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Trends in vertebrate pesticide use and development: alternatives to 1080 - what and when?

Charles Eason and Shaun Ogilvie. Faculty of Agriculture and Life Sciences, Department of Ecology, Lincoln University, PO Box 84, Lincoln, Canterbury, New Zealand.

SUMMARY

As a result of recent research and development:-

i) Feratox® cyanide pellets are now being registered for wallabies control as well as possums.
ii) Registration documents are currently being assessed by the Environmental Risk Management Authority (ERMA) for zinc phosphide as an alternative to 1080 for the control of possums.
iii) Registration documents are also being prepared for a combination of cholecalciferol and coumatetralyl to provide an anticoagulant alternative for effective possum control.
iv) Anticipated timelines for product availability are 2010 (zinc phosphide) and 2011-13 (cholecalciferol and coumatetralyl) subject to ERMA and NZFSA approvals and continued focused research and development effort.
v) In parallel we are pursuing the registration of *para*-aminopropiophenone (PAPP), a red blood cell toxicant, for 2010 – a novel poison for humane control of stoats and cats.
vi) On the platform of PAPP, alternative red blood cell (RBC) toxicants are being advanced for larger pests, possums and rodents. These "RBC" toxins are safer toxins, designed to minimise the impact of invasive animals, exhibiting humane performance and having a simple antidote
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The 1080 debate has become more polarised since the ERMA reassessment in 2007 and expenditure to meet increased compliance and consultation requirements continues to increase. Research on biocontrol of vertebrate pests has been an important and major focus for investment for more than 20 years in both New Zealand and Australia. Despite considerable commitment, effort and initiatives there is a gap between conventional poisons and the requirements of modern biocontrol that needs to be filled. More effective, safer alternatives to 1080 for the control of possums, predators, rodents and rabbits are required now to reduce over reliance on 1080 and provide greater flexibility. With continued focused research effort the next 1-6 years will see changes as improved, increasingly "ecofriendly," toxin products become available and additional products with novel active ingredients targeting possums and other major pests are delivered.

CURRENT VERTEBRATE PESTICIDES

Animal poisons, or Vertebrate Toxic Agents (VTAs) fall into two classes: non-anticoagulant and anticoagulant agents.

Non-anticoagulant compounds

Sodium fluoroacetate (1080) is effective for controlling pests in a variety of bait formulations and is the only poison commonly used for aerial control of pests in NZ. Carcasses of animals poisoned with 1080 are hazardous to dogs for many months and there is some debate about the humaneness of 1080.

Feratox®, cyanide pellets, were developed to increase the effectiveness of cyanide for possum control and reduce the risk of exposure of operators. Cyanide is potent, it does not cause secondary poisoning of dogs, it is favoured by some who oppose the use of 1080 and it is humane. Whilst Feratox® cyanide pellets are very effective for possums and now wallabies, they have not yet been formulated for predator control.

Phosphorus is used by only a few licensed operators and is usually added to paste bait for possum control. It is generally considered inhumane, and its use has been associated with the secondary poisoning of dogs.

Cholecalciferol (vitamin D_3) was developed in NZ for controlling possums (Eason 1991) and is now registered in Feracol® paste bait, Pestoff DECAL Possum Bait® and No possum gel®, with Feracol® paste bait also now used for rodent control. There is low risk of secondary poisoning of dogs, and birds are much less susceptible to cholecalciferol than to 1080, but current baits are deemed too expensive.

Anticoagulant compounds

First-generation anticoagulant rodenticides were developed in the 1950s and 60s, and second-generation anticoagulants in the 1970s and 80s.

Pindone, has proved most effective for rabbit control, and is also registered for possum control but is not so effective in this species. Diphacinone is more toxic than pindone and is registered for field control of rodents. They do not bioaccumulate like the second-generation anticoagulants. Coumatetralyl is registered for rodent control and more persistent than diphacinone and pindone.

Brodifacoum is the most well known second-generation anticoagulant and has been used successfully in recent rodent eradication programmes on offshore islands to protect populations of endangered indigenous birds. Although brodifacoum is effective for possum and rodent control repeat field use of brodifacoum can result in transfer of residues through the food chain.

REGISTRATION PROCESSES AND TRENDS

In NZ the requirements of the Hazardous Substances and New Organism (HSNO) Act (1996) legislation must be met, along with the requirements of the Agricultural Chemistry and Veterinary Medicines (ACVM) Act, 1997. The registration process requires approval from both the Environmental Risk Management Authority (ERMA) and the New Zealand Food Safety Authority (NZFSA); consultation with Maori is a prerequisite, and welfare considerations are a key component of the registration assessment process for vertebrate pesticides as well as the need for demonstrating effective control of pests with minimum non-target impacts.

THE PIPELINE

New NZ registration of established vertebrate pesticides

Part 1: Products that contain vertebrate pesticides already in use in NZ.

The use and registration of existing products and active ingredients that are already approved by ERMA and the NZFSA and viewed as "ecofriendly" are being extended. Since its registration in 1997 Feratox® has become an accepted method for cyanide baiting with more than six million pellets sold annually for possum control. As its use has strong community support and it is used by hunters and trappers as well as professionals, extending this registration to include Dama and Bennett's wallabies is a logical step.

Cholecalciferol has the advantage of low secondary poisoning risk and low toxicity to birds. Currently available commercial baits contain cholecalciferol at a concentration of 0.8%. The active ingredient cholecalciferol is expensive and if efficacy and humaneness can be achieved with lower concentrations of toxin in existing baits their price could be reduced. Field trials are planned in both paste and solid baits in 2009 to support product registration of affordable effective bait containing 0.4% cholecalciferol.

Part 2: Products that contain vertebrate pesticides NOT already in use in NZ.

Zinc phosphide has been in use for over 50 years with very few non-target hazards. It is still used in the USA, as well as in Australia, China and the Asia-Pacific region for field control of rodents and larger pests. It found favour because of the comparatively low risk of secondary poisoning of dogs compared with 1080. Zinc phosphide is a quick-acting compound with clinical signs first appearing from 15 minutes to 4 hours, and death after a lethal dose occurs generally in 3-12 hours. It is inexpensive and it has not been registered in NZ before now.

Cholecalciferol + coumatetralyl (C+C) as a combination also has a track record overseas eg. Racumin plus® has been used to overcome anticoagulant resistance in rats and mice. AHB has funded the development of 'C+C' for controlling possums, and it is currently being developed in multispecies baits for controlling rats and mice as part of the Lincoln University FRST programme. Bait containing 0.015% cholecalciferol and 0.03% coumatetralyl (C+C) has been developed, and dossiers are being prepared for registration later in 2009. C+C is effective at killing possums, rodents and rabbits even though the amount of cholecalciferol is a fraction of that used in current cholecalciferol baits.

Whilst zinc phosphide is more akin to 1080, in that it kills more quickly than anticoagulants, C+C by contrast is slower acting and offers the advantages of brodifacoum without persistent residues. For both zinc phosphide and C+C there is a common development strategy which is to first register a product for control of possums and then extend this registration to include rodents and rabbits. Zinc phosphide is initially being registered in a paste bait. Ultimately it is intended that there will be solid bait and paste formulations of both zinc phosphide and C+C.

NZ registrations of a new generation of vertebrate pesticides.

There have been no developments in this field since the development of brodifacoum and cholecalciferol in the 1970/80s. There is an opportunity, and a challenge, to develop new replacements which are ahead in terms of humaneness and safety. A new class of compounds is now emerging. At the core of the research is the discovery that targeting red blood cells (RBCs) induces a humane death. PAPP (*para*-aminopropiophenone) represents the first compound in this class and is a potent and selective toxin for stoat and feral cat control.

Recent progress, following field trials in 2008 (stoats) and June 2009 (cats), has been rapid. PAPP dossiers for chemistry and manufacturing, toxicology, efficacy, ecotoxicology and non-target impacts, and welfare were filed with the NZFSA in 2008 and ERMA in 2009. In field trials its potential has already been proven in kiwi protection programmes.

Amongst this class of compounds PAPP represents a partially selective toxin. PAPP is toxic to carnivores, with birds and humans being less sensitive. The onset of symptoms is rapid and stoats and feral cats are usually unconscious quickly. Methylene blue is an effective antidote to PAPP toxicity and is available from veterinarians.

Sodium nitrite is a common salt that is currently at an early stage of research and investigation for larger pests. The toxicology of sodium nitrite is well understood because of its use as a preservative agent in meat. The toxic effects of sodium nitrite, like PAPP, are related to its ability to reduce the oxygen carrying capacity of the red blood cell and methylene blue is the antidote.

In parallel screening of PAPP analogues has been initiated and compounds with a similar mode of action in rodents and possums. PAPP and sodium nitrite should be perceived as the prototypes, and we believe that we can improve on these compounds to produce more potent, broad spectrum and selective species specific toxins for a range of pest species, with low toxicity to birds, based on the PAPP platform which will facilitate more effective predator and multispecies control[1].

Other initiatives include the exploration of methylxanthines, components of chocolate, for their toxicity to possums, and research supported by Nag Pae o te Maramatanga to identify useful natural plant toxins. Whilst these avenues of research may appear as long shots the work on methylxanthines is linked with our colleagues at the USDA National Wildlife Research Center and a component of the toxic plant karaka, like PAPP, induces methaemagolbinaemia and has already been proven to be toxic to possums.

[1] Links to a new FRST's programme entitled "Pest Control for the 21st Century" involving Lincoln and Auckland University focused on novel vertebrate pesticides and delivery systems.

A forecast for the new registration pipeline subject to ERMA/NZFSA and continued focused research effort[2].

Type	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15
Products that contain vertebrate pesticides already in use in NZ.	Feratox® for wallaby control. Less expensive cholecalciferol paste and solid bait	Cyanide for pigs/ferrets				
Products that contain vertebrate pesticides NOT already in use in NZ.	Zinc phosphide 1.5% *paste* for possum	Zinc phosphide 1.5% *paste* for possums rodents	Zinc phosphide solid baits for possums and rodents C+C *solid bait* for multispecies control	C+C *paste bait* for multispecies control of possum, rats, mice and rabbits.		
NZ registrations of a new generation of vertebrate pesticides	PAPP paste for stoat and feral cat control	PAPP delivered in repeat dose tunnels	Sodium nitrite for larger pests	New red blood cell toxin for possums	More potent PAPP like rodenticide and/or combined rodenticide and mustelid toxin	PAPP like possum selective toxin + other RBC toxins Natural toxins and methylxanthines

CONCLUSIONS

Over the last three decades considerable effort has been put into improving and refining the use of 1080. By contrast the last six months (Dec 2008 – June 2009) has seen a record period for new product registration advancement. Extensive registration dossiers were filed for microencapsulated zinc phosphide (MZP) for possums, Feratox® for wallabies, and *para*-aminopropiophenone (PAPP) for stoats with ERMA & NZFSA. However, there are no "silver bullet" replacements for 1080. A suite of more effective and acceptable tools is being developed, to reduce over reliance on 1080 and to provide greater flexibility. There is now an intense focus on delivery of alternatives within 1-6 years. A new consortium, linked with Lincoln University, is working to a timeline, to deliver a suite of improved ecofriendly toxin products available by 2012, and additional products with novel red blood cell toxins targeting rodents, possums and other major pests delivered by 2015.

These new red blood cell (RBC) user-safe toxins will be unique, exhibiting humane performance, availability of an antidote, improved efficacy, cultural acceptability and species selectivity and will fill a gap between conventional poisons and the demands and expectations of modern biocontrol. Our short-medium term focus is on registering new compounds for ground control. This is a significant milestone in itself. If or when these registrations are achieved and experience has been gained over at least 2-3 years, the next logical step is to consider which compounds are suitable for aerial use. Research and development needs to be consolidated over the period 2010-15 if any of these new options are to become available for aerial control in the future. In parallel, work to improve the cost-effective use of ground control over larger areas with advanced delivery systems that can sustain control for months or

[2] These timelines are not only subject to regulatory approval but continued stakeholder support both in kind and also with contracted research.

years, should enable larger areas of land to be treated, reducing the need for aerial baiting.