting points

4.1.1.2 Target species active substance approval

4.1.1.2.1 First generation AR

Rationale

Scientific evidence

First generation anticoagulant rodenticides (FGAR) have been developed in the early 60s to control target rodent populations (rats and mice). Unfortunately, resistance was rapidly detected in three species (*R. norvegicus, R. rattus, M. domesticus*). In Norway rats, resistance may be linked to a genetic modification of the target enzyme VKOR (Li *et al*., 2004, Rost *et al*., 2004) or to increased metabolism (Ishizuka *et al*., 2006). The prevalence of resistance may be high in both rural and urban settings (Baert *et al*., 2012; Grandemange *et al*., 2009b)}. In Roof rats, there is very little published evidence on acquired genetic resistance. An early survey in the UK found warfarin resistance to be widespread in the north west of the country, with subsequent breeding studies indicating a multifactorial basis for resistance (Greaves *et al*., 1976). Genetic resistance has been reported for a Japanese strain (Tanaka *et al*., 2012), and metabolic resistance has been described in Japan and elsewhere (Ishizuka *et al*., 2006). It is generally accepted that House mice are less susceptible to FGAR than Norway rats (Buckle, 1994). In a recent publication, Pelz *et al*. (2012) showed that several mutations are present in House mice in Germany and confer resistance to FGARs (as well as some SGARs). One combination of the genetic mutations is associated with introgression of 3 mutations from the Algerian mouse (*Mus spretus*), as demonstrated by Song *et al*. (2011). There is also evidence of metabolic resistance against FGAR in House mice (Sutcliffe *et al*., 1990).

Amateurs are usually concerned with House mice infestations, but may sometimes be faced with Norway rat infestations.

Resistance in Norway rats and House mice is widespread, and will increase when ineffective ARs are used. Where resistance is suspected, the VKORC1 mutation should be determined, unless VKORC1 data is already available for the location of the infestation. ARs should only be used against rodent populations where there is good evidence that they will be effective. Resistance guideline documents should be produced and regularly updated (see RRAG, 2010; RRAG, 2012[a]), and restrictions on the use of selected ARs should be based on the VKORC1 mutations of the resistant population.

Amateurs should have access to effective anticoagulant rodenticides, with restrictions on pack size, and methods of bait application (e.g. tamper-resistant bait boxes). Provision of adequate information to the general public is essential. (see Section 4.3.6)

Recommendation: not recommended use for mice

FGARs should only be used against susceptible species, when there is no risk of selecting mutated individuals. Applying FGARs without prior evidence of the absence of resistance will select mutated rodents. This seems particularly of concern for House mice. As a consequence, label recommendations, training and information about rodenticides and their correct use should be available to the general public (see Section 4.3.6).

Norway rat: all first generation products may control susceptible Norway rat infestations, when properly used. Outside known resistance areas recommendation is made to consider resistance when correct rodenticide application fails to control infestation. In rural areas, Norway rats may

be present in/around buildings and be a source of nuisance for amateurs. It is important to maintain active substances that can be safely used for rat control by amateurs.

Roof rat: roof rats are less susceptible to FGARs than Norway rats and FGARs may fail to control infestations even when properly used. Recommendation is made to consider resistance when correct rodenticide application fails to control infestation. Roof rats are a minor threat in the northern parts of the EU but are more significant pests in the countries of the south.

House mouse: approval of FGARs for use in House mice should be conditional on the demonstration of appropriate efficacy in field trials. This recommendation should extend to bromadiolone and difenacoum. Restricting amateur use to FGARs is most likely to result in a severe lack of AR efficacy against most House mice infestations in Europe.

Benefits

- Decrease selection pressure for resistant rodents with low-efficacy rodenticides
- Limit resistance spread
- Better management results (i.e. improved efficacy) and limited use of rodenticides

Limitations

- Higher risk of primary poisoning of non-target species if improper use
- Higher risk of secondary poisoning

4.1.1.3 Low potency vs high potency SGARs

Rationale

Assumptions/Scientific evidence

In order to overcome resistance of rodents to FGARs, new rodenticides were developed (2nd generation AR or SGAR), with higher efficacy. These rodenticides are often active after a single feeding, but are also more toxic for non-target species than FGARs. SGARs can be further divided in "low potency SGARs" (bromadiolone, difenacoum) and "high potency SGARs"(brodifacoum, difethialone, flocoumafen). Some mutations or other genetic alterations may induce resistance to low potency SGARs, as observed in the UK and Germany for instance (Buckle, 2012, Pelz *et al*. 2007), and quite commonly in mice (Pelz *et al*. 2012). As of today, there is no evidence of practical resistance to any of the latter compounds (see 4.5 in preliminary report). It many situations, low potency SGARs will not control rodent populations effectively and this will result in resistance selection, prolonged use and risk to non-target species (Buckle, 2012).

Recommendation: use in case of resistance, all user categories

The use of high potency SGARs should be considered as a primary tool, when there is definite evidence of resistance (including lack of efficacy, *in vitro* or *in vivo* confirmation of resistance). The use of high potency SGARs in open areas should be considered only when there is documented evidence of resistance and for short duration of treatments (i.e. pulse baiting strategy). SGARs for amateurs may be considered in and around buildings only, especially for use against rats. High potency SGARs should be readily available for amateur use indoors against mice, considering the limited efficacy of other FGARs or low potency SGARs, and provided bait is only available in bait boxes, with limited pack size (see other RMMs).

Benefits

- Reduce outdoor uses

- Apply high potency SGAR when necessary.

Limitations

- Non-target Risk (primary and secondary poisoning)

4.1.1.4 Areas of use

General information

Unlike many other categories of biocide, which may be frequently applied in specific use situations, rodent infestations arise in a vast array of circumstances. Any attempt to list or to categorise these situations is extremely difficult because of their wide variety. Because of their inherent commensal behaviour, in which they actively select close co-existence with humans, rodents have the potential to impact adversely almost every human industrial, agricultural, commercial, social and personal activity in the EU. However, each rodent infestation is different from any other and each requires a different approach to obtain satisfactory rodent pest management.

Many industry hygiene standards, accreditation procedures for industry and commerce and auditing arrangements state categorically that procedures must be in place to prevent rodent infestation of any area involved in these processes. Therefore, it is not sufficient merely to manage extant infestations in places where they currently occur but it is mandatory to exert due diligence to prevent the establishment of rodent infestations in any areas where they may occur. This necessity makes even broader the potential use areas for rodenticides.

EUBEES Emission Scenario Document Use Areas

Four main rodenticide treatment scenarios were proposed during the review of rodenticides conducted by the European Commission (EC) for the Biocidal Products Directive (BPD) and the consequent Regulation (BPR).

1. 'In and around buildings'
2. 'Sewers'
3. 'Open areas'
4. 'Waste dumps'

These scenarios were explicitly described in the EUBEES Emission Scenario Document (ESD) for PT 14 active substances (ECHA). They encompass the majority of rodent control operations involving the applications of PT14 active substances in the EU. Other definitions of rodenticide use patterns may be applied in certain MSs and are mentioned below.

Rationale: "In and around buildings"

Assumptions

The most common use scenario for both rat and mouse control is the one described in the EUBEES ESD as 'in and around buildings'. This involves the use of rodenticides to control rodent pests infesting buildings and the environs of buildings.

In this context, no universally-applied definition is available for a 'building'. It is apparent that such a definition is required if the term 'in and around buildings' is to be used in the text of rodenticide product labels that proscribe a legally permitted pattern of use. It is beyond the scope of this document and the remit of the current project to propose such a definition, but consideration should be given to the following aspects:

- The materials from which the fabric of the building is constructed and whether or not they can be easily penetrated.
- The configuration of the structure in terms of wall, roofs, doors, etc.

- The capability of the structure to prevent access to the areas within, for example to humans, companion animals and wildlife, and hence the ability of the building to prevent access to rodenticide baits placed within it.
- The permanence of the structure.
- The behaviour of rodent pests when they encounter the structure and their ability to exist within it.

Whatever definition is applied, buildings capable of infestation by rodents may include domestic properties, commercial premises, farm buildings, store-houses, warehouses, grain stores, municipal buildings such as schools, hospitals and offices, animal husbandry facilities, such as stables, milking parlours, cow sheds, chicken sheds and pig arks, any building concerned in the storage, preparation, distribution, sale and consumption of food, any mode of transport including aeroplanes, trains, ships, commercial and private transport vehicles, etc.

Those applying rodenticides "in and around buildings" include "professionals", "trained professionals" and "amateurs" (i.e. the general public).

House mice usually restrict their activity to within the buildings they infest and, therefore, rodenticide applications within infested buildings may be fully effective in their control. Conversely, infestations of Norway rats and roof rats are very rarely restricted to the buildings that they infest. Indeed, it is universal throughout the EU that rat infestations comprise elements situated outside buildings. Therefore, rodenticide applications aimed at the removal of rat infestations in the built environment usually involve a major element in which rodenticides are applied around the infested building. Such applications have the added and essential benefit that the baits are set so as to prevent rodent ingress into building, which is precisely the area that rodent management procedures are aimed to protect. For this reason, the 'in and around buildings' scenario is fundamental in the EU to effective control of Norway rats and roof rats.

The permitted use of a rodenticide in this way is defined by the EU guidance as follows (European Commission, 2009):

'In and around buildings' shall be understood as the building itself, and the area around the building that needs to be treated in order to deal with the infestation of the building. This would cover uses in sewer system or ships but not in waste dumps or open areas such as farmlands, parks or golf courses.

Recommendation: all categories of users may have access to AR for use "in and around buildings"

Buildings are generally thought to be associated with human activity, although the degree of human activity will vary greatly depending on who has permission of access, location and type of use. Nevertheless, a reasonable assumption is that any restriction of bait application to the building and its environs will exert a reduction in the risk of non-target exposure. Two considerations underlie this position. The first is that there may be a greater degree of vigilance of rodenticide applications around buildings because those inhabiting them, or working within them, are present either continuously or periodically and may be required to conduct inspections of baits and to pick up and dispose of dead rodents. The second is that the potential for interactions between non-target wildlife and baits, and between poisoned rodents and predatory and scavenging wildlife, is likely to be less than in areas away from buildings because activity associated with the building, including human activity and disturbance caused by sound, light and any companion animals present, is likely to deter the presence of most wildlife species. Of course, once again, this protection will be variable depending on the same considerations as mentioned previously.

Therefore, a product authorisation, which restricts rodenticide use to 'in and around buildings', would be anticipated to offer a degree of risk mitigation against primary and secondary exposure of wildlife when compared to an authorisation which permits 'open area' use (see below). The degree of risk reduction will vary according to the type of building under consideration, as illustrated by the following examples. An isolated farm building, situated far from any area of human activity, may be considered by some species of wildlife to be merely another area of 'natural habitat', perhaps providing both cover and food. This building will provide only limited mitigation of exposure risk to wildlife. Conversely, an occupied human dwelling with frequent, and perhaps continuous, human disturbance will not be attractive to the majority of wildlife species. Baiting in and around such buildings may provide a significant degree of risk reduction of wildlife exposure. In reality, the majority of buildings which are referred to by the 'in and around buildings' use pattern scenario will fall between these two extremes in terms of the access of wildlife to them.

Of course, applications of baits around buildings, and therefore in places where human activity is found brings other exposure risks; specifically risks to humans and to companion animals. These risks would require appropriate mitigation by other means, such as the use of tamper-resistant bait boxes. **Consequently, all categories of users may have access to AR for use "in and around buildings" with other appropriate RMMs (bait boxes, pack size etc.).**

Rationale: Sewers

Assumptions

Sewer systems are ideal habitats for Norway rats, with a nearly perfect living environment including moderate temperatures, abundant cover when the fabric of systems is in a poor state of repair as is the case in most cities and the constant provision of foodstuffs. Attention is therefore given to these systems for the control of rat infestations within the scope of the public health and hygiene arrangements made by those agencies, such as water authorities and local government bodies, which are responsible for provision of pest control within sewers. Sewer systems provide permanent refugia for large rat infestations, which may make repeated incursions above ground. Consequently, sewers are often subject to regular control measures, especially in pre-determined critical infestation areas. Virtually none of the alternatives to rodenticides, such as habitat modification, gassing and trapping, are appropriate for use in sewers and rodenticide applications are the only practical option for the management of rats in sewers.

The treatment of sewer systems with rodenticides is a highly specialised task. A detailed explanation of the conduct of sewer baiting programmes is provided by the UK Chartered Institute of Environmental Health for instance (CIEH, 2013). Generally, sewer treatments are conducted by specialised teams. These are either employees of water authorities or local government agencies or they are provided by professional pest control companies contracted for the task by such agencies. Specialist equipment is frequently needed to free manhole covers, where they have been overlaid by road surfaces, and to lift the heavy manhole covers. Due to the position of sewer systems, rodenticide treatments often include a requirement for measures to control road traffic and the various legal provisions that this necessitates.

Because of the high humidity level in these systems, moisture-resistant wax blocks or similar formulations containing a rodenticide, which provide long palatability, are often used. Due to the extreme difficulties of gaining access to bait points, and to the size of sewer infestations, it is often necessary to employ larger than normal quantities of rodenticide baits. Also, the frequency of visits to check and to replenish baits is often less than normal.

Recommendation: use in sewers only for properly trained professionals

Due to the structure of the sewer systems and the extreme difficulties, and sometimes dangers, of gaining access to sewers, the risk of primary poisoning of humans and non-target organisms is relatively low, because access to bait is highly restricted. Likewise, pest animals that take the baits put in sewers, and subsequently die within them, are unlikely to be readily available to predators and scavengers, especially predatory birds. Therefore, a restriction placed upon the use of a rodenticide product that it may only be applied in sewers is likely to provide a very substantial level of mitigation against risks of both primary and secondary exposure of non-targets. **Considering the difficulties and dangers associated with access to the sewer system, usage in sewers is only acceptable for properly trained professionals.**

However, when sewer baits are poorly anchored, or where it is not possible to secure them in place because of the construction of the sewer, baits may be dislodged and may enter the sewer flow. The fate of these baits is then determined by the systems employed for the management of the sewer waste stream, including filters, screens, overflows etc. Similarly, when poisoned rodents die and fall into the sewer flow, an opportunity exists for secondary exposure, depending on the nature of the treatments applied at sewer outfalls.

Rationale: Open Areas

Assumptions

Rodent infestations, in particular infestations of rats, may become established away from buildings. This occurs in circumstances where food and cover is available, indeed these situations may be particularly attractive to rats because they are sometimes less disturbed by human activity. Therefore, it may also be necessary for rodenticides to be applied away from buildings. The sites where such applications are made are referred to in the EUBEES ESD (ECHA) as 'open areas'.

'Open areas' where rodents become established are extremely diverse. For example, within the urban environment, rats may be present in areas such as parks, gardens, playgrounds, private or public forests, and other amenity areas where people consume food and feed wildfowl. Railway embankments and sidings, canal banks and sports grounds may also provide rodent habitats. Other urban situations away from buildings where rat infestations may become established are railway embankments and marshalling yards, canal embankments and locks, airfields, building sites, waste ground etc. In all these places rats may inflict severe and sometimes hazardous damage to infrastructure. Other 'open area' scenarios are associated with a very wide range of agricultural activities, particularly those involving the rearing of free-range and outdoor livestock, such as pigs and poultry. It should be noted, however, in the context of agriculture that the protection of growing crops, both in the open field and in glass-houses as well as the protection of in-field crop storage facilities, is not a rodenticide use that is regulated within the Biocidal Products Regulations and is not, therefore, the subject of this document. Such use is, instead, regulated by the Plant Protection Products regulations (CE1107/2009). Other 'open area' use scenarios include where rodent infestations become established in hedgerows and at rearing-pens where supplemental food is provided in the husbandry of game-birds. Rodenticides are also used for the protection of wildlife, in particular ground-nesting seabirds on islands, and this is also an "open area" use.

Use of rodenticides away from buildings, and in open areas, is generally considered to bring with it greater risk to wildlife than use 'in and around buildings'. This is because of the general principle that there will be a greater abundance of wildlife in places which are not built-up and which do not have the human activity that is usually associated with buildings. It would be anticipated, therefore, that any permission for use of rodenticide biocidal products, which includes approval for application in 'open areas', will bring with it a greater risk of exposure to both primary and secondary non-target wildlife species.

The consumption of poisoned target rodents is only one of the sources of contamination for secondary non-target scavenging and predatory species. Certain species, such as barn owl and kestrel, that are reported to be widely contaminated with anticoagulants, are unlikely to consume target rodents, and would be expected to feed predominantly on non-target small mammals, in particular mice and voles. Such non-target small mammals are likely to have a ubiquitous distribution in open areas, and will readily consume rodenticides as soon as they become available. Thus in the absence of target species, there would normally be an active route of contamination for secondary non-target predatory and scavenging species as soon as the baits are set out.

Generally speaking, bait presentation systems specifically designed to avoid bait consumption by non-target species should be developed and these would be particularly appropriate for use in open areas.

Recommendation: use in open areas only for trained professionals

Open areas are frequently private lands from which human ingress is prohibited by legal denial of access. Therefore, bait applications in open areas, which are privately owned, such as farmland, woodland, hedgerows and other private land would not be expected to exert a significant risk of exposure to human bystanders and to companion animals. In some countries (Germany), private woodland may still be accessible to the general public and, therefore, be considered as situations of high risk of exposure, both primary and secondary, of non-target species.

Of course, an exception to these considerations are those 'open areas' in urban environments, such as parks, gardens, playgrounds and other areas of public access for amenity purposes. In this case the above considerations are reversed and there is a greater probability of exposure of humans and companion animals to any bait deployed in these areas, and a lesser likelihood of exposure to wildlife.

Consequently, use in open areas should be considered only for trained professionals, in order to ensure maximum protection and efficacy of the AR application.

Use of adapted devices preventing access to rodenticide by many non-target species including invertebrates, small mammals and birds, in the absence of the target rodents could also provide an interesting tool for use in open areas by trained professionals.

Rationale: Waste Dumps

Assumptions

Waste dumps are a very specific rodenticide use scenario, which was included in the EUBEES ESD (ECHA). They may be considered to be a special type of 'open area'. Waste-handling facilities, such as landfill sites, recycling centres and municipal composting facilities, provide good habitats for the development of rodent infestations because of the abundant food available, although the degree of food availability is greatly dependent upon waste management operations and practices carried out at the site. Frequent covering of the 'open face', where waste is deposited, reduces food availability.

Waste dumps also attract a wide range of wildlife species, and large numbers of individuals of these species may congregate at these facilities, once again because of the plentiful food available. Usually, access to waste dumps by humans is limited because of safety considerations and there are few risks to human bystanders and companion animals. However, as a special case, waste dumps might be considered to pose a greater risk of wildlife exposure to rodenticides than 'open areas' because of: 1) the greater concentration of wildlife at these sites, 2) the greater

numbers of pest rodents present and, 3) the larger quantities of rodenticides applied to combat the rodent infestations.

Recommendation: use in Waste Dumps only for trained professionals

There is ample evidence that a variety of wildlife species can visit waste dump facilities, notably because of the availability of food. Predators and scavengers may also be present and feed on dead rodents. **As a consequence, restricting use to trained professionals only should be considered in order to ensure maximum protection and efficacy of the AR application**. This is most likely in line with access restrictions for waste management facilities.

Rationale: use in and around buildings for rats

The use pattern in which baiting is restricted to 'indoors' is not one of the application scenarios proposed by the EUBEES ESD (ECHA). Consequently, we are unaware that any formal risk assessments have been conducted for this application method and the following discussion is based on qualitative assessment and the cited literature sources.

Clearly, a restriction of use of a biocidal product to 'indoors' is likely to provide the most effective mitigation against primary exposure of wildlife because wildlife does not usually frequent areas that might be considered 'indoors', with the possible exception of isolated and uninhabited farm structures, such as barns, stables and animal sheds.

Given the natural behaviour of House mice, which is frequently restricted to the 'indoor' environment (Murphy *et al*., 2005), it is likely that a regulatory mitigation restriction to 'indoor' applications would have no significant impacts on our ability to control House mouse infestations. However, the opposite is true for the control of rats. Throughout the EU, virtually all infestations of Norway rats and of roof rats will include an element of the infestation outdoors. Indeed, in many circumstances the dominant portion of any rat infestation will be harboured outside the infested building. The inability to bait the full infested area that is imposed by an indoor only restriction will radically adversely impact the ability to exert rapid and effect control of rat infestations.

It is worthy of repeating the statement that an 'indoor' restriction of a rodenticide biocidal product is equivalent to a ban on its use to control Norway rats.

In many situations, the absolute purpose of a rodent pest management strategy is to prevent any indoor incursion of rodents. Such a strategy is intended to prevent any risk of disease transmission to the humans, companion animals and farm livestock that may inhabit the buildings, to prevent structural damage to the fabric of the building and to avoid the contamination of the contents of the building with rodent faeces, urine and hair. Therefore, a restriction that only permits baits to be applied in the places where the absence of rodents is an absolute requirement appears to be entirely counter-intuitive.

Furthermore, in order to avoid the risk of possible contamination of foods with rodenticide baits, many food manufactures apply hygiene protocols that prevent the use of particulate rodenticides within factories and other facilities where foods are processed and stored. Obviously, an 'indoor' baiting restriction will prevent the use of any rodenticide anywhere at such facilities because the products would be effectively banned both 'indoors' and 'outdoors'.

Certain second-generation anticoagulants, namely brodifacoum, difethialone and flocoumafen, have been restricted to 'indoors' only in the use in the UK since their introductions. Surveys of rodenticide use conducted by the UK government (Figure 5) show the effects of this restriction in the very small quantities of the restricted active substance used. This is because of the consequent inability to apply them for the control of Norway rats. This restriction has resulted in three decades of the dominant use in the UK of the two active substances, bromadiolone and

difenacoum, that are capable of use against Norway rats. This in turn as resulted in the subsequent spread of Norway rats that are resistant to these two compounds during the prolonged period in which effective resistance-breaking anticoagulants could not be used (Buckle, 2012; Buckle and Prescott, 2013).

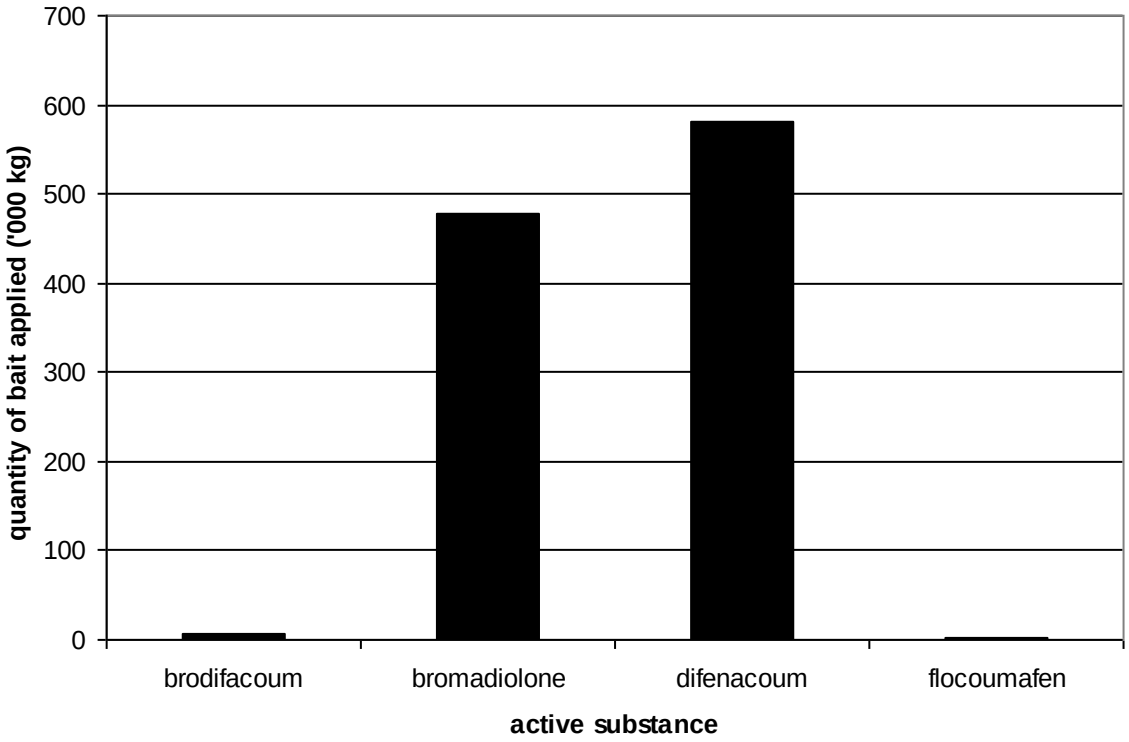


Figure 5: The quantities of brodifacoum, bromadiolone, difenacoum and flocoumafen used on farms in Great Britain growing arable crops. Results of a survey conducted by the UK Department for Environment, Food and Rural Affairs in the year 2000.

Recommendation: use in and around buildings for Norway rats and all user categories

It is suggested to allow in and around building use of AR, even for amateurs, in order to provide adequate control of Norway rat populations, usually associated with an outdoor burrow. The other RMMs (pack size limitation, duration of baiting etc.) should provide adequate restrictions to protect non-target species and limit the risk of resistance selection.

Benefits

- Clear definition of areas of use per user category
- Adapted restrictions

Limitations

- Risk of primary and secondary poisoning

4.1.2 RMMs addressing primary poisoning:

4.1.2.1 Dyes

Rationale

Assumptions

A safety measure intended to reduce the risk of the rodenticide bait being mistaken for a food item, for livestock feed or any other non-toxic product is the use of warning dye. Dyes mark the bait as unnatural or adulterated and may serve to indicate what toxicant is being used. This can simplify enforcement of proper rodenticide use in the field, as the dispersed grain is identified by its colour. The use of brightly coloured dyes is also thought to be valuable in deterring rodenticide bait consumption by birds, thereby reducing non-target hazards to some species and making control efforts more environmentally safe (Brunner and Coman, 1983; Moran,1999).

Scientific evidence

Colouring rodent baits helps people distinguish toxic baits from food or feed, thus preventing accidents caused by human errors (Marsh, 1985). Several studies have shown that the incorporation of dye to the rodenticide bait has potential to reduce the risk of birds feeding on the bait if accidental exposure occurs (e.g. Kalmbach and Welch, 1946) but see Jacob and Leukers (2008). While birds can see colours rodents cannot and therefore, food colour should not affect feeding behaviour (Godfrey, 1989). The addition of dyes to a grain bait resulted in no significant differences in consumption by Norway rats, California ground squirrels and pocket gophers (Salmon and Dochtermann, 2006) but it did reduce food consumption in common voles by 10% (Jacob *et al*. 2010).

Recommendations: add a specific dye in baits

Despite of somewhat lower bait consumption in some rodent species the inclusion of warning dye to rodenticides is a mandatory risk mitigation measure to indicate poison for human and avoid human poisoning. A single colour for all AR would be helpful to distinguish them from other pest control products and to detect spillage easily. Non-metabolised dyes may also be helpful in identifying exposure of both rodent target and non-target species by visual examination of stools. Use of a common blue or green dye could be a good warning sign of the presence of an AR. Modification of any formulation to include a dye should be regarded a minor change of formulation and not result in extensive rodent testing for product registration, since rodents are not affected by colours.

Benefits

- clear warning sign
- little impact on bait consumption
- indicator of potential non-target exposure if detected in stools

Limitations

- cost of introducing uniform dye
- regulatory requirements if animal testing is requested (may be limited)

4.1.2.2 Bittering agents

Rationale

Assumptions/Scientific evidence

Inadvertent consumption of rodenticide bait, particularly by children, is always a concern, and with this in mind, the human taste deterrent denatonium benzoate is frequently incorporated into rodenticide formulations to deter consumption by humans. Denatonium benzoate is

manufactured by several companies. Denatonium benzoate is a very effective human repellent when incorporated in baits at a strength of 0.001%, but with no measurable effect on consumption by rodents (Kaukeinen and Buckle, 1992). The incorporation of denatonium benzoate in bait formulations is unlikely to reduce the frequency of accidental exposure to humans, but is likely to reduce the amount of rodenticide consumed, and thus the severity of any possible adverse effects. However, the inclusion of a bittering agent may act to increase the number of reported exposure cases because of the very unpleasant experience of sampling a bait containing a bittering substance.

Recommendation: add a bittering agent at a harmonised concentration across MS

It is recommended that a bittering agent be incorporated in all rodenticide formulations. The current 0.001% concentration of denatonium benzoate is acceptable for that matter.

4.1.2.3 Area of use

4.1.2.3.1 Baiting area and survey

Rationale

Assumptions

Thorough survey of the infested area is an absolute prerequisite before any rodenticide treatments are considered. This survey covers commonly the pest species, their activity areas and the extent of the infestation.

The label instructions give guidance on the number and spacing of bait points. Guidance from best practice codes (e.g. CSL, 2002; CRRU, 2012) can be used to create a successful baiting strategy.

The area classification is based on assumptions concerning risks for non-targets, the suitability as reservoirs, breeding places and animal behaviour. Rodent infestations appear in various types of areas requiring different approaches to obtain satisfactory rodent control. Areas types are classified in “sewers”, “in and around buildings”, “open areas” and “waste dumps”.

Sewer systems are very suitable as reservoirs and breeding places for rat infestations. Due to their structure a risk for primary and secondary poisoning of humans and non-target organisms seems to be very low (CEFIC, 2013). House mice infestations seem to be mainly restricted within buildings. Consequently their control in buildings with SGARs is normally effective and constitutes little risk to non-target wildlife outside. In contrast, Norway rats are very rarely restricted to buildings and their movement within the wider environment presents a risk of secondary poisoning.

The application of baits around buildings and in open areas is generally considered to be associated with greater risk to wildlife because of the comparative abundance of wildlife in these places and easy access to bait if best practice guidance is not followed (CEFIC, 2013).

Waste dumps often contain a source of plentiful food and may attract a wide range of wildlife species, and large numbers of individuals of these species. Waste dumps are considered to pose a greater risk to wildlife than other open areas during SGAR application (CEFIC, 2013). There are usually few risks to human bystanders, because in general access to waste dumps by humans is strictly limited.

In all scenarios one important point of best practice codes is to ensure an optimal number and distribution of bait points (CRRU, 2012 http://www.thinkwildlife.org/crru-code/). Rodenticide applications often fail to eradicate rodent infestations quickly because too little bait and/or too few bait points are used (CEFIC, 2013). Treatments are conducted most safely when they are efficient and quick. Poorly applied bait left out for long periods is both ineffective and creates a long-term risk to non-target animals and the environment (CEFIC, 2013). The risk of primary and secondary poisoning and the ability of selecting resistance may increase.

The label may provide a range of bait point sizes to permit the user to judge infestation size and bait different infestations appropriately.

Besides the placement of surface bait stations, it is a common practice to place rodenticide baits directly into rat burrows. This may result in rapid bait uptake and efficient treatments, especially when rodents are neophobic and avoid bait stations. It is unlikely that non-target animals utilise active rodent burrows (CEFIC, 2013). It is recommended to put bait as deep into the burrow as possible and to block the burrow with grass, paper or foliage. Such baiting may result in spillage of bait outside the treated burrow, because baits may be ejected by rats from the baited burrows. In most cases, it may be difficult to retrieve uneaten baits from baited burrows after rodent control. In addition the documentation of bait consumption is almost impossible. According to HSE (2012) it is agreed that in certain circumstances burrow baiting has been found to be an efficient method of bait placement offsetting the risk for bait to be spilled or pushed out of the burrow into the surrounding area, with the potential for primary poisoning of non-target species. To minimise such risk it should be mandatory to visit burrow baited sites daily, preferably in the early morning, to monitor spillage and if necessary clean up spilled bait.

RMMs follow the area classification and product permissions for selected areas are possible.

Scientific evidence

House mice in most of northern Europe restrict their activities predominantly to within buildings (Lund, 1994; Murphy *et al*., 2005).

A study by Endepols *et al*. (2003) showed that Norway rat feeding activity on farms was predominantly located outdoors at 'old materials' and 'stacks', which indicates that complete reliance on indoor baiting might reduce control success. The control of rodents around building constitutes a potential risk to human bystanders, non-target companion animals and wildlife. In the direct surrounding of in and around treated farm buildings anticoagulant residues in non-target animals occur (Broll *et al*., 2014).

Rat control treatments conducted under best practice codes are highly effective (Endepols *et al*., 2003). By using enough bait points the rodent control treatment will be conducted most efficiently and in the shortest possible time. Especially for the rodent control on livestock farms, an interactive rodent control program can support in allocating baiting-points to specific structural elements to ensure complete rodent eradication (Endepols *et al*., 2003).

In resistance areas infested with Norway rats carrying Y139C polymorphism the use of bromadiolone or difenacoum is inappropriate, because high amounts of bait are released into the environment with no effect on rodent control (Endepols *et al*. 2012a, Buckle *et al*. 2012).

Recommendation: survey sites before rodenticide use

Thorough survey of the infested area should be an absolute prerequisite before any rodenticide treatments are considered. The survey should cover beside the pest species, their activity areas

and the extent of the infestation, the indications of the presence of non-target animals including humans, children, domestic animals and wildlife (CRRU, 2012). Rat control treatments should follow best practice codes (e.g. CSL, 2002; CRRU, 2012). When infestation extends beyond the boundaries of the site, the neighbouring infested sites should also be treated.

It is strictly recommended to follow label instructions concerning the number and spacing of bait points, the range of bait point sizes to permit the user to judge infestation size and bait different infestations appropriately.

The differentiation between areas "sewers", "open areas" and "waste dumps" seems to be meaningful. The differentiation between "in buildings" and "around buildings" is sensible because of differences in risk for non-targets and pest species behaviour.

4.1.2.3.2 Baiting area and information on baiting area

Rationale

Assumption

Some CAs advise putting up notices to indicate to the public, or warn the public, that rodenticide baits are being used.

For the reasons given in section 3.5 of this report, it is the experts' experience that putting up information / warnings on the presence of toxic substances in a given environment may result in illicit use of the product. A Plant Protection Product issued specific warnings on the toxicity of aldicarb and other carbamate insecticides in France in the early 2000 and this campaign resulted in an increased number of poisoned dogs and cats as a consequence of deviant use (Vetagro Sup, Toxicology laboratory personal communication).

Recommendation: avoid posting information on baiting areas

From the previous discussion, it appears that displaying information on bait application may be a reasonable RMM, but also that it may draw unwanted attention to the presence of baits and of rodents. It is the experts' opinion that information should be clearly available on the bait box itself to prevent accidental exposure, but that requiring general information such as signposting on the application of AR in any given site does not provide increased security for the general public and non-target animal species. In some instances, it is even counterproductive and people may look for and steal bait boxes if a sign is posted. The baiting of public areas is invariably conducted by professional pest control technicians, often under the control of local government officials. The decision about displaying warning signs should be made on a site-by-site basis at the discretion of competent and trained professionals after an appropriate risk assessment. It should not be a mandatory requirement.

This issue should also be considered on a regulatory basis to determine liability of rodenticide applicator in case of accidental exposure with or without posting general information.

Benefits

- Simplify management of baiting area
- Increasing safety of application of bait boxes without undue attraction

Limitations

- regulatory requirement and liability of PCO

4.1.3 RMMs addressing secondary poisoning:

4.1.3.1 Duration of baiting

Rationale

Assumptions

Until now the duration of anticoagulant application depends on the kind of compound, rodent species, recommendations of the producers, experience of controllers, persistence of infestations and management strategies. Applications of rodenticides are usually, and preferably, conducted over a limited period of time. They commence when an operational necessity for such an application is identified. Usually, this is the discovery of an extant rodent infestation. The baiting operation begins, is conducted over a period time, and ceases when the pest infestation is either completely removed or is reduced to such a level at which it is no longer considered to be problematic.

The duration of the application is influenced by a very wide array of factors, which include, but are not limited to, the following:

- The pest species involved. House mice and roof rats are generally less susceptible to the anticoagulant rodenticides and infestations of them may take longer to control than those of Norway rats.
- The size of the infestation. Larger infestations may take longer to control than smaller ones.
- The efficiency of the rodenticide application. Where bait points are deployed appropriately, and they are effectively and regularly replenished with bait so that baits remain available throughout the baiting effort, the duration of applications required to eradicate rodent infestations will be short. However, baiting will be prolonged if insufficient bait points are set out and if these are permitted to run out of bait during the treatment. Greaves *et al*. (1988) showed that the quantity of bait put out at bait points, the frequency of bait replenishment and the toxicity of baits all play an important role in treatment duration.
- The type of bait used. Some baits, and active substances, are more palatable to rodents than others and the less palatable biocidal products may take longer to control infestations than those that are more palatable.
- Availability of alternative food. All bait applications rely on the fact that rodents will forego their habitual foods and will switch to rodenticide baits. The willingness of rodents to switch is affected by many considerations including (among others): the nature (i.e. attractiveness) of alternative foods and the baits that are presented, the ease of access to foods and to baits, the degree of intraspecific competition for both natural foods and baits, the positions of competing foods and baits in terms of the protection that placements may offer from predators. It has been shown that, where Norway rat infestations have long-established feeding behaviours because they have been feeding for very long periods from a single, easily available food source, it is extremely difficult to cause the infestation to sample any new food, including rodenticide baits (Quy *et al*., 1992). In such situations, very prolonged applications may be required in order to achieve removal of rodent infestations (Greaves *et al*., 1982).
- Behavioural traits. It has been shown in field experiments (Quy *et al*., 1992) that some rodent infestations have specific behavioural mechanisms, which may be genetically-determined, which make them reluctant to sample new foods, such as rodenticide baits. Once again, treatments of such infestations with rodenticides would be expected to be prolonged.
- Immigration from neighbouring untreated sites. Although such situations should generally be avoided by comprehensive surveys of infestations conducted prior to bait application, it is occasionally the case that undiscovered neighbouring, or small satellite, infestations

adversely affect the conduct of bait applications. Baiting periods may be prolonged when rats from neighbouring areas come onto treated sites during applications in order to exploit resources which they have been denied by resident rodents until these succumb to the rodenticide application.

- Resistance status of the treated infestation. Of course, where resistance occurs, application of fully resisted active substances against resistant infestations will result in ineffective, and consequently prolonged, treatments. However, when applications are made against resistant rodents using active substances to which they are not resistant in practical terms, the possession of a degree of resistance may result in prolonged treatments. In such circumstances, the proportion of resistant rodents in the infestation will affect treatment duration and, similarly, among the resistant rodents, the proportion that is homozygous resistant will also have an effect.

Prolonged baiting, permanent baiting and proactive baiting are techniques used by professional pest controllers with the intention of controlling persistent infestations, of preventing new infestations and of intercepting any immigrants into the area. Long-term preventive baiting strategies should be available as an option to deal with high-risk sites and/or those sites with a high potential for reinvasion and/or those sites where quality assurance schemes require it (e.g. food-industry, hospitals).

This could increase however the likelihood of primary and secondary poisoning of non-target species. Long baiting periods increase the duration of exposure to non-target species. Long-term baiting is assumed to result in the accumulation of rodenticides residues in wildlife (U.S.EPA, 2008). Permanent baiting is thought to be a prime cause of wildlife contamination where non-target small mammals rather than target rodents take the bait (Cefic, 2013). In this way, predatory bird species such as Kestrel and Barn Owl are more readily contaminated with anticoagulant. There are also concerns that permanent baiting will lead to the selection of genetically based anticoagulant resistance (RRAC, 2003), and many best practice guidelines advise against the routine use of anticoagulant rodenticides for permanent baiting. Permanent baits should only be used where there is a clear and identified risk of immigration or introduction, or where there is a requirement for protection for high-risk areas. HSE (2012) recommend that long-term preventive baiting strategy should be available as an option to deal with high risk sites and/or those sites with a high potential for reinvasion and/or those sites where quality assurance schemes require it.

The use of long-term or permanent baiting is a common practice. It is mainly employed by professional pest control technicians. Many professional pest control companies base their service contracts on the placement of an arrangement of fixed permanent baiting points deployed both outside and (where permitted) inside buildings, with regular site visits to check these baiting points and to replenish the bait. These visits are usually every 4, 6 or 8 weeks according to the requirement of the contract between the professional pest controller and the customer. Permanent baiting is at the foundation of much of the service of professional rodent pest control currently provided in the European Union by professional pest control companies.

The normal justifications given for the practice are:

- When checked at regular intervals, the bait provides a tool for monitoring the presence or absence of rodents
- The bait which remains in position is perpetually available for rodents that may come onto the site. The intention is that these rodents encounter bait, and are killed, before they are able to become established.

No quantitative evidence exists on the frequency at which these permanent bait points are visited by target rodents. However, many reports from practitioners are that they are also frequently visited by non-target small mammals. This is a primary route of contamination of wildlife because small mammals form the prey base of many mammalian and avian predatory species across the EU.

The schedule of visits to check and replenish these permanent bait points, such as every 4, 6 or 8 weeks, is usually in contravention of label requirements for checking visits to bait points. Permanent baiting is frequently written into biosecurity protocols for commercial sites and compliance with permanent baiting procedures is mandatory within many schemes of audit and accreditation for manufacturing sites, especially those of the food industry.

Is permanent baiting bad practice? At some sites there is a constant threat of reinvasion of rodents. One example of this is food outlets in city centres, which may be quickly infested with mice from neighbouring untreated premises. In this case, indoor permanent baiting for house mice presents very little risk of non-target wildlife exposure and may be justified on the grounds of the requirement to protect public health and promote food hygiene.

However, where outdoor permanent bait points show heavy use by small mammals, and not the target rodents, such practice is a considerable an unjustifiable risk to wildlife.

Some suggested measures to deal with permanent baiting:

- The permanent deployment of live rodenticide baits (i.e. containing active substance,) in the absence of an extent rodent infestation, should not be a routine pest control procedure.
- Each time baits are deployed for a long period a site specific environmental risk assessment should be conducted.
- The justification for any long-term bait deployment should be made in writing and kept on record. This may be in terms of a proven record of re-infestation of the site and an ongoing risk to human health of animal health and hygiene.
- Contrary to this, recording long-term deployment of bait at sites without consumption by target rodents signal the requirement to remove the poisoned bait from bait points.
- The decision to use long-term baiting should be reviewed at regular intervals and at least each time the site is visited for bait checking.
- Outdoor permanent baits should be removed where they show feeding on baits by non-target small mammals.
- Bait presentation system technology (see baiting in open areas) avoiding non-target access would be an option for long-term not permanent baiting

There should be a maximum duration for a rodenticide treatment of around 4-6 weeks. In a field trial where rodenticide is applied optimally, failure to obtain control in a 4-week period would strongly suggest that there is a problem concerning physiological resistance, or a problem concerning acceptance of the bait formulation (which has been reported in central southern England e.g. Quy *et al*., 1992). For an operator to continue a treatment beyond 6 weeks he/she should produce a detailed risk assessment to justify such actions.

Scientific evidence

Several studies have shown that complete eradication of infestations can usually be reached within 35 days (Drummond and Rennison, 1973; Buckle *et al*., 2013; BPCA, 2001; CRRU, 2012). It can take as little as 2-3 weeks to be effective, but particularly if the infestation is heavy, it can also last for up to 5 weeks (CSL, 2002). Individuals do not feed consistently during treatments

(Buckle *et al*., 1987), and social interactions may have an influence on the individual duration of bait consumption (Barnett and Spencer, 1951). If eradication is not reached within this time, reasons for the failure of control efficiency could be non-compliance with best practice codes (CSL, 2002), possible re-invasion, immigration of rodents (e.g. Brown and Tuan, 2005), high levels of neophobia to the bait station or formulation of bait (Brigham and Sibly, 1999), resistance to the AVK (e.g. Endepols *et al*., 2012a ; Buckle *et al*., 2013). Long-term application of rodenticides increases the likelihood of primary and secondary poisoning of non-target species (HSE, 2012). Long-term baiting is also likely to result in residues of rodenticides in wildlife (Bradbury, 2008) and may also lead to the selection of anticoagulant resistance (RRAG, 2003).

Recommendation: limit treatment application to 35 days in a first step

'Expected' duration of rodenticide treatments

From the foregoing discussion it is apparent that **no absolute value can be derived for the 'normal' duration of rodenticide treatments**. However, there is abundant evidence in the literature from practical field trials of how long bait applications take to achieve eradication of Norway rat infestations. This phenomenon was first studied systematically by Drummond and Rennison (Drummond and Rennison, 1973), who conducted warfarin treatments against warfarin susceptible infestations of Norway rats. They found that the mean duration of treatments was 15 days, and that the lower and upper 95% confidence intervals of the mean were 8 and 30 days respectively (see also EPPO, 1982). Thus, it may be supposed that these values would hold true for any anticoagulant used against Norway rats to which the infestation is fully susceptible.

No equivalent information is available for roof rats, although eradications of this species would be expected to take longer than that of Norway rats because they are generally less susceptible to anticoagulants than Norway rats and are also less likely readily to consume cereal-based rodenticide baits.

Similarly, such extensive information is scarce for House mice. However, more published data are available for this species showing the necessary duration of treatments for eradication of mice using a range of anticoagulant rodenticides in UK farm buildings. Rowe and co-workers, working during the 1980s, showed that substantial infestations of House mice could be removed from infested buildings when baits were efficiently deployed for periods of between 21 and 35 days.

From this analysis it is apparent that, in the case of anticoagulant baits used against rat and mouse infestations that are susceptible to the active substances they contain, it might be reasonably anticipated that **properly conducted treatments would be concluded in no more than 35 days**. In circumstances when baiting has continued for a period longer than this without substantial reduction, or complete removal, of the infestation, it is obvious that a review of the treatment process should be conducted and alternative measures implemented.

This duration of baiting is in accordance with several codes of best practice, such as the ones provided in the UK by the British Pest Control Association (BPCA, 2001) and for the countries of the EU by the European Chemical Industry Council (Cefic, 2012).

For amateurs: when eradication is not reached within this period, amateurs should turn to professionals for advice. Permanent and proactive baiting should not be allowed.

For professionals and trained professionals: when eradication is not reached within this time the baiting strategies have to be re-evaluated and improved. After justification **it is essential that**

capacity to bait beyond 35 days when required exists, because the survivors may be problematic rodents, which are resistant to anticoagulants or which develop an increased neophobic behaviour. Based on the on-site evaluation, the strategy could be to change to a more potent SGAR.

It is suggested that where long-term preventive baiting is carried out, it is necessary to conduct an appropriate risk assessment by:

- documenting the reasons why long-term baiting is needed,
- recording the reasons that the increased risk posed by long-term baiting is outweighed,
- the potential benefits to human and/or animal health on that particular site,
- re-visiting the site at intervals appropriate to the degree of risk posed by the application,
- monitoring the effectiveness of the rodenticides in use to be able to take corrective measures if resistance occurs (CEFIC, 2013).

However, mandatory documentation is only meaningful if authorities control them and if evaluations are done for improving management strategies and minimising risk.

Permanent baiting and pro-active baiting with SGARs should never be used as a standard procedure especially in open areas, such as waste dumps, but it should be available as an option to deal with high-risk sites and/or those sites with a high potential for reinvasion and/or those sites where quality assurance schemes require it. In situations where it does not appear to be safe, permanent monitoring should be considered as an alternative, including the use of electronic devices.

Benefits

- Long-term and permanent baiting could be applied where risk to non-target animals and the environment is very low, i.e. indoors such as in case of rat control in sewers systems or House mice control of indoors (see bait stations).
- Permanent baiting with SGARs outside of buildings, in open areas and at sites where no rodents are currently present should not be used because the likelihood of primary and secondary poisoning of non-target species and the possibility of the development of anticoagulant resistance.
- The same risks apply for the proactive baiting, which should not be allowed. Where baiting is carried out for more than 35 days it is necessary to conduct an appropriate risk assessment following for example (CEFIC, 2012).

Limitations

- The benefit of mandatory documentation is questionable if no evaluations result to improve management strategies and if there is no control by authorities.
- Regular visits to monitor a site
- Associated cost for PCO/clients

4.1.3.2 Frequency of visits

Rationale

Rodenticide baits are deployed for the removal of rodents at infested sites and baits are consequently consumed by the target rodents. It is ineffective, uneconomical and unsafe to apply quantities of bait that are so large that sufficient bait is put out initially so that bait remains available for rodent consumption throughout the predicted duration of the treatment. Therefore, it is normal practice, indeed it is considered best practice, to put out limited quantities of bait

and to return to the treated site at regular intervals to check the baits and to replenish them if it is considered necessary.

There are several reasons that make it necessary to check bait points during rodenticide applications including:

- To replenish any bait that has been consumed by rodents.
- To replace bait that has been spoiled by damp or by other adverse events.
- To check that baits remain properly protected from non-target animals and that bait points have not been removed or damaged by accidental of purposeful human interventions.
- To check that the initial placement of bait points is effectively presenting bait where it is needed over the entire area of the infested premises.
- To check that bait consumption is sufficient to result in a rapid effective treatment.
- To check for signs of access to baits by non-target animals. For example, where mouse droppings are found at outdoor bait points to determine if these are from target rodents or are from non-target small mammals, such as wild mice and voles.
- To search for, pick up and dispose of safely any bodies of dead and dying rodents.

No hard and fast rules can be applied to the required frequency of bait checks. However, two main considerations, from those listed above, determine when visits are needed. Sites with large and extensive rodent infestations need to be visited more frequently than those with smaller infestations in order to make sure that sufficient bait is available throughout the treatments. Sites where a pre-treatment assessment of non-target activity, or an environmental assessment, has identified the possibility that baits may be disturbed by human, or other agencies, also require more frequent checking visits to ensure the integrity of bait covers and bait boxes.

Rodenticide labels usually dictate, within a limited range of variation, the schedule of required visits to replenish bait points. Of course, any label instructions on this matter should be carefully followed because they reflect the combined assessments of the manufacture and of the CA that authorised the sale of the product in question. These recommendations are usually derived, however, from data generated during efficacy evaluations of the products in question. They are therefore determined mainly with respect to considerations of efficacy and not any consideration of safety and risk of non-target exposure at the treated site. Therefore, label recommendations about the frequency of checking visits should be regarded as the <u>minimum</u> needed to ensure efficacy, but this frequency may need to be increased depending on other characteristics of the treated site.

<u>Assumptions</u>

It is agreed good practice for all users of SGARs to revisit bait points frequently (HSE, 2013). The minimum frequency for revisiting bait points is rarely stated. CEFIC (2013) and previously HSE (2011) consulted with rodenticide suppliers and users on the feasibility of agreeing on a minimum frequency of anticoagulant bait revisiting and proposed that the first follow up should be no later than 7 days after the initial application, and subsequent follow up visits should be no more than 14 days apart. With saturation baiting, where the objective is to provide bait stations with a surplus of bait at all times, CSL (2002) recommend that 5 or more visits during the first 2 weeks may be necessary. As the treatment progresses, the bait take declines and rodents´ signs are clearly decreasing, they recommend that 1-2 visits per week may suffice thereafter, unless there are concerns about the safety of the baits, in which case extra visits should be made.

The CRRU (2012) guidelines state: "Never fail to inspect bait regularly. Where the risk assessment or treatment records show that multiple visits are required, then those should be made as frequently as is considered necessary. Daily inspection may be required in some circumstances".

An absolute minimum bait revisiting frequency is one visit every seven days. However, each site must be assessed by the experienced operator in the light of their site survey, taking into account variations in baiting practices, the practicalities of SGAR baiting in diverse scenarios (domestic, industrial, urban and rural settings), the size of the rodent infestation and the behaviour of the target species. It is the operator's responsibility to ensure the safety of humans, companion animals and non-target species at the treatment site. These risks will fluctuate over the course of the treatment depending upon activities on the treatment site, and with the reductions in the quantity of bait used and the number of bait point set, as the pest species is controlled. The operators should modify their bait revisiting frequency accordingly.

During the course of an anticoagulant treatment, usually most activity at the baiting points is found during the first two weeks of baiting (e.g. CSL, 2002). Consequently, the highest proportion of bait is consumed during this period. After that period, bait consumption and the number of dead or dying rodents decrease. Nevertheless the risk of primary and secondary poisoning is still present. Regular visits to the bait stations to maintain a constant supply of bait, which will also facilitate bait transfer to immigrants and ensure rapid removal of dead or dying rodents. With surplus or saturation baiting, rodents should be able to find sufficient bait whenever they want to, so that they ingest a lethal dose as soon as possible (CSL, 2002). This may mean that baits are replenished more frequently at first in order to keep the amount of bait in line with the rodents' needs. Moreover, by matching bait quantity to the number of rodents willing to eat it, there will be less surplus bait available should non-target animals accidentally get access to it.

Scientific evidence

No clear pattern of the number and frequency of bait inspections could be identified in the scientific literature, as adequate requirements are highly variable and depend on many factors, e.g. area of baiting and pest species. For Norway rats, CSL (2002) summarize their experiences from many practical studies and found that in standard controls during the first two weeks of baiting five or more visits to the bait stations are appropriate and thereafter a lower frequency of visits may suffice.

For more potent SGARs only small amounts of bait are necessary to reach the lethal dose. In such a case the pulsed baiting technique (see section 5.1.3) is suitable that replaces limited amounts of bait at longer time interval, e.g. every five to seven days (Dubock, 1979; Greaves *et al*., 1988[a]). The primary purpose of the pulsed baiting technique is to permit effective rodent control while reducing the quantities of rodenticide used and, thereby, the quantity of the active substance released into the environment (Greaves *et al*., 1988[a]). This may minimise primary and secondary poisoning (Buckle *et al*. 2012[a]). Field trials on farms with the high potency SGAR compound brodifacoum were fully effective against Norway rats with the Y139C resistance mutation and showed that the applied pulsed baiting regime reduced the quantity of bait required to control resistant Norway rat infestations to relatively low levels (Buckle *et al*. 2012[a]). There is good evidence that brodifacoum baits are fully effective against Norway rats when applied in quantities of only 50 g per bait points with replenishment visits only once or twice each week (Greaves *et al*., 1988[a]).

Experts strictly recommend following label instructions regarding the frequency and number of visits to the site. It is agreed good practice for all users of SGARs to revisit bait points frequently (HSE, 2013). The frequency of bait inspections should largely depend on the rodents' response, but also the likelihood of non-targets taking bait or eating poisoned rats. CSL (2002) recommend that during the course of anticoagulant treatments, especially during the first two weeks of baiting, it is important to visit the bait stations frequently to check how rodents react to the bait. During each visit it has to be ensured that fresh bait is available, possible spillage of bait is eliminated and dead or dying rodents are recovered.

When high potency SGARs are required, e.g. for treating a resistant infestation, the pulsed baiting regime with a low frequency of bait application may provide an opportunity to reduce bait amounts and the risk to non-target animals (see below). To ensure the regular recovery of dead or dying rodents additional visits to the site (without bait application) are necessary (Greaves *et al*., 1988).

Recommendation: provide indicative recommendations for regular visits – to be adapted with local risk assessment

The frequency of bait inspections should largely depend on the rodents' response, but also on the access of bystanders to the site and the likelihood of non-targets taking bait or eating poisoned rats. To check how rodents react to the bait it is required during the course of anticoagulant treatments, especially during the first two weeks of baiting, to visit the bait stations frequently. **It is recommended to state a frequency bait inspection interval, because the word "frequently" is unspecific**.

Recommendations concerning the frequency of bait inspections made by CSL (2002) are reasonable. In standard controls during the first two weeks of baiting 5 or more visits to the bait stations are appropriate and thereafter a lower frequency of visits may suffice. The minimum interval during a standard control operation should be no later than 7 days after the initial application, and subsequent visits should be no more than 14 days apart. When potential risks for non-target organisms are indicated, more visits (maybe daily visits) are recommended. During permanent baiting operations (see 4.1.3.1 Duration of baiting), after a detailed risk assessment, intervals might be every two weeks.

Codes of best practice, such as those provided by the European Chemical Industry Council (Cefic 2013) and the German Umweltbundesamt (UBA, 2014), propose minimum frequencies as shown in the table below. These values should always be regarded as indicative.

Table 5: Proposed indicative treatment schedules for anticoagulant rodenticide baiting at infested sites (other than sewer systems)

Code of Practice	Time of first visit after bait placement	Frequency of subsequent visits
Cefic (2013)	No later than 7 days	Not less than every 14 days
UBA (2014)	No later than 5 days (preferably 2-3 days)	Not less than every 7 days

During each visit it has to be ensured that fresh bait is available, possible spillage of bait is eliminated, protection of baits is checked and dead or dying rodents are recovered.

When highly toxic SGARs are required, e.g. for treating a resistant infestation, the pulsed baiting regime with a low frequency of bait application may provide an opportunity to reduce bait amounts and the risk to non-target animals (see below). To ensure the regular recovery of dead or dying rodents additional visits to the site (without bait application) may be necessary.

Benefits

- Provide a basis for reasonable frequency of visits during rodenticide application

Limitations

- Frequency of visits is highly variable depending on the site, its environment, food availability
- No standardised suggestion for all situations

4.1.3.3 Removal of dead rodent bodies

Rationale

Assumptions

The search for dead bodies during and at the end of the treatment is a mandatory risk mitigation measure. To help prevent the risk of secondary poisoning, dead and moribund rodents and non-target animals should be searched for at least on every visit to the site– at least when checking bait stations as mentioned above, removed and disposed of according to local regulations (CEFIC, 2013). It is agreed good practice for all users of SGARs to search for dead or moribund rodents, but the frequency of searching is not clearly described (HSE, 2012). In compliance with a report by HSE (2013) carcasses should be searched for and removed at least as often as when baits are checked and/or replenished. While professional pest controllers may often only revisit baiting points in a low frequency, they suggest that in some cases clients, who are supervised by a pest-controller, may survey sites for rodent bodies (e.g. poultry pens) on a daily basis (HSE, 2013). Wildlife organisations recommend a daily carcass searching and safe disposal in order to minimise risk to scavengers such as red kites (HSE, 2013). According to the risk assessment daily inspection are required in some cases. In any case, the frequency should be sufficient to meet the operators' safety assessments.

The period of searching for carcasses has to comprise the time the bait is available for consumption by rodents and furthermore two additional weeks after bait removal, because rodents may succumb several days after the last take of bait.

Regulations covering the safe disposal of bodies may differ greatly among MS. PCOs would normally be trained and know the appropriate rules. For amateur use, the safe disposal of dead bodies should be done "according to local regulations", which may vary greatly. A common approach usually suggests to wear gloves and place the body in two sealed plastic bags and dispose of them with household waste.

Scientific evidence

One potential risk to wildlife, predators or scavengers, and also to domestic animals is the uptake of poison through the consumption of dead or moribund animals containing rodenticides in body tissues (e.g. Laakso *et al*. 2010; Langford, 2013; Hughes, 2013; Dowding *et al*., 2010;

Hughes *et al*., 2013; Langford *et al*., 2013). During the course of treatment the first rodents dead or dying of anticoagulant poisoning may appear after about 3-5 days and then others in the population may succumb over the following days and continue doing so for several days after the last take of bait (CSL, 2002). Secondary exposure to the SGAR is particularly problematic due to these compounds' high toxicity (Buckle, 1994) and long persistence in body tissues (e.g. Fisher *et al*., 2003; Eason *et al*., 1996). The most potent SGARs are designed to be toxic in "a single night's feeding," but since time to death are several days, the target rodent and also non-target animals can feed multiple times before death, leading to a carcass containing residues that may be many times the lethal dose (Bradbury, 2008). This may be exacerbated in resistant individuals that consume and carry multiple lethal doses (Brown, 2007). Additionally, the extended persistence of second-generation anticoagulants in the body of a predator or scavenger may result in adverse effects from additive exposures through multiple feedings that are separated by days or weeks.

No published data could be located with respect to the fraction of dead animals removed during search activities in relation to the total number killed during a baiting programme.

Recommendation: search for and remove dead bodies based on local risk assessment

Searching for and removing dead bodies should be conducted at frequent time intervals, for instance during each site visit by PCOs. It is the operator's responsibility to minimize the risk to human, domestic animals and non-target species. Monitoring frequency should be the result of the operator's safety/ risk assessment analysis performed during the first visit.

For amateur use, regulatory aspects should be confronted in order to provide a harmonised way of safe disposal of bodies (wearing disposable gloves, place in two plastic bags sealed and eliminated in municipal waste) explained in leaflet.

Benefits

- Reduce potential exposure of non-target predators and scavengers
- Provide more precise rules for amateurs

Limitations

- Time-consuming
- Requires appropriate information/protection of person responsible
- Requires regulatory harmonisation

It seems likely that the **rapid removal of dead or moribund animals during SGAR baiting is an appropriate measure for minimising non-target risk**. However, there is no published information how effective that approach is.

4.1.3.4 Removal of uneaten bait

Rationale

Assumptions

When it is decided to terminate the treatment, uneaten bait has to be removed and disposed of safely to minimise the duration of exposure to children, domestic animals and non-target animals. Bait should not be left at the site for a possible future infestation, because the remaining bait is a continuing risk to non-target wildlife and the source of residues of rodenticides in a

wide variety of non-target wildlife (CEFIC, 2013). It may make sense to leave bait stations in place for future applications, as old and familiar bait stations can reduce neophobic behaviour and increase future rodents´ bait take (Quy, 2011).

If the label suggests a reduction of bait amounts during the treatment according to bait take, the user should strictly follow the advice. Especially for trained professionals/professionals it makes sense to reduce bait amounts at bait points during the treatment under strict observation of the progress of control and when they ensure that best practice codes are applied.

Scientific evidence

Several studies demonstrate the high exposure of (small) non-target rodent species feeding on rodenticides from bait boxes during routine rat control treatments. Brakes and Smith (2005) showed that a large proportion (48.6%) of individuals in local wild small mammal populations ate bait and entered the bait boxes. After feeding, the non-target species may contain high residues of anticoagulant compounds, which can result in secondary exposure to predators and scavengers.

Recommendation: remove uneaten baits at the end of the baiting period

To reduce the duration of exposure of non-target organisms when using ARs outdoor, the removal and safe disposal of uneaten bait at the end of the treatment is a mandatory risk mitigation measurement.

If the label suggests a reduction of bait amounts during the treatment according to bait take, the user should strictly follow the advice. **Remove all uneaten bait at the end of treatment (<35 days), including bait boxes, and burrow entrances.**

Benefits

- Minimise non-target species exposure (domestic and wildlife species)- Minimise consumption over extended period of time and selection of resistant strains.

Limitations

- Time and cost of last visit to retrieve all uneaten bait

4.1.4 RMMs addressing resistance selection

Detailed recommendations have been made under the "General recommendations" "resistance management" section. Summarised information is given below.

Rationale

Scientific evidence

FGAR efficacy is severely affected by all resistance mechanisms, especially VKORC1 mutations in rats (Pelz *et al*., 2005) and mice (Endepols *et al*., 2012b). Bromadiolone and difenacoum are partially affected (Buckle *et al*., 2012; Endepols *et al*., 2012a; Endepols *et al*., 2007), but there is no evidence of field resistance to brodifacoum, difethialone and flocoumafen.

Norway rats are usually more susceptible than Roof rats, and House mice are known to be resistant to FGARs (Song *et al*., 2011).

Recommendation: adapt treatment to rodent species and information on resistance

It is strongly recommended to adapt the active substance used for rodent management to the local resistance situation.

House mice: FGARs should not be used against House mice, unless there is evidence that the strain is susceptible.

Norway rats: FGARs, bromadiolone, difenacoum should always be considered first choice products against Norway rats, unless there is local evidence of resistance. If infestation persists after five weeks despite correct application and bait consumption, resistance should be considered and tested for. If resistance is identified and information available on the practical level of resistance, using the most potent AR should be considered immediately.

Roof rats are intermediate and FGARs may not be effective and rapidly select resistant individuals. Consequently, SGARs should be considered first choice, unless there is prior evidence of susceptibility of the local strain.

4.1.5 Overview of proposed RMMs within the active substance approval

An overview of the proposed RMMs to be implemented through the active substance approval is provided in Annex 4 to this report.

4.2 Other RMMs or conditions to be set at the stage of product authorisation:

4.2.1 By user category

4.2.1.1 Trained professionals

General

The ubiquitous nature of infestations of Norway rats, roof rats and House mice in the MSs of the European Union brings these pests into contact with a wide range of human interests, including personal, societal and commercial. This in turn means that a wide variety of people have an interest in rodent control, and this leads to a wide range of potential users for the ARs. These user groups are generally considered to fall into two main categories, professionals and amateurs. However, there is great diversity within these groups and consequently there is no clear line of separation between them.

Across the EU it is a common feature of biocide regulation that products sold to professionals and to amateurs are different. These differences may affect the quantities of biocidal products that can be purchased, they packs in which they are sold, the ways in which they can be used and the places where they can be applied. Where terms such as 'professional' and 'amateur' are to be used in the regulation of biocides it is essential to have clarity in the definition of terms and, so far as practically possible, to have terms that are unambiguous.

Up to this point there are no universally-agreed definitions of the terms 'amateur' and 'professional', as applied to the purchase and use of biocides. This situation is a serious impediment to the harmonious and uniform regulation of the biocides market.

Rationale

It is necessary that those who employ workers to keep them safe from foreseeable harm (for example in the UK the Health and Safety at Work Act 1974). Those who employ others to make applications of chemicals for the purpose of pest control would be expected to establish procedures in which these chemicals are used safely by their employees. In this respect, safety refers to the security of the individuals making the applications, other workers employed at treated sites, to bystanders who may have legal access to treated sites without knowledge of those conducting the treatment or who may enter sites without legal authority, to non-target animals and, more generally, to the environment.

In many regulatory jurisdictions, specific training courses are available on rodent pest management. These courses are offered either as a part of a wider qualification in pest management practices or as stand-alone courses which cover rodent pest management alone. Where these courses lead to the formal the award of a qualification, and the registration of qualified personnel by an approved training body, untrained professionals who obtain such a qualification may then be considered to be 'trained professionals'.

A specific type of 'trained professional' is the pest management professional (PMP) or the professional pest controller (PCO). These technicians would usually be trained in a wide array of pest management techniques, including rodent pest management. Their principal professional working activity is pest management and therefore this is performed on a daily basis. It is to be anticipated that they will use rodenticides more frequently than other 'professionals', such as farmers, store keepers and janitors, and apply larger quantities of them. A consequence of this is that they should be expected to be trained at a higher level than those who use rodenticides only occasionally. Once again, there is a wide array of training courses for PMP/PCOs in the MSs of the EU. See under section 4.3.4 for appropriate training of "trained professionals"

4.2.1.2 Professionals

Rationale

This term has many meanings. Its original and primary use was to define the membership of a 'profession' – such as the medical and legal professions. This implies the existence of a 'professional body', which sets standards and makes judgements about the suitability of members to operate within the profession. Its counterpoint is a member of a 'trade'.

However, when applied in the context of the use of pesticides, and by extension biocides, the definition of a professional user is provided as follows in the Sustainable Use Directive:

> *'professional user' means any person who uses pesticides in the course of their professional activities, including operators, technicians, employers and self-employed people, both in the farming and other sectors;*

This very wide definition applies the term professional to anyone who uses a pesticide (or a biocide) while carrying out their working duties (i.e. professional activities). Therefore, under this definition, anyone who applies a rodent control intervention, such as the application of a rodenticide, while at work is considered a professional. This might include a wide range of workers such as farmers and growers, those involved in animal husbandry, store-keepers, janitors, those employed in food preparation, packaging, storage, distribution and sale and many other types of employees.

An immediate potential for confusion arises because those whose commercial activity is to provide a professional service of pest management are commonly called professional pest controllers (PCO) or, more recently, pest management professionals (PMPs). These 'professional' personnel are thought to have the following characteristics in relation to other 'professionals' who do not offer such a service:

- They are likely to use greater quantities of biocides because they conduct applications as a part of their daily activities. Other professionals apply biocides only occasionally.
- They are more likely to have attended specific training courses related to the biocides that they commonly use.
- They are more likely to be in possession of, and consistently and correctly to use, personal protective equipment. This is associated to the fact that they use greater quantities of biocides and are more likely to be habitually exposed to them.

Many who fall under the above definition of a 'professional', and who apply rodenticides either only on their own land or in and around premises that they own or exert control over, may have no specific training in the use of rodenticides. Many farmers who apply biocidal rodenticides would be expected to be in this category of user i.e. "untrained professional", although they may have

habitually used rodenticides throughout their working lives and may consider themselves to be competent in their use. There is evidence that these "professionals" are generally aware of the risk associated with AR for non-target species, but also that they may not know and apply all RMM (Hughes *et al*., 2013). See under Section 4.3.5 for appropriate training of Professionals.

4.2.1.3 Amateurs

Rationale

Those members of the public who purchase pesticides and apply them are generally referred to as 'amateurs'. Alternative terms are the 'general public', 'house-holders' and 'home-owners'. Another term sometimes applied to this user group is the 'non-professional'.

The following general assumptions are often made about the characteristics of this category of user:

- 'Amateur' users will have received no specific training in the use of the pesticides that they purchase and use.
- Therefore, they will have a very low degree of understanding of the mode of action of the pesticides they are using and of the various risks that are inherent in their use.
- They will have no access to any apparatus that may be termed personal protective equipment (PPE), other than (perhaps) gloves.
- The main access that they may have to information about the correct use of the product purchased and the risks of its use will be that available from the label of the purchased product.
- Various assumptions may be made about the willingness of amateurs to read label instructions and their ability correctly to interpret and apply them. In some regulatory jurisdictions the assumption is made that label instructions will be read and applied by amateurs. In other jurisdictions the opposite assumption is made, that is that amateurs will not read and apply label instructions. Obviously, the latter provides the more protective but the more restrictive approach.

There is evidence (see report by Edworthy *et al*., 2011 at HSE), that amateurs are less likely to read and interpret correctly safety instructions on product packaging and especially if it is inserted on a separate information sheet. It is a generally held assumption, that rodenticides purchased by amateurs are mostly used for the control of House mice, or other species of small rodents, which are active within the home environment. In many regulatory jurisdictions there are rules that limit either the quantities of bait that can be purchased by amateurs or the sizes of packs that they can purchase.

A specific category of amateur user is the agricultural smallholder, sometimes called the 'hobby farmer'. Such people may comply with each aspect listed above to describe an 'amateur' user. Conversely, and usually depending on the scale of the enterprise engaged in, they may be much more like a farmer, and therefore fall more correctly into the 'professional' category which is described below.

Recommendation: restrict pack size and ensure safe packages for amateurs

If amateurs are mainly concerned with control of small scale rodent infestations, it is apparently wholly proportionate that amateurs should be restricted to small packs of rodenticide baits that are appropriate for such use *(see UK HSE Risk assessment document ref. for instance).* Detailed proposals for pack size restrictions are made under section 4.1.1.

Special attention should also be paid to safety of packages with regard to primary poisoning by children or pets. Additional recommendations on this field (e.g. children-proof packages) are provided under section 4.2.4.

4.2.1.4 Bait boxes

Rationale

Assumptions

A well-established means of risk mitigation are rodent bait stations. Their use is obligatory in the US in most circumstances (U.S.EPA, 2008) and recommended in Europe (EC, 2007). The idea was to mitigate risks by using tamper-resistant bait stations: these are resistant against manipulation by non-target species (including humans, especially children) and typical non-catastrophic weather (e.g. rain, moisture). Moreover, the bait may be placed in a way that it cannot be spilled or removed from the bait stations. The principal purpose of tamper-resistant bait stations is to prevent access to bait contained in them by non-target animals that are: (i) larger than the target rodents (Kaukeinen 1987, Lund 1988), and therefore cannot pass through the access apertures, or (ii) deter them from entering the boxes because of their confined nature (Buckle and Prescott 2011). Tamper resistant bait stations have no mitigation influence on mammals smaller than the target species, because they can enter bait stations and feed on bait.

After feeding, the target species (and also non-target species) leave the bait stations. Therefore, bait stations have little if any impact on secondary exposure of predators and scavengers that feed on rodents that have consumed rodenticides (Bradbury, 2008).

The material and material properties also have influence on bait station attractiveness. Rodent bait stations are made from a variety of materials, including plastic, cardboard, wood or metal.

Norway rats are neophobic (Brigham and Sibly, 1999), and bait stations introduce a new situation for food uptake, which is usually not easily accepted (Quy, 2011).

Testing methods for establishing the robustness of tamper-resistant bait boxes have been described by Jacobs (1990). Kaukeinen (1987) and Schmolz *et al*. (2008) proposed a standardised laboratory test method for the evaluation of the efficacy of rodent bait boxes. It allows an objective estimate if a bait station product is sufficiently attractive for target rodents for a successful rodent control operation and also presents a method for comparative test of bait station characteristics (Schmolz *et al*., 2008). However, the natural behaviour of wild rodents when bait boxes are deployed within their familiar foraging areas is only fully exhibited in the field (Buckle and Prescott, 2011).

Besides the placement of surface bait stations, it is a common practice to place rodenticide baits directly into rat burrows. This may result in rapid bait uptake and efficient treatments, especially when rodents are neophobic and avoid bait stations. It is unlikely that non-target animals utilise active rat burrows. Such baiting may result in spillage of bait outside the treated burrow, because baits may be ejected by rats from the baited burrows. HSE (2012) recommends that in certain circumstances burrow baiting has been found to be an efficient method of bait placement offsetting the risk for bait to be spilled or pushed out of the burrow into the surrounding area, with the potential for primary poisoning of non-target species. In most cases, it may be difficult to retrieve uneaten baits from baited burrows after rodent control. In addition the documentation of bait consumption is almost impossible.

Scientific evidence

Several studies, e.g. Brakes and Smith (2005), demonstrate the high exposure of (small) non-target rodent species feeding on rodenticides from bait boxes during routine rat control treatments: A large proportion (48.6%) of individuals in local populations ate bait: wood mouse *Apodemus sylvaticus* were most exposed, followed by bank vole *Myodes glareolus* and field vole *Microtus agrestis*.

In spite of their widespread and sometimes mandatory use, it has been found that bait stations have an adverse effect on the uptake of bait (see review Quy, 2011). Studies revealed that the bait station design has strong influence on bait acceptance. Bohills *et al*. (1982) found that House mice (*Mus musculus*) prefer bait placed in small bait stations to bait in large bait stations or open trays. Rats prefer larger stations, where they can adopt their normal posture for feeding (Clapperton, 2006). It is known that wooden boxes are preferred by rodents over those made from other materials (Lund 1988; Schmolz *et al*. 2008). Buckle and Prescott (2011) conducted a study to determine the uptake of bait from three tamper-resistant bait boxes of different designs and from open wooden bait trays, designed as safe as possible for non-target species using naturally-available materials present at the trial sites. The amount of bait eaten by rats from the protected bait trays was approximately eight times greater than the quantity eaten from the tamper-resistant bait boxes. The three bait box designs appeared to deter bait consumption by rats to a similar extent.

Recommendation: use of tamper-resistant bait boxes mandatory for amateurs, recommended (covered bait points) for professionals

Tamper-resistant bait boxes are essential tools in the application of rodenticides in many circumstances. Bait boxes are considered to give a higher level of protection for bystanders than covered bait points. A hierarchy of risk mitigation options is presented in Table 6. Option 1 provides the highest degree of protection for humans (in particular children) from the toxic hazards of the rodenticide. However there are public hygiene and socioeconomic considerations, which may require a less stringent control regime be considered (HSE, 2011). Some bait boxes include a small transparent window on the top, which gives users a view on the bait chamber and bait consumption. This appears to be an interesting monitoring tool.

Table 6: Hierarchy of risk mitigation options with predicted implications for human exposure, efficacy and economic viability/cost of rodent control (according to HSE, 2011; modified).

Levels		Protection from human exposure	Efficacy	Cost
1	Baits supplied in factory-filled **non-refillable tamper-resistant bait stations**	High from exposure to laid bait, high protection from exposure to stored bait.	May be low for problematic infestations. Aversive effect of bait station type and form of bait (Block, Paste)	High
2	Baits to be used in **refillable tamper-resistant bait stations** and supplied as inner packs or units, each containing bait for one bait point	High protection from exposure to laid bait, intermediate protection from exposure to stored bait.	May be low for problematic infestations. Aversive effect of bait station type (especially rats)	Moderate. Requirement to buy bait stations and bait in small pre-measured units.
3	Baits to be used in **refillable tamper-resistant bait stations**, and supplied loose in refill packs.	High protection from exposure to laid bait, lower protection from exposure to stored	May be low for problematic infestations. Aversive effect of bait station type (especially rats)	Moderate.

Levels		Protection from human exposure	Efficacy	Cost
		bait.		
4	Baits to be used in covered bait points, with bait to be supplied as inner packs or units, each containing bait for one bait point.	Low protection from exposure to laid bait, intermediate protection from exposure to stored bait.	Generally high	Low. No requirement to buy bait stations.
5	Baits to be used in covered bait points, with bait to be supplied in bulk packs.	Low protection from exposure to laid bait, low protection from exposure to stored bait.	Generally high	Low. No requirement to buy bait stations.
6	Baits to be used in covered bait points, with bait to be supplied as loose bait.	Low protection from exposure to laid bait, low protection from exposure to stored bait.	Generally high	Low. No requirement to buy bait stations. Less costs as loose bait is cheaper than in small packs.

Professionals and Trained Professionals

Given professionals use their experience and training to store and apply a rodenticide bait securely, and understand and fully carry out the label instructions for biocidal products, they should be able to buy packs of loose bait and be able to apply bait in tamper-resistant bait stations, covered bait points or uncovered in locations inaccessible to bystanders or non-target species that would also not be able to enter bait stations.

Experts recommend that the use of tamper-resistant bait stations should not be mandatory for professional users when it is possible to prevent access of non-target animals by other means (Buckle and Prescott, 2011). In the UK, guidelines for good practice in the application of rodenticides, in both rural (HSE Information Sheet 1999) and urban (HSE Information Sheet 2003) situations, propose that a risk assessment, conducted by the person making the rodenticide application, should precede the placement of rodenticide baits. The outcome of the risk assessment determines the need for different forms of protection of rodenticide baits from human disturbance and non-target animals, including the use of tamper-resistant bait boxes.

Especially for problematic rodent control, it is recommended that the use of tamper-resistant bait stations is not mandatory for professional users. Options 1-3 in Table 5 may prolong the time taken to establish control over problematic rodent infestations and increase the potential for anticoagulant resistance to develop and the potential for humans to be exposed to rodent-borne diseases. In particular when rodent control is an urgent necessity such equipment should not be employed.

Amateurs

For non-professionals it is proposed that products provide a level of protection equivalent to or greater than option 2/3 (Table 6). In view of the potentially high exposure at bait points and the view that amateurs may not always place bait in inaccessible locations, a risk

mitigation measure should be a mandatory use of tamper-resistant bait stations. For problematic rodent infestations, e.g. when rodents avoid the tamper-resistant bait stations, a professional control may be required anyway. Options 2 and 3 (Table 6) allow the non-professional to refill bait stations. The protection from human exposure to laid bait is still as high as under option 1, but the protection from exposure to stored bait may be reduced. In combination with other risk mitigation measures, such as clear label instructions, options 2+3 make rodenticides simple and safe for non-professionals to use, especially under option 2 when bait is supplied as inner packs or units, each containing bait for one bait point. The possibility of refilling bait stations significantly reduces the costs and may also raise efficacy of the control measurement, as other AR compounds or products than under option 1 may be used and rodents have a better chance to get used to a particular bait station.

Some experts recommend different options for non-professional rat and mouse control, as rat bait points contain more bait than mouse bait points and human exposure is potentially greater for bait laid for rats than for mice. For non-professional use against mice, it is discussed that products provide a level of protection equivalent to or greater than option 5 (HSE, 2011). The requirement for bait to be included in factory-filled inner packs or units containing a fixed bait amount would reduce the likelihood of a non-professional applying more than the required amount of bait. Nevertheless we should bear in mind that mice are generally less neophobic and more willing to enter tamper-resistant bait stations than rats and under most circumstances an efficient mouse control is ensured under options 1-3. When (rarely) problematic mice infestations were found and control could not be reached under options 1-3, the need of a pest controller is recommended. The costs of mouse control under options 1-3 (moderate costs) may be higher than under options 4+5 (low costs).

Bait box classification and specific regulation

There is no regulation with respect to proper definition of the qualities expected for an effective tamper resistant bait box and the level of protection achieved. As a consequence, there is no specific information with respect to the level of protection offered (e.g. child-proof, pet-proof). In the US, the US EPA promulgated specific recommendations for bait box testing (Pesticide Registration PR notice 94-7) as early as 1994. **It seems advisable to have some basis for classification and labelling of tamper-resistant bait boxes on the basis of validated tests in the EU**.

The USEPA classifies bait stations under 4 tiers:

- Tier I are tamper-resistant, weather-resistant bait stations and are resistant to tampering by children and dogs
- Tier II are tamper-resistant but not weather –resistant, to be used indoors only. They are resistant to tampering by children and dogs
- Tier III are tamper-resistant for children only, to be used indoors only.
- Tier IV is where tamper-resistance is unknown may not claim to be tamper resistant and should only be used indoors in areas not accessible to children and pets.

Providing some regulatory basis and recommendations for testing for tampering by children and dogs would be of value and provide good information on the actual protection status offered by the bait station. Before any specific guideline is available, USEPA-approved Tier I to III could be mentioned on the package. Testing for child resistance is developed in ISO norm 8317 and 13127 and these could be effectively applied to rodenticide packages. We were not able to locate any specific ISO/CEN norm with respect to domestic animals or tamper resistant boxes specifically in the EU.

Benefits

- Accurate and determined tamper-resistance level
- Provision of precise information to users

Limitations

- Cost of testing
- Cost to develop guidelines

4.2.2 By bait formulation:

4.2.2.1 Grain

Rationale

Assumptions

Grain formulations represent the least expensive and most commonly known bait type in the amateur sector. Loose grain, however, represents a potential threat in terms of primary poisoning of children and pets. Even when deployed in tamper-resistant bait boxes, spillage may occur and bait may be available outside.

In terms of efficacy, grain-based baits are highly attractive to most rodent species and will certainly be consumed readily, provided food-competition is limited. As a consequence, rodent infestations should be rapidly controlled.

Recommendation: availability to all user categories

Grain baits should be available to all user groups, with limited pack size for amateurs (or even tamper-resistant bait boxes distribution only for House mice and Norway rats). Grains should be recommended for roof rat infestations. Grains should always be provided in sachets for amateur use. For professionals, this decision should be taken after consideration of risk assessment.

4.2.2.2 Pellet

Rationale

Assumptions

As discussed with grain baits, pellets are easy to use, but may represent a threat in terms of primary poisoning of children and pets. Even when disposed in tamper-resistant bait boxes, spillage may occur and bait may be available outside the bait box. Dust contaminated with ARs may be present.

Recommendation: availability to all user categories

Pellet baits should be available to all user groups, with limited pack size for amateurs (or even tamper-resistant bait boxes distribution only for House mice and Norway rats). Pellets should be recommended for roof rat infestations. Pellets should always be provided in sachets for amateur use. For professional, this decision should be taken after consideration of risk assessment.

4.2.2.3 Paste

Rationale

Assumptions

Paste baits are commonly used today as a good surrogate for grain baits, because of their good palatability and rapid acceptance by rodents. They can be fixed in bait boxes and safely kept inside, with very limited spillage.

Recommendation: availability to all user categories

Paste baits should be available to all user groups, with limited pack size for amateurs (or even tamper-resistant bait boxes distribution only for House mice Roof rats and Norway rats).

4.2.2.4 Block

Rationale

Assumptions

Block baits are usually less consumed than grain or paste baits. They are useful in wet areas, including sewage, cellars, etc. they can be securely fixed in bait boxes and very limited spillage is expected to occur.

In terms of efficacy, blocks are less attractive and may be poorly and slowly consumed. As a consequence, poor consumption may result in limited efficacy.

Recommendation: availability to all user categories

Block baits should be available to all user groups, with limited pack size for amateurs (or even tamper-resistant bait boxes distribution only for House mice and Norway rats). SGAR should be considered first choice for block baits, because of limited palatability.

4.2.2.5 Gel, liquid formulations

Rationale

Assumption

Liquid / gel formulations are ready-to use baits designed to deliver small amounts of AR. Liquid formulations may easily contaminate the skin and it is advisable to avoid refilling these formulations.

Recommendation: availability to all user categories – non refillable for amateurs

Use only non-refillable ready-to-use formulations for amateurs. Depending on the results of risk assessment, refills may be accessible to professional users.

4.2.3 Quantity of bait applied and pulsed baiting

Rationale

Assumption

The recommended quantity of bait to be put out at bait points is a function of many different considerations. The active substance in the bait, the size of the rodent infestation being treated

and the intrinsic palatability of the bait are all important factors. Manufacturers and other scientists conduct experiments, both in the laboratory and the field, to investigate and demonstrate efficacy and to develop label recommendations about the quantities of bait that should be applied. However, given the risks presented to non-target animals when AR baits are applied, it must be an absolute requirement that the minimum quantity of bait is applied that can be reasonably expected to be efficacious in most practical circumstances.

The FGAR active substances and the less potent SGARs (i.e. bromadiolone and difenacoum) are usually applied using the technique called 'surplus baiting' or 'saturation baiting' (Dubock, 1982). In this, sufficient bait is applied at each bait point so that the bait does not run out between the visits of the applicator. Against Norway rats, this usually requires the application of quantities of bait at each bait point in the range 100-300 g and against house mice the amount is usually 20 to 50g. As stated previously, and in contrast, the most potent ARs (e.g. brodifacoum, flocoumafen) have been shown to be effective against anticoagulant-susceptible and anticoagulant-resistant rats and mice when small quantities of bait are consumed only once (see for example Redfern *et al*., 1976; Lund, 1981). This permits their use with the 'pulsed baiting' technique, which employs smaller quantities of rodenticide at each bait point (commonly 20-50 g against Norway rats and 5 to 20g against house mice) and requires less frequent bait replenishment. A consequence of this is that less AR active substance is available to enter the environment and to present risk to non-targets.

Scientific evidence

Many early studies of the potent SGARs showed that they are effective when small quantities of bait are consumed over very short periods of feeding (for brodifacoum see for example Redfern *et al*., 1976; Lund, 1981; for flocoumafen see for example Buckle, 1986; Lund, 1988). These observations led to speculation that brodifacoum could be potentially effective as a 'single application' rodenticide (Rennison and Dubock 1978). Trials were therefore conducted with brodifacoum baits against Norway rats on UK farms to test the efficacy of single bait applications of 1, 4 and 7 days duration. Contrary to expectations, complete control was not achieved with any of these regimens. They resulted in 41, 51 and 68% mortality respectively. It was concluded that, to achieve satisfactory levels of control, bait must be available for longer than a seven-day period because, clearly, a proportion of rats do not feed sufficiently from bait points in the first week to acquire a lethal dose. It was also concluded that those rats that took bait during the first week, and succumbed, were likely to have fed on several occasions thereby consuming more bait than necessary to cause death.

These considerations gave rise to the concept of 'pulsed baiting' (Dubock 1982) in which limited quantities of bait are applied at approximately weekly intervals. Those animals that feed during the early stages of the treatment consume the available bait completely, finding none left when they return to the bait points subsequently. They die before another application, or 'pulse,' of bait is laid for those animals that are more reluctant to begin feeding on the poison. Two or more additional pulses may be required to achieve complete control of rat and mouse infestations. The mechanism of this process was displayed during field trials of flocoumafen (Buckle 1986).

The comparative performance of three compounds, difenacoum, bromadiolone and brodifacoum, in pulsed baiting programmes was compared by Greaves *et al*. (1988). These authors found that treatment efficacy was directly related to the toxicity of the baits used. Thus, fewer baiting rounds and less bait were required to achieve complete control of resistant *R. norvegicus* infestations with brodifacoum baits than with baits containing either difenacoum or bromadiolone. The use of pulsed baiting with compounds such as brodifacoum and flocoumafen offers valuable advantages to the rodent control practitioner. Firstly, relatively small quantities

of bait are required and less labour is needed to apply it during baiting programmes, resulting in lower treatment costs. Also, for periods during treatments, no bait is exposed because it has all been consumed by the target rodents (Buckle 1985), thus reducing the primary hazards of the treatment. There is also a reduction in the quantity of bait eaten by rodents resulting in reduced levels of residues in targets and potentially lower secondary non-target hazard (Dubock 1982).

More recently, the advantages of pulsed baiting has been demonstrated against Y139C-resistant Norway rats in Germany (Buckle *et al*., 2012) and its significant benefit in terms of reduction quantity of active substance entering the environment has been demonstrated (Daniels *et al*. 2011).

Recommendation: require pulsed baiting programmes whenever possible

Where scientific data is available to confirm the efficacy of a biocidal product containing one of the potent SGARs (e.g. brodifacoum, difethialone, flocoumafen) in a pulsed baiting application programme, this mode of application should always be used both by professionals and amateurs. Conversely, consideration should be given to restricting the use of these active substances, especially in open areas, where pulsed baiting is not used.

4.2.4 By packaging type and/or pack size

Recommendation: limited pack size and child-resistant packages for amateurs

As discussed under section 4.1.1.1, specific pack size restrictions are proposed for non-professionals depending on the active substance (FGAR vs. SGAR) and the bait formulation (see table 4).

In order to avoid cases of primary poisoning by children or pets, **AR for amateurs should be placed on the market on reclosable or non-reclosable packages meeting the standards from the CLP Regulation**, annex II, section 1:

4.2.4.1 Reclosable packages

Child-resistant fastenings used on reclosable packages shall comply with EN ISO standard 8317 as amended relating to 'Child-resistant packages — Requirements and methods of testing for reclosable packages' adopted by the European Committee for standardisation (CEN) and the International Standard Organisation (ISO). Such packages could be considered for larger packs (>250g for instance)

4.2.4.2 Non-reclosable packages

Child-resistant fastenings used on non-reclosable packages shall comply with CEN standard EN 862 as amended relating to 'Packaging — Child- resistant packaging — Requirements and testing procedures for non- reclosable packages for non-pharmaceutical products' adopted by the European Committee for Standardisation (CEN).

Benefits

- Minimise non-target species exposure (children and pets)

Limitations

- Regulatory implications (changes)

- Cost to adapt current packages

4.2.5 RMMs addressing resistance selection

See § 5.2.1. and 5.2.2

4.2.6 Post-authorisation monitoring of resistance

Rationale :

Assumption

As of today there is no specific requirement and only one MS currently requires Authorization holders to conduct post-authorisation monitoring of resistance. As developed in other parts of the document (see section 3.5), resistance is primarily related to the active substance. Different commercial products with the same active substance should, therefore, have a somewhat similar efficacy profile provided they are similarly palatable. Hence, these products should be subject to a harmonised approach when it comes to post-authorisation monitoring of resistance.

Recommendation: set up national registries / collaborative monitoring programmes / risk maps of resistance

When resistance is suspected/demonstrated (via PCR or other resistance assessment methods), the provisions in the biocides Regulation (Article 47(1)(c)) oblige authorisation holders to report the case to competent authorities. These cases should be recorded in a local/national registry, in order to map precisely resistance and resistance type for all target rodent species.

Competent Authorities or identified structures should coordinate registries / risk maps / information on resistance foci in each MS.

Collaborative resistance monitoring strategies at MS level should be developed between the companies selling products containing the same AR.

These strategies should be coordinated at EU level and designed in consultation with CAs, interested parties (authorisation holders, PCOs, etc.) and following advice from an independent scientific panel. In so doing, high quality data would be generated and made available on-line and kept up to date.

4.2.7 Standardised SPC template and harmonised label information

Rationale

Assumption

Regulatory, mandatory information needs to be placed on labels and packages, based on the product authorisation (SPC) and the CLP Regulation. It is suggested that most of the information should be placed on the label inserted in the package and the most important information on packages. Warnings such as *"keep out of reach of children"* for instance, need to be clearly visible. Regulatory requirements (H and P statements) must appear clearly. Review of existing labels and instructions shows highly different requirements among MSs. Labels are also extremely complex and the amount of information provided is extensive, and sometimes confusing.

Recommendation: provide a harmonised label information

Labels include regulatory information, which are quite similar across Europe. Because Mutual Recognition under the previous biocidal products Directive leaved some room for the

application of different RMMs, each MS may have required specific information on label. It appears desirable to have a common approach (at least in a given MS) for similar products (i.e. same active substance, same formulation), to identify key points on the package itself and include all mandatory information in a separate document. Use of web-based QR codes or applications could provide accurate and user-friendly information about Good Practice, Resistance or any other information. The basis for such a harmonised document could be the SPC, which should be used consistently across the EU.

Common sentences to be found and harmonised for the key RMMs; e.g. "Keep out of reach of children" and "Baits must be securely deposited in a way so as to minimise the risk of consumption by other animals or children. Where possible, secure baits so that they cannot be dragged away". The most important recommendations should be placed on the package itself, but it is also strongly recommended to limit package recommendations to the most important H and P statements.

An example of SPC template with standardised sentences for the main RMM is provided in Annex 8.

Benefits

- Consistent information across Europe, harmonisation
- Less cost for label translation / adaptation

Limitations

- Adaptation to existing MS regulations
- Standardized Mutual Recognition (less adaptability to local requirements)

4.2.8 Authorisation holder to ensure that information is provided to users

As part of the authorisation process, a detailed list of information media should be provided (documents, diffusion, hotlines, website information etc.).

Small leaflets listing all pertinent information needed for correct use of AR should be designed and provided to all categories of users.

This is of particular interest for amateur users, where the label on small packages can include limited information provided that an accompanying leaflet integral to the packaging is provided with the product.

Recommendation: authorisation holder should provide a a list of information media to be used for user information

Benefits

- Detailed list of communications tools
- Adaptation to user category

Limitations

- Cost
- Not a regulatory requirement unless limited information is provided on the label of small packages
- Time needed to revise, review, distribute documents

4.2.9 Overview of proposed RMMs at the product authorisation stage

An overview of the proposed RMMs to be implemented through the products authorisation is provided in Annex 5 to this report.

4.3 General recommendations:

4.3.1 Resistance evaluation and monitoring

4.3.1.1 Resistance evaluation

Rationale

Testing for resistance is required to provide objective data that can furnish the basis on which to establish effective resistance management strategies. Today, several testing procedures exist.

The major disadvantage of *in vivo* investigations is that they must be conducted on sentient wild animals live trapped from resistant infestations. Such procedures, where tests are conducted on live vertebrates, are conducted at specialised facilities with strict adherence to licensed protocols. Such studies, which involve the testing of a range of anticoagulant active ingredients against rats and mice from suspected resistance foci are both time consuming and expensive. Methods that have been successfully used in the laboratory include feeding tests, where resistant animals survive a lethal feeding period (LFP) that would be expected to kill susceptible animals, and Blood Clotting Response (BCR) tests, where animals are dosed with anticoagulant, and sometime later, susceptible animals are found to have a much longer clotting time than resistant animals. A recent development of the BCR test allows both the identification and quantification of resistance (Prescott *et al*., 2007), by providing an estimate of the Resistance Ratio. Such BCR tests have been used alongside field trials for a particular active ingredient to investigate the link between the Resistance Factor and treatment outcome (Endepols *et al*., 2007).

The detection of resistance using the *in vitro* methodology based on DNA sequencing of the VKORC1 gene has simplified the resistance monitoring process. This technique is the most cost-effective, and has identified a number of mutations in resistant populations of Norway rats and House mice, that were the subject of research publications as far back as the 1960's (Pelz *et al*., 2005), (Grandemange *et al.,* 2009b), (Prescott *et al*., 2010). In many cases, the potential impact of a VKORC1 mutation can be inferred from previous research (Buckle 2012), while for new mutations, or mutations that have been less well studied, other *in vitro* or *in vivo* tests are available to provide this information (Grandemange *et al*., 2009a), (Hodroge *et al*., 2011), RRAG, RRAC).

In vitro and in vivo evaluation

In situations where rodenticides are used correctly, but bait consumption plateaus and remains stable over 2-3 weeks, with no obvious further reduction in the rodent population, anticoagulant resistance would be suspected. If the infestation is located within an area where resistance has previously been documented, it could be assumed that the resistance will be of a similar type.

Where such information is not available, tissue samples should be collected from between 4 and 10 individual animals from the infestation (avoiding individuals that have died as a result of anticoagulant poisoning), and a VKORC1 resistance assessment should be conducted. Testing a number of animals from the infestation will provide information about the incidence of

resistance in the population, and in particular, the proportion of homozygous resistant animals which will possess a higher degree of resistance than heterozygous animals.

Once the VKORC1 mutation has been identified, the likely impact on treatment outcome can be determined from published information, and the recommended management strategy can be determined from published guidelines. The Rodenticide Resistance Action Group has produced such documents for the UK pest control industry (RRAG 2010, RRAG 2012[a], RRAG 2012[b]), and it is recommended that similar documents be made available on-line to the pest control industry in all MSs, so that the distribution maps and the likely impact on treatment outcome for each of the VKORC1 / species combinations can be regularly updated, in the light of work conducted across MSs and elsewhere.

Recommendation: recommend *in vitro* testing for resistance

The detection of resistance using the *in vitro* methodology based on DNA sequencing of the VKORC1 gene has simplified the resistance monitoring process. This technique is the most cost-effective, and has identified a number of mutations in resistant populations of Norway rats and House mice, that were the subject of research publications as far back as the 1960's (Pelz *et al*., 2005; Grandemange *et al*., 2009b; Prescott *et al*., 2010). For mutations already described and when the resistance potential has already been evaluated (see Buckle, 2012), *in vitro* DNA sequencing should be recommended as the first step.

In vivo evaluation should be considered when *in vitro* evaluation is negative or as a complementary tool in field trials for the development of new rodenticides.

Results of resistance evaluation should be posted on dedicated networks to complete nation-wide surveillance objectives.

Benefits

- Rapid, cost-effective detection of resistance in all commensal rodent species
- Documented evidence for proper rodenticide treatment

Limitations

- Laboratories to screen for the most common mutations need to be identified in MSs
- Procedures for reliable testing need to be validated in MSs

4.3.1.2 Resistance monitoring

Rationale

Scientific evidence

The preliminary report describes the biological basis of resistance as well as the various resistant strains identified in the EU and will not be further presented here.

Since the early 60s, resistance to anticoagulant rodenticides has been described across Europe and appears to be quite common in Norway rats (Pelz *et al*., 2005;, Grandemange *et al*., 2009b; Baert *et al*., 2012; Prescott *et al*., 2010) and in House mice ((Pelz *et al*., 2005); (Song *et al*., 2011)). However, to date our understanding of the geographical distribution of the different types resistance in these species is lacking in many MSs. With the development of the new molecular resistance testing methodologies, it could be demonstrated that the extent of resistance is now expending rapidly in many EU MSs, while in others no information is available. A major concern is the increased severity of resistance that has now been demonstrated at many resistance foci,

and that is posing a significant threat to the sustainable use of these compounds. This problem is compounded because of our virtual complete reliance on these active substances for rodent control in the EU, due to the limitations of alternatives. Anticoagulant resistance management is therefore essential if the future of these rodenticides is to be prolonged. See Annex 1 for more details about resistance in the EU.

Recommendation: set up national registries / collaborative monitoring programmes / GIS risk maps of resistance

It is recommended that nationwide surveillance systems are set-up at MS level in order to monitor resistance in the different target species for each AR substance. As the surveillance is based on the active substance, these systems should be supported in a collaborative manner by the companies selling products containing the same AR in that MS. The outcome from this monitoring system should recorded in a local/national registry together with any other notifications submitted by authorisation holders on cases of suspected lack of efficacy or resistance. The overall information in that register would enable mapping precisely resistance and resistance type for all target rodent species.

These national systems should be coordinated at EU level and designed in consultation with CAs, interested parties (authorisation holders, PCOs, etc.) and following advice from an independent scientific panel. In so doing, high quality data would be generated and made available on-line and kept up to date.

The surveillance system would be primarily based on the new molecular resistance testing methodology (which detects mutations of the VKORC1 gene), in order to understand adequately the extent of anticoagulant resistance in rats and mice. In the first instance, such monitoring would need to be conducted in collaboration with the laboratories that are currently set up to conduct the molecular analysis, and it is envisaged that a network of such laboratories would eventually become established across all MSs.

The monitoring system would be reliant on effective tissue sample collection that could be conducted by all stakeholders, including local governmental authorities, PCOs, farmers, and Industry. Subsequent restrictions on the use of the different anticoagulant active ingredients could then be based on objective available data, such as the Resistance Factor data for the different active ingredients and resistant strains that is currently being generated by the Rodenticide Resistance Action Committee (RRAC), and the guidance documents produced by the Rodenticide Resistance Action Group (RRAG) that considers the potential impact of the different VKORC1 mutations on treatment outcome.

Focusing primarily on VKORC1 mutations appears to be the most feasible approach, since these mutations represent the vast majority of resistance cases in Norway rats and, most likely, in House mice. A comparison with antibiotic resistance, for instance, shows that laboratories testing for resistance report their results to a common database.

It is proposed that the results from the resistance testing methodology should be widely disseminated using an on-line database with GIS mapping technology, to present the extent of each of the VKORC1 mutations, and the ratio of homozygous to heterozygous resistance. The database could be set up to include other relevant information such as land use (agricultural, industrial, urban etc.), and could include a time axis that could be used to monitor both the expansion of resistance in certain populations, and the success of resistance management strategies.

Benefits

- Optimise post-authorisation monitoring resources for products containing the same AR
- Provide valuable information about the extent and spread of resistance in commensal rodents
- Adapt local management strategies based on resistance information available and accurate
- Evaluate different strategies with respect to potential efficacy to control the spread of resistance
- Effective detection and management of anticoagulant resistance in populations of Norway rats, roof rats and House mice
- Permits sustainable use of ARs and prolongs their viable life in practical use

Limitations

- Cost and organisational aspects for collaboration between different authorisation holders
- Time required to generate results and establish a functional on-line database
- Spatial accuracy

4.3.2 Resistance management

Rationale

Scientific evidence

The control of rodent infestations should always be conducted using integrated pest management (IPM) and should never be solely dependent upon the use of chemical rodenticides. This is particularly the case with ARs when dealing with rodent populations that possess a degree of physiological resistance. In addition to chemical rodenticides, an IPM programme can involve the management of the environment and habitat (to restrict access to food, water and harbourage), proofing (to exclude or restrict access), and trapping (see RRAC, 2003).

Across Europe, many populations of Norway rat and House mice have been found to possess mutations of a resistance gene (VKORC1) that is known to confer a degree of resistance to the animal. However, the incidence of the resistance gene in populations can be variable. At one extreme, the majority of animals in a population will possess the resistance gene in the homozygous state, while at the other extreme, only a few animals in the population will possess the resistance gene in the heterozygous state, and the majority of animals will be homozygous for the wild type susceptible genotype. When ARs are used that are ineffective against most animals that possess a resistance gene, they will selectively kill the susceptible animals, and rapidly increase the incidence of the resistance gene within the surviving population. As heterozygous resistant animals are more easily controlled by ineffective AR rodenticides than homozygous resistant animals, the continued use of these rodenticides will eliminate susceptible animals, and increase the proportion of homozygous resistant animals in the population. In surveys of VKORC1 mutations in Norway rats, it is not uncommon for all animals sampled to be homozygous for the VKORC1 mutation, indicating a prolonged history of selection through the use of ineffective “resisted” anticoagulant rodenticides. This has been the case for many populations of Norway rat in the UK, both for the VKORC1 resistance mutations L120Q in central southern England and Y139F in Kent, due to a misguided regulatory policy which prevents the use of effective resistance-breaking ARs against Norway rats in the UK (Buckle, 2012).

In laboratory strains of Norway rats (that are homozygous susceptible or homozygous for a particular resistance gene), their dose response, which is distributed according to the normal statistical distribution, can be analysed using Probit analysis (Prescott *et al*., 2007). Thus in any population of Norway rats that are homozygous for a particular VKORC1 mutation, not all

individuals will be equally resistant to the AR; and continued use of ineffective AR against such a population is likely to achieve some mortality of homozygous resistant animals.

Independently, Greaves and Cullen-Ayres (1988) and MacNicoll (per. com.) have produced a "selected line" of homozygous resistant Norway rats over several generations by repeatedly administering AR to groups of animals at a rate insufficient to achieve complete mortality, and then breeding from survivors. These "selected lines" were shown to have higher Resistance Factors than the original homozygous resistant strain, and have thus become considerably more resistant to ARs. It is very likely that the prolonged use of ineffective AR in practice, will have a similar effect on wild populations, and will result in homozygous resistant animals with higher Resistance Factors, that are increasingly more difficult to control.

Greaves and Cullen-Ayres (1988) further demonstrated that the enhanced Resistance Factors of the "selected line" occurred with all three of the active ingredients tested; difenacoum, bromadiolone and brodifacoum. Thus the prolonged use of an ineffective AR against a wild population of Norway rats possessing a VKORC1 mutation will result in increased Resistance Factors for all AR active ingredients; progressively as susceptible animals are eradicated, the incidence of the resistance gene increases, the proportion of homozygous resistant individuals increases, and the "selected line" develops.

It is well known that resistance is not compound-specific, but can be selected for by an ineffective AR and will result in enhanced Resistance Factors for all ARs, although for the most potent ARs, these Resistance Factors are small and are unlikely to have any perceptible effect on treatment outcome. It is also evident that continued use of ineffective AR has the potential to produce a "selected line" of resistant animals that will be increasingly more difficult to control, even with effective ARs.

Recommendation: restrict use of AR to those known to be effective

In case of lack of efficacy with good bait consumption, resistance may be suspected and actively identified by one of the means described in other sections of the document (see 4.3.1.1).

Where it has been demonstrated that a rodent population possesses a resistance gene, the use of ARs should be restricted to active ingredients that are known to be fully effective against the resistance mutation in question.

Studies are on-going for a number of the VKORC1 mutations to estimate the resistance factor for each AR active ingredient. Using data generated in the UK, Germany and France, the Rodenticide Resistance Action Group (RRAG) has considered the effect of five VKORC1 mutations on treatment outcome when FGARs or SGARs are used (see RRAG, 2010). With two mutations (L128Q and Y139S), the concern is that FGARs are likely to be ineffective, and for three mutations (Y139C, Y139F and L120Q), the concern is that FGARs, bromadiolone and difenacoum are likely to be ineffective. The document captures the current view of the potential impact of the difference VKORC1 mutations on treatment outcome using FGARs and SGARs, and should be adopted across MSs for guidance on which active substances should not be used against resistant Norway rat populations possessing a known VKORC1 mutation.

This document should be actively updated, and expanded to include all VKORC1 mutations in both Norway rats and House mice, to provide a basis on which to decide which active ingredients not to use against a resistant rodent infestation.

In order to implement these Guidelines, it is essential for each MS to initiate a VKORC1 resistance monitoring program to map the geographical distribution for each of the VKORC1

mutations identified. Ideally this would be conducted by laboratories (i.e. from Universities or Government Agencies) in all MSs. This monitoring program is currently operational in our laboratories in the UK, France and Germany. We would be happy to collaborate with all MSs, initially by conducting the analysis on samples shipped to our laboratories, and subsequently by providing assistance to set up the monitoring program in laboratories from each MS.

The Resistance Management Program should be implemented and maintained across all MSs by a Committee consisting of participants from each MS, in order to ensure that the Guidelines are updated appropriately, and to oversee and review the resistance management program.

4.3.3 Non-target poisoning monitoring

4.3.3.1 Exposure to humans

Rationale

Monitoring exposure of human beings to anticoagulants is a well-established procedure across Europe and all over the world (see for instance Bronstein *et al*., 2011; Bronstein *et al*., 2010; Bronstein *et al*., 2009; Berny *et al*., 2010). In most countries, human exposure cases are referred to human poison control centres and it is widely agreed that the vast majority of non-intentional exposure cases result in minimal harm with no requirement for subsequent follow-up, even in children (Ingels et al., 2002) ; (Caravati et al., 2007) Comité de coordination de toxicovigilance, Paris, 2010. The medical profession has extensive experience with ARs because these compounds are routinely used for medical intervention in humans, and has basic procedures in place to quickly determine any adverse effects. This measure is also strongly supported by stakeholders who usually refer questions regarding human exposure to Poison Control Centres (see Annex 6).

Recommendation: use poison control centres to retrieve human exposure cases

It is recommended to reinforce the role of poison control centres (or any similar structure) and add phone numbers on labels / packages and to constitute databases available for retrospective surveys and evaluation of prevalence of anticoagulant exposure. Information on emergency phone numbers should also be available on websites, leaflets and documents distributed in retail shops.

For professionals, it seems advisable to recommend an annual evaluation of potential exposure to ARs. Routine procedures usually include complete evaluation of haemostasis, as can be performed for human patients under anticoagulant therapy.

Benefits

- Provide an immediate access to human toxicologists for any exposure case.
- Protect professionals

Limitations

- Cost and time for label/package modification
- Cost of data collection

4.3.3.2 Exposure to pets

Rationale

Scientific evidence

The use of anticoagulant rodenticides can result in unwanted non-target exposure cases in domestic animals and many publications have identified this problem (Berny *et al*., 2010; Bradbury, 2008; Waddell et al., 2013). There is, however, no consistent reporting of pet exposure in European countries, with the exception of WIIS in the UK, and different systems or poison control centre-like units may have experience in collecting pet poisoning cases (Guitart *et al*., 2010). In other parts of the world, like in the US, specific centres have been identified, either private or public, like the National Pesticide Information Centre (Buhl *et al*.,, 2013). As stated in the preliminary report (see Annex 1), developing/identifying specific hotlines, either within existing poison control centres or as dedicated units would certainly provide valuable information to evaluate the actual impact of rodenticides on pets, as well as the efficacy of RMMs on long-term retrospective or prospective surveys. This type of information is used in human and veterinary drug development to assess secondary adverse events, the circumstances of these accidents and the products involved in order to re-evaluate drug safety and modify label recommendations (Anses, 2012).

Recommendation: identify veterinary structures to collect domestic animal exposure data and collect data on actual uses of AR

Identify Animal Poison Control Centres (or equivalent)

It is recommended to have dedicated monitoring systems for domestic animal poisoning. Several countries already have specialised units, either in Human Poison Control Centres or dedicated Animal Poison Control Centres. The availability of hotlines/specialised units would provide effective service to deal with anticoagulant poisoning cases in animals (mostly pets but also food-producing animals).

Rodenticide manufacturers and PCOs may have specific hotlines or services to deal with non-target poisoning. It appears, however, that many situations will require specific advice from a veterinarian. It is not conceivable to have a veterinarian online for each company producing, selling or applying anticoagulants. Therefore, relying on dedicated structures (governmental offices or private structures officially recognised by the local CA to deal with anticoagulant poisoning issue in animals) appears as the most reasonable option.

Animal poison control centres (or equivalent structures) should also have access to analytical facilities to confirm clinical poisoning cases, especially when legal actions are being considered.

Private companies using/selling anticoagulant rodenticides may receive calls/requests regarding potential pet exposure. They should transfer these inquiries to identified structures.

Benefits

- Provide references and emergency numbers to pet owners primarily, in order to cover for unexpected exposure
- Retrieve data for later evaluation of the efficacy of RMMs

Limitations

- Availability of services across Europe
- Cost

Include information to report pet incidents in existing documents (labels, leaflets) in each MS

Information about these structures should be made available by CA (website, QR codes…), by companies (label or leaflets), in points of sale.

Establishing or recognising existing structures should help MSs to have updated information on the actual frequency and severity of non-target pet poisoning with anticoagulant rodenticides.

The expertise of poison control centres is essential in order to gather important information on each incident, especially with respect to circumstances of exposure. Long term monitoring can provide valuable data to identify and quantify the impact of each rodenticide product. It is also possible to monitor trends and changes in the type of incidents and relate these changes to product modifications, if documented. It seems advisable to have published information (website, scientific journals, CA…) providing general (anonymous) data about anticoagulant pet exposure to the general public (as it is done by the WIIS in UK for instance).

Benefits

- Information readily accessible for pet owners faced with an unexpected exposure case
- Provision of emergency phone numbers or recommendations for unexpected exposure cases

Limitations

- Time and cost of development
- Diffusion to points of sale
- Avoid redundant documents

Collect information on actual uses of anticoagulant rodenticides

In order to provide quantitative data, companies should provide key figures of the volume/volume of products placed on the market of each MS (by active substance / product name…). Such data are highly confidential and should only be used under the supervision of CA for re-evaluation of products for instance. Sales figures are used in veterinary and human pharmaco-vigilance structures to assess the prevalence of adverse events, the circumstances of such events and to provide and modify label accordingly. These figures are not available for other purposes. Another possibility would be to conduct general surveys to identify uses, amounts being used, category of user, circumstances of use…

In return, companies should also have access to incident record data on their products.

Benefits

- Provide realistic information on uses (and approximate amount) of anticoagulant rodenticides by categories of users
- Provide a basis for rational evaluation of the prevalence of poisoning (by product, product type, user type…)
- Post-marketing surveillance

Limitations

- Highly confidential information should only be accessible to CA or officially recognised structures, to evaluate potential risks associated with different products
- Cost, time, evaluation of data

4.3.3.3 Exposure to wildlife

Rationale

Scientific evidence

There are widespread concerns about wildlife exposure to SGARs across Europe and elsewhere; where predatory and scavenging mammal and bird species consume rodents that have been poisoned with ARs, and other wildlife species consume the rodenticide bait directly.

The occurrence of AR residues as a result of secondary exposure in predators and birds of prey is widely recognised (Berny and Gaillet, 2008; Stone et al., 2003;Sánchez-Barbudo *et al*., 2012) , with low-level exposure being frequently reported (Elmeros *et al*. 2011; Langford *et al*., 2013), although there is very little understanding about the likely impact of such exposure at the individual and population level (Lemus *et al*., 2011). In the UK, the long-term data set provided by the work of the Predatory Bird Monitoring Scheme (PBMS) is particularly comprehensive and instructive (see for example Walker *et al*., 2011).

Several schemes have been established in MSs to collect and analyse wildlife carcasses where screening for SGARs is carried out routinely. Such screening is essential to effectively monitor the environmental impact of SGARs, and should consider:

1. The involvement of SGARs in wildlife mortality where pesticide poisoning is suspected

2. The presence of SGARs in wildlife where pesticide poisoning is not suspected, in order to provide a measure of 'SGAR Exposure'

3. The likely impact of sub-lethal SGAR residue levels on the wildlife species, both at the individual and population level.

Recommendation: use wildlife surveillance schemes to collect suspected poisoning incidents and support epidemiological surveys of wildlife exposure

Establish / identify networks to collect data on wildlife suspected incidents

There are a number of schemes operating across Europe that are investigating SGAR residue levels in wildlife species. The objective of these schemes is either to investigate the cause of death of wildlife where pesticide poisoning is suspected (UK Wildlife Incident Investigation Scheme; France's SAGIR network, Germany's reporting scheme); or to assess the exposure of certain wildlife species to pesticides including SGARs (UK Predatory Bird Monitoring Scheme; Vigilance Poison in France). These schemes regularly report the presence of SGARs in liver tissues of the screened animals. However, there is no consistency in the operation of these schemes across MSs.

A collaborative network of laboratories should be set up across all MSs to provide data on the occurrence of SGARs in wildlife. These laboratories must be adequately resourced.

Additional information that would be useful to document include gross necropsy, circumstances of discovery, the organ analysed, and the possible source of the anticoagulant, if this is known.

The collation of such data across Europe would provide baseline information on the current impact of SGARs to wildlife, and could subsequently be used to assess the effectiveness of the Risk Mitigation Measures deployed.

With respect to the interpretation of residue level, some work needs to be done to interpret data correctly. For instance: Mineau *et al.* (2005) conducted an avian reproduction study on mallard ducks dosed with 0.05 mg/kg brodifacoum. They found no obvious breeding impairment, with surviving animals having brodifacoum liver residue levels up to 0.42mg/kg. Sorex (2006) conducted an avian reproduction study on Quail, feeding them on 0.1mg/kg difenacoum bait over 10 weeks pre-egg laying and 10 weeks egg laying, concluded that the "no observable effect

concentration was above 0.1 mg/kg difenacoum, and found surviving animals with difenacoum liver residue levels up to 0.46 mg/kg.

Collect information on actual uses of anticoagulant rodenticides

In order to provide quantitative data, companies should provide key figures of the volume/amount of products placed on the market of each MS (by active substance / product name…). Such data are highly confidential and should only be used under the supervision of CA for re-evaluation of products for instance. Sales figures are used in veterinary and human pharmaco-vigilance structures to assess the prevalence of adverse events, the circumstances of such events and to provide and modify label accordingly. These figures are not available for other purposes. Another possibility would be to conduct general surveys to identify uses, amounts being used, category of user, circumstances of use…

In return, companies should also have access to incident record data on their products.

Benefits

- A common framework for the assessment of non-target poisoning incidents across Europe, including data on circumstances of exposure, active substances, species involved, that could be used for the long term access and re-evaluation of RMMs.
- Experience from several EU countries, which already have efficient incident monitoring networks, could be expanded to develop an effective network across all MSs.

Limitations

- Because anticoagulant rodenticides have a delayed action, it will often be difficult to assess circumstances of exposure.
- Wildlife incidents can only be confirmed using a combination of analytical evidence and clinical evidence. Such work is expensive and will require funding.
- Liver residue levels as low as 0.1 mg/kg have been used to indicate potential lethal poisoning, although some available data do not concur with this.
- This relationship between SGAR liver residue concentration and survival or mortality outcome requires further investigation.

Support epidemiological surveys of wildlife exposure and effects

This second level is a recommendation to support large epidemiological and experimental work on wildlife exposure and potential health effects. These studies should investigate different vertebrate/non vertebrate species and understand how anticoagulants can be detected in so many different species (food-web transfer) as well as potential population health effects associated with low level exposure.

Benefits

- Provide scientific data on the contamination of the food-web
- Provide scientific investigation on potential health effect of low-level anticoagulant exposure

Limitations

- Limited scientific knowledge on any detrimental effect of low-level exposure so far
- Complex epidemiological surveys, financial support from funding agencies needed

4.3.4 Training for Trained Professionals

Rationale

Assumption

For the purpose of Biocidal Product application, trained professionals have been considered as a specific user category. This includes pest control operators only. Qualification of professionals is an issue that needs to be addressed with respect to Biocidal Product application, since there is, up to now, no common background of knowledge or regulatory requirements across Europe, as it is the case in the US (http://www.cdc.gov/nceh/ehs/eLearn/IPM.htm). Some countries have developed PCO certification as part of the general Plant Protection Product application certifications, or as separate trainings, but this not a general procedure in the EU (CEFIC, 2013).

Training and continuing education is part of the professional career. It is required for PCOs as well as other professionals to provide proof of their regular training (Germany, France, the Netherlands, UK, USA for instance). Both PCOs and manufacturers of rodenticides strongly support the need for adequate training and certification (see Annex 7).

Recommendation: recognize standards for Pest Management Services

Implement a European Standard for Pest Management Services

In 2013, a project has been submitted to the CEN (Comité Européen de Normalisation – European Committee for Standardization) regarding Pest Management Services – Requirements and Competences (prEN16636) and is currently under review. This project covers both the general approach of Pest Management and the specific requirements in terms of competence and training. Approbation of this European Standard would clarify the general regulatory requirements and provide a reasonable basis for PCO certification. In several MSs, training / certification programs already exist. There is no need to duplicate existing procedures but rather to harmonise the level of requirements with existing national schemes.

Benefits

- Provide a standard framework to officially recognise a professional working in pest control

Limitations

- This standard has to be validated by an external structure (CEN)
- Time for implementation in MSs (delay)
- Licence documents, which have to be controlled

Develop/Identify specific training programs for PCOs

It is suggested that formal and validated training should be required, as in the CEN project, as a pre-requisite to serve as a "professional user" (i.e. applicator). Furthermore, competences should be regularly evaluated and updated as suggested in the project. Companies and professionals unable to provide proofs of initial, as well as regular, training should not be considered as PCOs and allowed to have access to all products and procedures available for "trained professionals". Similar recommendations in terms of qualification and training of personal should apply to local authorities or governmental bodies acting as PCOs in the public service.

In many regulatory jurisdictions, specific training courses are available on rodent pest management. These courses are offered either as a part of a wider qualification in pest management practices or as stand-alone courses which cover only rodent pest management. Where these courses lead to the formal the award of a qualification, and the registration of

qualified personnel by an approved training body, untrained professionals who obtain such a qualification may then be considered to be 'trained professionals'.

The characteristics of any training courses, which provides formal qualification as a 'trained professional', optimally will have the following characteristics:

- The syllabus of the course will have been audited as suitable for the purpose of training by an independent qualification/education authority. If the course is considered to be fit for award of a professional 'certification' it will have met appropriate national or international training standards.
- Trainers who offer the course will have shown themselves to be sufficiently knowledgeable in the subject to be capable of training others and will be registered with an appropriate awarding body or training institution.
- The examination for award of the qualification will conducted under conditions of independent invigilation, or if conducted on-line will be carried out in an environment that is appropriately controlled.
- Exam marking will be independent of those who offer the training and marking will be moderated by an independent awarding body or training institution to ensure a consistent approach among different awarding bodies.
- The register of those awarded the qualification will be maintained by an appropriate trade association, awarding body or training institution

There is a justifiable expectation that all those workers who apply rodenticides as a part of their duties should be so trained and registered as qualified and should therefore be competent in their use. However, this expectation is not present in the case of 'professionals' who apply rodenticides either only on their own land or in and around premises that they own or exert control over.

A specific type of 'trained professional' is the pest management professional (PMP) or the professional pest controller (PCO). These technicians would usually be trained in a wide array of pest management techniques, including rodent pest management. Their principal professional working activity is pest management and therefore this is performed on a daily basis. It is to be anticipated that they will use rodenticides more frequently than other 'professionals', such as farmers, store keepers and janitors, and apply larger quantities of them. A consequence of this is that they should be expected to be trained at a higher level than those who use rodenticides only occasionally. Once again, there is a wide array of training courses for PMP/PCOs in the MSs of the EU.

Where professional qualifications, such as those referred to above, have been audited and approved by professional bodies and trade associations and have been found to meet certain national or international training standards set by government bodies, such a biocides Competent Authorities, those who attain these qualifications may be registered with the awarding bodies and therefore become "certified".

Online training may be considered as well as continuing education programs.

Benefits

- Provide a common standard for training of PCOs
- Identify and develop specific training programs for rodenticide use
- Increase professional skills and reduce risks associated with anticoagulants

Limitations

- Cost for smaller business units
- Implementation in MSs and coordination with existing programs (if any).

*when available

4.3.5 Training of Professionals (farmers, gamekeepers)

Rationale

A Professional user is a broad category encompassing PCOs, farmers, game-keepers. In this document, PCOs are considered under the "Trained Professional" category only (see previous chapter above). There is published evidence (Tosh *et al*., 2011) demonstrating that farmers do not know and apply all RMM for anticoagulant rodenticides. As a consequence, the agricultural use of AR may result in substantial non-target exposure (Hughes *et al*., 2013). Training, therefore, appears as a necessary tool to increase knowledge and awareness of professional users such as farmers.

Recommendation: provide training for professional users of AR

Adapt existing training programs on plant protection products for farmers to include sessions on rodenticides

Farmers and other professionals usually have training in a variety of specialised issues. Application, storage, disposal of plant protection products is usually considered in special training programs with certification. There is no similar program for Biocidal Products at the moment (except for the recent Certibiocid developed in France). These training programmes should be slightly modified to integrate specific training sessions on rodenticides and, more generally on rodent population control in their common environment, if this is not already part of the training program. MSs should consider either developing a specific program or adding specific training units to existing programs for farmers.

Training should cover (not exhaustive list of items): rodent biology (including identification and behaviour), problems caused by rodents, rodent control methods (including trapping, physical, chemical method, rodent-proofing…), non-target and environmental impact of rodenticides, resistance to rodenticides and resistance management strategies, regulatory aspects. Information from PCOs and accredited teachers/trainers could help develop these specific training programs to be included as part of general Pesticide use/application certification packages. Training sessions of about 1 day should cover most topics necessary for a correct use of rodenticides around farm buildings.

It is also suggested to encourage training of sellers involved in delivering rodenticides to farmers or amateurs (see 4.3.6.1)

Benefits

- Provide a common standard for training of professionals
- Identify and develop specific training programs for rodenticide use
- Develop professional skills and reduce risks associated with anticoagulants

Limitations

- Time and cost of training for individuals

- Availability /development of appropriate training programs
- Licence documents, which have to be controlled

Provide information on rodenticides in points of sale and via professional organisations

Information should be available via the professional bodies, but also at points of sale (in the form of Best Practice Codes or Guidelines) and on specialised websites for farmers.

Benefits

- Remind farmers of the potential risks associated with the use of anticoagulant rodenticides
- Provide valuable information on correct and sustainable use of rodenticides and control of rodents in farms
- Provide valuable information on risk mitigation measures
- Reinforce former training sessions

Limitations

- Time and cost of developing leaflets or websites/smartphone applications

4.3.6 Provision of information for the general public

It is not possible to envisage comprehensive training for amateurs, either on-line or in the classroom. Therefore reliable sources of information should be readily available to them on labels, packages and leaflets available at points of sale, to be distributed by competent / trained staff only.

However, the provision of validated, accurate information is necessary. For example, in the UK many retail outlets have Specially Qualified Persons (SPQ) present to provide information and training for amateurs (http://www.amtra.org.uk/index.php?page=sqp). Training materials could also be presented in store using video loops. MSs are required to have a website to display information on Biocidal Products authorised. It seems important to provide more information about proper use of rodenticides or other rodent control measures (rodent-proofing, removal of food and shelter…), risk to non-target species and risk mitigation measures, resistance. This information should be easily accessible, in the form of leaflets, documents, webpages (including smartphone applications) in a user-friendly format. Dedicated hotlines usually provide a complementary service and can provide rapid information or refer callers to the appropriate emergency unit (NPIC see website).

4.3.6.1 Point of sale

Rationale

We were unable to locate information that could be used to assess the advantages of displaying information and the provision of specifically trained persons at the point of sale. Some interesting work has been conducted with veterinary drugs in France (Delhaye, 2008). Pesticides used for external parasite control for pets are available to the general public by three different means:

- by the veterinarian (62.6%)
- by a pharmacist (32.8%)
- in general stores and garden stores (4.6%)

The study focused on permethrin use in cats, as permethrin is contra-indicated in this species but still the most common cause of adverse drug reaction in cats (Anses, 2012). The

retrospective survey showed that most cases (63%) occurred after purchase in a pharmacy store while general stores and veterinary clinics represented 19 and 18% respectively. The relative prevalence of accidents compared with veterinary clinics was 1.9 in pharmacy stores and 3.9 in general/garden stores. This survey concluded that the presence of at least one person with specific knowledge on the toxicity of the product in cats was required to reduce the risk of misuse by the owner. At the same time, the author reviewed the prevalence of adverse reactions in cats after the implementation of a recommendation to use specific labels warning potential users about the toxicity of permethrin to cats. This survey also concluded that having simple, straightforward recommendations, icons and labels resulted in a significant decrease in the prevalence of adverse reactions related to misuse in cats (Delhaye, 2008).

Recommendation: provide various media in points of sale for amateurs

Provide Leaflets / Boards / Videos in points of sale

Information should be available in points of sale. There is already a lot of information available on the label/package of rodenticides, the idea would be to simplify the label and have more useable information in dedicated leaflets available at retail outlets. Information on proper use, risk to humans, pets and the environment, emergency phone numbers should be clearly identified, reference to websites for the provision of information should also be included. In-store video loops may also be displayed to provide information to deliver correct information about proper use and safety procedures for AR.

Benefits

- Provide valuable information on correct and sustainable use of rodenticides and control of rodents to users who cannot be reached by conventional training procedure
- Provide valuable information on risk mitigation measures

Limitations

- Risk of redundant documents
- Cost of production, diffusion

Presence of Specifically Qualified Persons in retail stores

It is currently the case in many garden shops to have specifically trained persons to deliver pesticides and provide advice and safety information. It seems advisable to encourage the presence of such persons in all stores delivering rodenticides to amateurs, with information displayed in the sale area. These qualified persons could undergo the specific training programmes designed for farmers for instance (see above 4.3.5).

Benefits

- Contact person in retail stores
- Availability for documentation, information, right application of RMM

Limitations

- Initial and regular training
- Cost (salary, documentation production, control of licences)

4.3.6.2 Online

Recommendation: develop or support non-commercial websites to provide adequate information on AR

Provision of information via internet

Dedicated non-commercial/official user-friendly websites should be available to provide information on authorised rodenticides, their proper use and the risks (see for example the website of the UK and Ireland Campaign for Responsible Rodenticide Use; www.thinkwildlife.com). CAs should have specific web pages dedicated to rodenticides, their proper use and RMM. An actualised list of products and SPC (without confidential information) could be suggested to provide regulatory and accurate information to all rodenticide users.

Private companies should also keep their own websites to provide information on their products and refer to appropriate emergency hotlines. It is also advisable to encourage European cooperation to develop common documents and recommendations, available on all affiliated websites.

This information could also be made available as a QR code on the package itself.

Benefits

- Provide readily accessible valuable, accurate and validated information

Limitations

- Internet accessibility in remote areas or at the site of application

4.3.6.3 Product information

Rationale

Assumptions

The UK and Ireland CRRU initiatives have produced a very thorough document on stewardship of AR. Specific recommendations have been suggested by user groups in order to adapt the label recommendations and information available to the category of user.

Commercial products may be available in small packages and the amount of information, which can be placed on the package or on the label, may vary greatly. Products with a similar intended uses may have very different package information and /or label recommendations (CRRU, 2014).

Recommendation: provide a harmonized SPC

A harmonized SPC should contain all information necessary for proper amateur use and RMM. Products for amateurs should be clearly distinguishable from other products. This SPC should be readily available (online, provided by the company and/or the CA). Information to be included should contain the following items :

- product description (name, authorization number and authorization holder, active ingredient, concentration, formulation, total amount available, target species)

- recommended use and applicable guidelines (if any) with recommendations on storage, bait elimination, rodent elimination
- mandatory safety and hazard sentences, poison control centre/ emergency phone number

It is suggested to have stakeholders and CA working together to design acceptable product information and presentation for amateurs. Products designed for similar uses (same formulation etc.) should display similar information. This element will be helpful not only for a better understanding by the general public but also from inspector in charge of the enforcement and compliance checks on the field.

4.3.7 Best practice guidelines

There is a very wide variety of best practice guidelines currently available in the EU. Some of these deal with general circumstances of rodent pest management and rodenticide applications, others are intended to cover specific use scenarios, while others still are intended for specific user groups. A list of the most relevant and up-to-date best practice guidelines is given in the table 7 below.

Table 7: Best Practice Codes for Rodenticide use

Available at https://circabc.europa.eu/w/browse/35e2633a-b322-4c6b-8aa5-d18233f726e6

Recommendation: provide existing codes of best practices to all user categories in MS

General guidelines and good practice guides should be available in each MS, either via CA or Professional organizations for all professionals.

Benefits

- Existing guidelines cover all common uses of AR
- Potentially available for translation and adaptation to MS specificities

Limitations

- Time/cost of translation / adaptation/ harmonisation
- Inclusion in list of documents provided to users

4.3.8 Overview of the general recommendations

An overview of the proposed general recommendations is provided in Annex 6 to this report.

4.3.9 Support new active substances development

Rationale

Both the preliminary report and the present document provide ample evidence of the advantages and limitations of AR. Because rodenticides are almost restricted to one group of compounds in the EU, resistance is likely to occur and be selected if only AR can be used against rats. No new active substance has been developed since the late 80s' for the control of rodent populations.

Recommendation: support development of new strategies for rodent control in EU research programmes

The EU and MSs should include rodenticides as a key word in funding programs, in order to support new initiatives and developments in this comparatively small market (by comparison with drugs or plant protection products) and to help produce new or improved rodenticides minimising the disadvantages of anticoagulants (persistence, resistance, high toxicity) but maintaining their advantages (overcoming of bait shyness, excellent efficacy, antidote available).

Benefits

- Develop new rodenticides, both effective and less toxic
- Provide alternatives to existing compounds to control resistance development

Limitations

- Long-term effort (5-10 years)

- High cost and size market results in limited research

4.3.10Survey and discussion

An online survey has been conducted to collect information and views of stakeholders, namely PCOs (contacted thanks to CEPA) and rodenticide manufacturers (contacted thanks to CEFIC). A total of 109 answers were received from 17 different countries, encompassing all kinds of companies (from small companies to very large groups). All the results are attached as an excel file (Annex 7).

Some key data could be obtained from both groups.

On the detrimental impact of AR, both groups acknowledge receiving calls regarding accidental human or animal poisoning. Among PCOs, 60 to 70% receive calls regarding potential accidents in either humans or animals.

Table 8: Survey results – accidental exposure in humans and animals

During a rodenticide application, are you sometimes asked about accidental exposure to rodenticides? (PCOs)		
Answer Options	**Response Percent**	**Response Count**
Yes, for children	58,1%	25
Yes, for pets	69,8%	30
Yes, for animals other than rats, mice and pets	27,9%	12
No	14,0%	6

Are you sometimes asked about accidental exposure to rodenticides? (Chemical industry)		
Answer Options	**Response Percent**	**Response Count**
Yes, for children	48,5%	16
Yes, for pets	81,8%	27
Yes, other animals than rats, mice and pets	42,4%	14
No	9,1%	3

Secondary poisoning is suspected by 14% of PCOs and 45% of rodenticide manufacturers.

Resistance is commonly suspected by both groups in both rats and mice.

Table 9: Survey results - Resistance

Do you encounter rodenticide resistance problems (i.e. rodenticide applied, bait consumed and poor efficacy)? (PCOs)		
Answer Options	**Response Percent**	**Response Count**
Yes, for rats and mice	25,6%	11
Yes, for rats	11,6%	5
Yes, for mice	16,3%	7
No	46,5%	20
Not concerned	4,7%	2

Do you encounter rodenticide resistance problems (i.e. rodenticide applied, bait consumed and poor efficacy)? (Chemical Industry)		
Answer Options	**Response Percent**	**Response Count**
Yes, for rats and mice	34,3%	12
Yes, for rats	14,3%	5
Yes, for mice	5,7%	2
No	25,7%	9
Not concerned	20,0%	7

Generally speaking, resistance is associated with warfarin, chlorophacinone, bromadiolone and difenacoum.

There is also a general agreement on the needs for harmonised requirements across MSs for rodenticides, as well as common labelling. Similarly, both groups consider that appropriate training and certification should endorse PCO qualification, and appropriate training should be available for all categories of professional users.

Availability of rodenticides to amateurs is usually considered as necessary for both groups (>60%), for use indoors for mice (61%) or in and around buildings (62%) for rats. The suggestion of specialised shops for product delivery is considered as the best option for rodenticides, but it is also generally agreed (59%) that specifically qualified personnel should be present.

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6 ANNEXES:

6.1 Annex 1 – Preliminary report

Available at https://circabc.europa.eu/w/browse/345908ed-e071-460b-8206-253fd6fa1de2

6.2 Annex 2 – List of RMMs in authorised products

Available at https://circabc.europa.eu/w/browse/0f2dda65-9f45-48a0-a760-b33aed25d70e

6.3 Annex 3 - List of RMMs applied by MSs

Available at https://circabc.europa.eu/w/browse/a054c700-2b9d-4f98-8d22-c7f369370e0b

6.4 Annex 4 – Summary table of proposed RMMs within the active substance approval

RMM	Species	Amateur	Professional	Trained Professional	See §
Area of use	Mus musculus	Indoor	Indoor / Outdoor	Indoor / Outdoor	4.1.1.3
	Rattus norvegicus	Indoor and around buildings	Indoor and around buildings/Outdoor	Indoor/Outdoor	
			Open areas	Open area	
			Sewage	Sewage	
				Waste dumps	
	Rattus rattus	Indoor and around buildings	Indoor and around buildings/Outdoor	Indoor and around buildings/Outdoor	
			Open areas	Open area	
				Sewage°°	
				Waste dumps	
Pack size	Mus musculus	Limitation depending on bait type / active substance	No specific limitation	No specific limitation	4.1.1.1
	Rattus norvegicus	Limitation depending on bait type / active substance	No specific limitation	No specific limitation	
	Rattus rattus	Limitation depending on bait type / active substance	No specific limitation	No specific limitation	
Restriction of the active substance	Mus musculus	(FGAR) SGAR	(FGAR) SGAR	(FGAR) SGAR	4.1.1.2
	Rattus norvegicus	FGAR/SGAR	FGAR/SGAR	FGAR/SGAR	
	Rattus rattus	FGAR/SGAR	FGAR/SGAR	FGAR/SGAR	
Dye	All species	Blue / green suggested	Blue / green suggested	Blue / green suggested	4.1.2.1
Bittering agent	All species	Denatonium benzoate 0.001%	Denatonium benzoate 0.001%	Denatonium benzoate 0.001%	4.1.2.2
Baiting area info	All species	On bait box	On bait box	On bait box	4.1.2.3
Duration of	All species	<35 days	<35 days	<35 days	4.1.3.1

RMM	Species	Amateur	Professional	Trained Professional	See §
baiting	All species	No permanent baiting	Permanent baiting subject to risk assessment	Permanent baiting subject to risk assessment	
Frequency of visits	All species	Not specified	7-14 days, subject to risk assessment	7-14 days, subject to risk assessment	4.1.3.2
Removal of bodies	All species	Yes. Provide disposal recommendations. Regular visits	Yes-during regular visits	Yes-during regular visits	4.1.3.3
Removal uneaten bait	All species	Yes. Provide disposal recommendations.	Yes-end of treatment	Yes-end of treatment	4.1.3.4
Marketing authorization	All species	Distinct products for different user categories			

6.5 Annex 5 – Summary table of proposed RMMs at the product authorisation stage

RMM	Species	Amateur	Professional	Trained Professional	Section
Bait box	*House mouse*	Mandatory. Refillable ?	Recommended	Recommended	4.2.1.4
	Norway rat	Mandatory. Refillable ?	Recommended	Recommended	
	Black rat	Covered bait point	Covered bait point	Covered bait point	
Formulation					
Grain, pellet	*House mouse*	Yes <50*/250°g	Yes	Yes	4.2.2.1
	Norway rat	Yes <150*/750°g	Yes	Yes	
	Black rat	Yes <150*/750°g	Yes	Yes	
Wax block	*House mouse*	Yes <100*/500°g	Yes	Yes	4.2.2.4
	Norway rat	Yes<300*/1500°g	Yes	Yes	
	Black rat	Poor efficacy	Yes	Yes	

Paste	*House mouse*	Yes <50*/250°g	Yes	Yes	4.2.2.3
	Norway rat	Yes<150*/750°g	Yes	Yes	
	Black rat	Yes<150*/750°g	Yes	Yes	
Gel	*House mouse*	1 tube <50*/250°g	Yes	Yes	4.2.2.5
	Norway rat	NA	NA	NA	
	Black rat	NA	NA	NA	
Children resistant packages	All species	Yes (above 250g)	NA	NA	4.2.4
Information to user	All species	Described in Marketing Authorization	Described in Marketing Authorization	Described in Marketing Authorization	4.2.8
Label	All species	Standardised (harmonised) label across MSs, based on SPC			4.2.7

**SGAR/°FGAR/°°On farm*

6.6 Annex 6 – Summary table of proposed general recommendations

General recommendations				
Resistance evaluation	All species	NA	In vitro testing if necessary	In vitro / in vivo testing if necessary
Resistance monitoring	All species	NA	Submit tissue sample for analysis and report to reference structure for precise GIS mapping	
RMM	Species	Amateur	Professional	
Resistance management	All species	Contact PCO	Adapt AR to local mutation. Apply specific guidelines	
Non-target exposure – Humans	All species	Contact Poison Control Centre	Contact Poison Control Centre or refer to Poison Control Centre	
	EU /CA : revise labels to include Phone number			
Non-target exposure – Pets	All species	Contact Poison Control Centre / veterinary unit	Contact Poison Control Centre / veterinary unit Refer to veterinarian	
	EU/CA : identify specialised structures/ collect information on ARs sales			
Non-target exposure – Wildlife	All species	Contact specialised unit	Contact specialised unit	
	EU/CA : identify specialised units / collect information on ARs sales			
Training	All species	NA	Recommended	Required – Standardisation – Certification
Provision of information	All species	Leaflets, board, videos. Internet QR codes Simplify package	Guidelines Dedicated websites (companies / institutional)	Guidelines Dedicated websites (companies / institutional)
Point of sale	All species	Specialised Presence of Specially Qualified Persons	Specialised	Specialised
Best practice guidelines	All species	NA	Available and specialised. Provided during training	

6.7 Annex 7 – Survey results

Available at https://circabc.europa.eu/w/browse/67dae291-644f-44bd-bd1d-010bf2eeb2a6

6.8 Annex 8: Proposal for harmonised information on RMM in the Summary of Product Characteristics

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