Submitted by: Individual, UK

I am one of the four independent experts who were recently commissioned by the European Commission to provide a comprehensive Report on Risk Mitigation Measures for Anticoagulant Rodenticides as Biocidal Products. The other three independent experts were Dr Jens Jacob, Dr Alexandra Esther and Professor Philippe Berny. As a group we have decided to provide you with a joint response to this public consultation, which I have attached.

References: Berney, P., Esther, A., Jacob, J. and Prescott, C., (2014) Risk mitigation measures for anticoagulant rodenticides as biocidal products. Report. European Union, Luxembourg. pp104. ISBN 9789279449925 doi: 10.2779/241180

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Submission of information for the public consultation on active substances considered as potential candidates for substitution

As the independent experts commissioned by the European Commission to provide a comprehensive report on Risk Mitigation Measures for Anticoagulant Rodenticides as Biocidal Products, we have decided to submit a joint response to this public consultation.

Rodent pest control worldwide relies heavily 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, prevents the development of conditioned taste aversion, and makes them particularly effective against neophobic species such as the Norway rat (*Rattus norvegicus*).

A major problem with the ARs is that their intensive use since the 1950's has been followed by the selection of resistant strains of rats and mice that are difficult to control with the least potent ARs.

Currently in Europe, alternatives to ARs are limited. 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 conditioned bait aversion has been demonstrated against Norway rats. Old compounds (such as 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 effective antidotes). Methaemoglobin-forming compounds are currently being investigated as rodenticides but usually act too fast to be effective.

Thus in Europe today, the ARs are almost the only rodenticides available to control rodent infestations. To rely so heavily on a single class of compounds to control infestations will always be problematic, and it is therefore <u>considered very important</u> to support research that will develop the next class of substances (or strategies) for the control of rodent populations. With the above in mind, there is no evidence that chemical alternatives to ARs will be available in the next 5 years, (so no new developments regarding registered products are anticipated before 2020).

Alternatives to chemical rodenticides are limited. Trapping can be effective but is labour intensive and impossible to conduct on a large-scale. 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.
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With ARs, environmental risk is greatest in situations where effective control of the rodent infestation is not achieved; for example, where there is resistance. In such situations, both the rodenticide and the surviving rodents will be available in the environment to non-target species over prolonged periods, the rodents will be a high environmental risk because they have a high body loading of anticoagulant, and their behaviour may well be affected, thus making them more susceptible to predation. A similar situation can arise where the AR concentration in the bait is too low, where the bait is unpalatable or where baits are used permanently around buildings or in the open.

In contrast, where control is effective, both the rodenticide and the surviving rodents will decline rapidly over the 3 to 5 week treatment period, after which there will be no rodenticide and no surviving rodents carrying AR residues available to non-target species.

With all chemical rodent control products, situations will always arise where children and domestic animals (particularly dogs) will come into contact with the rodenticides, and there will be uncertainty as to whether or not any formulation has been consumed. For all of the anticoagulant active ingredients, all medical centres, hospitals and veterinary surgeries are set up to measure prothrombin time, and in the vast majority of 'potential cases of exposure', where the patients prothrombin time is normal 24-48hr after exposure to the rodenticide, it can rapidly be concluded that life threatening exposure has not occurred. With patient that do have a prolonged clotting time, the antidote to all ARs, vitamin K_1, can be administered, and exposure to the anticoagulant can be managed routinely. It should also be noted that worldwide large numbers of human patients are given daily doses of anticoagulant as part of long term medical treatments for the control thrombosis, without any major health side-effects. The use of bittering agents in AR commercial baits is extremely effective in controlling and preventing accidental exposure in people and there is a general consensus from Poison Control Centres that exposure to ARs do not need follow-up calls.

In contrast, where the patient has been exposed to any of the other rodenticide active ingredients (with the possible exclusion of powdered corn cob), the medical or veterinary practitioners are placed in a very difficult position, and may be obliged to consider intensive care monitoring, but with no effective complete antidote, management of the symptoms as they develop may be the only option available to them.

According to Brooks (Brooks & Bowerman, 1973), the eleven features of the ideal rodenticide are:
1- The onset of symptoms should be slow to avoid conditioned bait avoidance
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 and bird species. The development of rodent specific toxicants will always be problematic, and it will therefore be inherent for virtually all effective rodenticides to pose a risk to non-target vertebrates including humans and domestic animals (features 10/11). However for ARs, their delayed action and the availability of a complete antidote provide important safeguards, particularly for humans and domestic animals.

In the foreseeable future, ARs are likely to play a key role in the integrated management of rodent pests (where ARs are used in combination with a number of other management tools). The main drawback of this group of compounds is the development of anticoagulant resistance. Much of the current research conducted at our laboratories are focused on the identification of the different VKORC1 mutations that confer physiological resistance, on the determination of the magnitude of resistance for the different VKORC1 mutations by estimating resistance factors against each anticoagulant active ingredient, and on the identification of anticoagulant active ingredients that are potentially ineffective against specific VKORC1 resistant populations. Thus resistance management strategies are under development, and the work is on-going.

Recent research has indicated widespread resistance to the first generation anticoagulants, and the two least potent second generation anticoagulants. Continued use of these active ingredients against rodents that possess a low incidence of resisted VKORC1 mutations, will result in an increased incidence of the resistance gene, and an increased magnitude of the resistance (with higher resistance factors).

Effective control of the most resistant populations of rodent will most likely be achieved using the three most potent second generation anticoagulants, and selection for resistance in a rodent population will most likely be reduced by restricting the use of the least potent anticoagulant rodenticides; although for population of rodents where it has been established that there is no resistance, the least potent anticoagulants will remain fully effective.

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