Management of Damage Caused by Mammals

Is America Ready for a Humane Feral Pig Toxicant?

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ABSTRACT In 2005 the Invasive Animals Cooperative Research Centre undertook an extensive literature review in an attempt to discover possible pharmacological weaknesses of pigs that could be inherently targeted with specific chemicals. For a chemical to have utility it ideally had to be: safe for human operators, highly toxic to pigs, bait deliverable, target specific, humane, residue-less, reversible, inexpensive, already registered for other purposes, patentable, acceptable to trading partners, and have a well documented toxicological profile. Numerous weaknesses and associated candidate chemicals were discovered, but only one, sodium nitrite, proved appropriate in gavage and bait delivery proof-of-concept pen trials. This paper details the discovery process, two years of research towards formulating an article-of-commerce, and three years of development and registration. Discussed is what is required in relation to lobbying and funding, dealing with bureaucracy, intellectual property protection, formulation, target-specificity and nontarget safety, humaneness, ground and aerial baiting field efficacy, product stability, environmental fate and residue data in order to register a commonly available human food preservative as a new vertebrate pesticide in Australia. Also discussed is the development of a novel bait delivery device that increases the target-specificity and cost-efficiency of feral pig control.

KEY WORDS feral pig, swine, hog, Sus scrofa, omnivore, pesticide, humane, registration

The feral pig, Sus scrofa, is an extremely adaptable species with the ability to colonize most environments with reliable food, water and shelter. It inhabits a wide range of Australian habitats, with populations spread over 40% of the continent (Choquenot et al. 1996). Feral pigs cause a large and diverse range of impacts where they occur in Australia (Choquenot et al. 1996), including agricultural losses to crops and livestock (lambs) conservatively estimated at $106 million annually (McLeod 2004). They cause numerous environmental impacts, including wildlife predation and habitat destruction. In 2004 feral pigs were listed as a key threatening process in New South Wales (NSW), and in 2005 nationally, resulting in additional resources and management focused on this species. They spread endemic diseases (Choquenot et al. 1996), and will potentially spread exotic diseases, such as foot-and-mouth disease, should it enter Australia (Pech and Hone 1988).

Coblentz and Baber (1987) estimated that the use of toxicants for feral pig management was 11 times cheaper than removal by shooting and 80 times cheaper than removal by trapping when attempting to eradicate feral pigs from Isla Santiago, Ecuador. Similarly, the use of toxicants to manage feral pigs in Australia is reportedly the most efficacious and cost-effective control technique (Choquenot et al. 1996). Currently three toxicants are used for feral pig control in Australia—sodium fluoroacetate (1080), warfarin and yellow phosphorous (sold as C.S.S.P.). Each of these toxins has potential problems. 1080 is required in doses that may impact nontarget species and safety. 1080 can sometimes lead to profuse vomiting in feral pigs which may cause nontarget risks as well as animal welfare concerns. The use of 1080 as a toxicant in pen trials has not shown to be 100% effective in killing all targeted feral pigs.
pigs, even at higher doses. In addition, there is no known antidote in the event of nontarget poisoning. The use of phosphorus as a feral pig toxicant causes severe clinical disease in pigs over several days and almost certainly raises animal welfare concerns. In addition, typical application involves the incorporation of the toxicant into animal carcasses which can expose nontarget scavengers to potential poisoning. Phosphorus use is no longer supported in NSW by land management agencies or NSW Primary Industries who considers phosphorus inhumane and unacceptable for use. Warfarin is an efficacious chronic feral pig toxin; however, it is not currently registered for use by the Australian Pesticides and Veterinary Medicines Authority (APVMA). Agencies, such as the NSW National Parks and Wildlife Service and the Australian Capital Territory (ACT) Parks and Conservation Service, which may have historically used the toxin under experimental permits, are phasing out its use due to animal welfare concerns. NSW Primary Industries considers warfarin inhumane and unacceptable for use in controlling feral pigs. The withdrawal of inhumane pest animal control methods and the development and adoption of best practice methods for animal pest management is an action item outlined in the 2008 Australian Pest Animal Management Strategy (http://www.daff.gov.au/data/assets/pdf_file/0008/749204/aaws-strategy-jun08.pdf). Furthermore, the need to develop improved feral pig management tools is acknowledged in the 2005 Federal Feral Pig Threat Abatement Plan (http://www.environment.gov.au/biodiversity/publications/tap/pubs/feral-pig-tap.pdf).

Feral pig control on farms has historically been costly and inefficient and can often cause increased conflict in rural communities between landholders and trespassing hunters. Also, feral pig control in Australia is often reactive in nature rather than systematic and proactive. Control is often undertaken when the impact of the species is greatest (such as lamb, crop or pasture damage), or conducted annually with no real opportunity to measure if management objectives have been achieved. However, to effectively manage a highly fecund and highly mobile vertebrate pest, control needs to be proactive, collaborative and ongoing. One constraint to this in Australia is the access restrictions imposed on the main poison used for feral pig control (1080), which must only be supplied by authorized government officers.

In 2003, the Pest Animal Control Cooperative Research Centre (PAC CRC)-Meat and Livestock Australia Ltd (MLA) co-sponsored The Feral Pig Action Agenda workshop. Participants identified the need for greater feral pig control as well as the need for improved tools to manage the species (Lapidge 2003). Between 2004 and 2008, PIGOUT®, a new feral pig-targeted bait was developed by Animal Control Technologies Australia P/L (ACTA) and the PAC CRC with support from MLA to effectively deliver sodium fluoroacetate (1080) to feral pigs. The product was nationally registered in December 2007 and launched in March 2008. Lapidge et al. (2004), Cowled et al. (2006a,b) and Lapidge et al. (2006) all provide details on the development of PIGOUT. The bait matrix has also been designed to deliver other actives, such as contraceptives or vaccines, to feral pigs (Campbell et al. 2006, Cowled et al. 2008a). Recently there has been renewed interest to find an improved feral pig toxicant and bait combination that like the PIGOUT bait matrix, reduces the risks to nontarget species while increasing target species efficacy. A suitable new toxin was identified in 2005 and preliminary tests in 2006 showed that it is highly efficacious
whether administered by gavage or in PIGOUT baits (Cowled et al. 2008b). These results were recently presented to the APVMA, who were encouraged by the findings and supported the development of this new feral pig toxin. Ironically, it is a chemical that is used to preserve pig meat that is also highly toxic to the live animal. The active agent is sodium nitrite. There is a considerable amount of data on the chemistry and toxicology of this compound because it is approved for human consumption in low doses. Sodium nitrite’s mode of action is methemoglobinaemia, which was recently supported in theory by The Royal Society for the Prevention of Cruelty to Animals (RSPCA) (Sherley 2007). Pigs are highly susceptible to the effects of methemoglobinaemia as they contain uniquely low levels of methemoglobin reductase (Smith and Beutler 1966, Agar and Harley 1972), the enzyme required to reverse the methemoglobin formation process. This inherent weakness has previously resulted in numerous reported cases of domestic pigs being poisoned with nitrite (Robinson 1942, Gwatkin and Plummer 1946, Winks et al. 1950, London et al. 1967).

The paper details the steps involved in developing and registering this new humane toxicant for enhanced feral pig management in Australia under the trademarked name HOG-GONE®. The project is currently three years into an anticipated seven year process, with the pesticide registration review, proof-of-concept gavage and bait pen trials, APVMA and RSPCA engagement, Chemical and Animal Ethics Committee permitting, dose scoping and final formulation trials, and an independent nitrite toxicosis humaneness assessment all complete.

OBJECTIVES
The objective of this project is to reduce the economic, environmental and social impacts of feral pigs on Australia. Sodium nitrite / HOG-GONE has the ability to do this because:

- it is more efficacious in controlling feral pigs, and safer and easier to use than existing feral pig poisons;
- the active ingredient of the toxicant is readily-accessible and has an accepted antidote (methylene blue). When registered this product will be more widely available, with fewer restrictions due to its lower classification as a poison; and
- in turn, a change in end-user practice is anticipated, as baiting can be carried out proactively in conjunction with routine tasks such as checking stock waters if pig presence is detected, and farmers who have previously been concerned with the deployment of 1080 baits (and hence potential primary poisoning of farm dogs) will be more likely to use HOG-GONE.

METHODS
This project builds on the success of the PIGOUT bait, which was demonstrated to be an attractive, palatable and near target-specific product in Australia (Cowled et al. 2006b). Unfortunately, this has not been the case in the USA as a result of the greater diversity and possibly density of opportunistic omnivore species in the vertebrate assemblage (Campbell et al. 2006, Campbell and Long 2007). Gavage and bait-delivered sodium nitrite proof-of-concept trials have already been successfully completed and have shown that this toxin kills pigs quickly (~ 2 hrs) and humanely (unremarkable symptoms) (Cowled et al. 2008b). International protection on this intellectual property has already been achieved with a patent on the invention of bait-delivered sodium nitrite as a vertebrate pesticide.
The project design and methods used are similar to those used during the development of PIGOUT. Between 2006 and 2009 we established the ideal bait dose that best balances lethal dose for individual pigs, target-specificity, humaneness, operator safety and manufacturing issues by exposing feral and domestic pigs to various doses and bait formulations. In addition, we conducted or commissioned the following studies in 2008 and 2009, all of which will be used to form the final APVMA registration package for HOG-GONE.

- Commissioned an independent assessment of the chemical product data available for product registration of sodium nitrite as a new vertebrate pesticide by Golder Associates, Melbourne. The report reviewed all data in the public domain that addresses the eight-part APVMA registration requirements for a new vertebrate pesticide, including Chemistry and Manufacture, Toxicology, Metabolism and Kinetics, Residues and Trade, Occupational Health and Safety, Environment and Efficacy and Crop Safety.

- Commissioned native nontarget species testing of brush-tailed possums (Trichosurus vulpecula) and Tammar wallabies (Macropus eugenii). Both are native species in Australia that have previously sampled feral pig baits, and therefore a risk assessment is required for the proof-of-concept and registration application. However, both species are introduced and invasive species in New Zealand where pen trials are more likely to be approved. Results from these studies will be used to provide proof-of-concept for a model looking at published lethal nitrite doses and known methemoglobin reductase levels for ten other species. Should the predicted lethal doses for the two species concur with the model, published methemoglobin reductase levels found for over 40 native Australian species will be used to predict lethal doses and therefore the susceptibility and risk of these species to HOG-GONE exposure.

- Population level efficacy ground baiting field trials have been conducted on Glenrock Station, NSW (April 2009) and in Namadgi National Park, ACT (May 2009). Each trial generally involved baiting a population of up to 50 feral pigs in a maximum 100 km² area whilst treating a similar population with placebo nontoxic baits (Fig. 1). A population decline of 70% or greater must be demonstrated using three or more conferring population assessment techniques for registration purposes.

The following studies will be undertaken:

- Aerial baiting field trials will be conducted on rangeland properties in Kimberley, Western Australia, in October 2009 and Windorah, Queensland, in 2010. Other potential trial sites include the Cloncurry, Charters Towers and Goondiwindi areas, Queensland (Fig. 1). All baits in aerial
baiting trials are deployed from helicopters, and generally involve more expansive and inaccessible locations.

- Domestic stock nontarget testing will be conducted by the Institute of Medical and Veterinary Science, South Australia. Although domestic stock consumption of unprotected PIGOUT/HOG-GONE baits is rare in Australia, an assessment will be undertaken as to the number of toxic HOG-GONE baits sheep and cattle would need to consume to receive a lethal dose for the nontarget safety data package.

- A study to assess sodium nitrite residue levels in various organs of field poisoned feral pigs to ascertain the likely risk of secondary poisoning of scavenging carnivores.

- HOG-GONE stability trials. A minimum shelf life of 12 months is generally required for a commercial bait, and conversely, the product is required to rapidly break down in the environment.

In 2010 the project team will:

- Prepare an eight-part Category 2 Australian Pesticides and Veterinary Medicines Authority product registration package for sodium nitrite-containing HOG-GONE baits.
- Prepare results for popular articles, scientific publication (where possible, and with commercial confidentialities in mind) and international promotion.
- Prepare and print product extension information, promotional material, and advertising.
- Prepare for product launch, following the legislated 18-month APVMA registration process.

Separate to this project, but not unrelated, is the development of a feral hog baiting system (Boar Buffet®) by the Invasive Animals Cooperative Research Center (IA CRC). To minimize nontarget exposure to the toxicant in bait form intended for feral pigs and to improve dose compliance (via reducing bait gorging and monopolization by individual animals), plans for a feral pig-specific bait hopper were developed in 2006. The device was initially intended for selectively targeting feral pigs in the face of native rats, bandicoots and cassowaries at the IA CRC Daintree Rainforest Feral Pig Demonstration Site (Bengsen et al. 2009). The Boar Buffet was designed to target unique behavioral characteristics of the feral pig (feeding behavior, reach, size and strength), thus preventing nontarget species from gaining access to toxic bait material during feral pig baiting campaigns. The Boar Buffet is also designed to be portable (flat packs), easy to set up and dismantle and is low maintenance. The device can hold up to 200 baits stored in a weatherproof hopper. This type of feeding station will help maintain bait quality, enable land managers to control feral pigs in key hotspots and allow them to set up semi-permanent bait stations for long-term control.
RESULTS
The discovery, development and registration of nitrite as a vertebrate pesticide for feral pigs is expected to take seven years. The overall project timeline is detailed in Fig. 2.

Lobbying, Funding, and Bureaucracy
Despite the development of improved feral pig management tools being a priority of the 2005 Federal Feral Pig Threat Abatement Plan and the 2008 Australian Animal Welfare Strategy, it took two years of writing funding applications and political lobbying to raise the near AUS $1M cash required to take sodium nitrite through to registration and commercialization. All funding sources for the project are detailed in Fig. 2.

Intellectual Property Protection
Based on information in the public domain, and the data of Cowled et al. (2008b), a provisional patent for bait-delivered nitrite as a new vertebrate pesticide was filed in February 2007. The final patent was filed in February 2008, and was published in September 2008. The International Publication No. is WO 2008/104028 A1, with the title *Nitrite salts as poison in baits for omnivores*. The decision was made to protect our intellectual property due to the substantial investment required to commercialize nitrite as a pesticide. This also means that countries wanting to register nitrite as a pesticide will need to work with the IA CRC and its commercial partners.
Formulation
Following the initial gavage and bait-delivery pen trials conducted in early 2006 (Cowled et al. 2008b), product formulation pen trials with wild-caught and domestic pigs commenced in October 2007 on Kangaroo Island, South Australia. Due to the salty taste of nitrite, which pigs are naturally averse to, and the instability of the chemical, formulation of the product has proven technically difficult and time consuming. Finalizing the article-of-commerce was achieved in February 2009 after 17 months of pen trials on Kangaroo Island, at the Biosecurity Queensland Robert Wicks Pest Animal Research Centre (Inglewood, Queensland), and at the Connovation animal research facilities at Lincoln University, New Zealand. Final chemical presentation, bait doses and bait matrix formulation remain the intellectual property of the IA CRC, Animal Control Technologies Australia P/L and Connovation P/L.

As part of the formulation research, the IA CRC commissioned Professor Eason from Connovation Research P/L, New Zealand, to conduct a review of potential nitrite synergists that could be used to reduce the dose of nitrite required per bait for effective feral pig control, or reduce the risk to nontarget species through including a pig-specific synergist in the final formulation or both.

The results of this review will remain confidential, but are available for those wanting to work with the IA CRC (Eason and Lapidge, Connovation Research P/L, unpublished report).

Independent Welfare Assessment
The independent humaneness assessment of nitrite toxicosis was undertaken by the Institute of Medical and Veterinary Science (South Australia) in March 2009. The results of this review are currently being prepared for publication in the journal Animal Welfare. In summary, four of the five baited animals that voluntarily consumed nearly one final-formulation HOG-GONE bait or more died in 64±13 min. The symptoms of the toxicosis, and relative time frames, are detailed in Fig. 3. A fifth pig that consumed less than 40% of one bait took nearly three hours to die, but showed no symptoms or increase in stress hormones until 2 ¼ hrs after bait consumption, then progressed through the similar symptoms as the other test pigs depicted in Fig. 3. Porter and Kuchel (2009) reported “In the opinion of the authors, the symptoms leading to death and duration of display of these symptoms would suggest that sodium nitrite satisfies a general understanding of what a humane poison would be.”

![Figure 3. Symptoms of sodium nitrite toxicosis in four pigs involved in an independent welfare assessment. A fifth pig received a very marginal dose and took 3 hours to die, but showed no symptoms for the first 2 ¼ hours.](image)

Nontarget Species Risk Analysis
As of May 2009, Brush-tailed possum trials were initiated. Tammar wallaby trials are set to be completed shortly. Indicative results conferred with the predicted lethal possum dose from the lethal dose-methemoglobin reductase model developed. Predictions for an additional 40 species of Australian marsupial, reptiles and birds are currently being completed, and the results are being prepared for journal publication. Recommendations for limiting exposure of
susceptible species will be made. In the future, predicted lethal doses for other species, including United States wildlife, may be able to be calculated based on methemoglobin reductase levels, which are obtainable from a simple blood test.

Field Trials
Prior to any new pesticide being tested in the field, a Category 23 field trial permit must be obtained from the APVMA. The Category 23 permit for HOG-GONE was submitted in March 2007 and requested approval for up to 12 trial sites. The application was granted in September 2008. However, some 18 months later, despite nitrite being a well-known and relatively safe chemical, approval has been obtained for only six trial sites (Fig. 1). In April 2009, the first successful field trial was undertaken on Glenrock Station, NSW, which resulted in an 89% decline in the baited population compared to the control. Field trials will remain ongoing throughout 2009 and 2010 in a variety of feral pig habitats until sufficient data is obtained for the product to achieve registration. Impact to nontarget species is closely monitored in each trial through remote photography as part of the environmental safety data collected for the registration package.

Environmental Fate and Residue Data
The initial and extensive data on the environmental fate of sodium nitrite was compiled by Golder Associates in early 2009. In addition, data collection will commence on the field decay of HOG-GONE baits exposed to various environmental regimes (e.g., temperature, rainfall, soil type). Residue data will also be collected from field-poisoned feral pigs to ascertain the likely secondary poisoning risk to nontarget scavengers. However, as nitrite is known to be rapidly eliminated from the body, with a half-life of 30–60 min in those species tested (Fig. 4), residues are predicted to be minimal.

![Graph showing rapid decay of plasma nitrite](image)

Figure 4. Rapid decay of plasma nitrite in male (A) and female (B) rats following intravenous (20 mg/kg) or oral (40 and 80 mg/kg) administration of sodium nitrite (adapted from Kohn et al. 2002).

Boar Buffet Bait Hopper
The first Boar Buffet prototype was developed in early 2008 for US $900. In July, 2008, the device underwent nontoxic trials in a large pen containing 20 wild caught feral pigs at Inglewood, Queensland. The pigs quickly worked out how to use the device, with bait consumption times (for 40 nontoxic PIGOUT baits) ranging from 20 minutes in trial 1 to 5 min in trial 4. Subsequently 10 naïve pigs were radio tagged and released into a 16 ha free-living enclosure at Inglewood in September 2008. One week after their release and...
acclimatization, the Boar Buffet was introduced and baited with toxic PIGOUT on night 1 (no pre-feeding). By morning all animals had consumed a lethal dose, with all 10 pigs succumbing to PIGOUT (Fig. 5). This was an encouraging result, as no 1080 field trial has ever managed to kill all feral pigs. These results may be related to the self-regulating approach to bait consumption provided by the use of the Boar Buffet because pigs remove one bait at a time from the device, preventing bait monopolization by individuals within a mob and gorging. This device may also be suitable for USA situations, although it is possible that bears may be able to enter the device.

Figure 5. Feral pigs feeding on PIGOUT® baits from the Boar Buffet® bait hopper. All (n = 10) feral pigs fed from the device on the first night of exposure and subsequently died.

DISCUSSION

The development and registration of new, humane vertebrate pesticides is a complex, long-term project. The time frame for the development of nitrite as a feral pig toxicant will be seven years, and cost in the order of AUS $1–2M (in-kind salaries included). Furthermore, there are still significant registration hurdles to overcome that could impact the time frame or budget. However, as feral pigs are known to cause at least AUS $100M per annum damage to agriculture alone in Australia, and an estimated US $800M in the USA (Pimentel et al. 2000), the potential benefits from improved feral pig control products will ultimately outweigh the costs of development.

The Invasive Animals Cooperative Research Centre, which consists of 41 partners, including the United States Department of Agriculture, Animal and Plant Health Inspection Service, Wildlife Services National Wildlife Research Center, has as one of its priorities collaborating with leading international research organizations. These collaborations are currently happening to a large degree in research being conducted on immuno-contraception in wildlife. It is hoped that the same type of collaborative efforts can be achieved in other areas of research including toxicants. The IA CRC partners believe they can help each other achieve some form of global coordination in the development and testing of new products for invasive species management (Lapidge and Humphrys 2008). Should the United States decide to pursue the registration of nitrite as a feral pig toxicant then the extensive Australian data package will be made available in return for a royalty on product sales. As nitrite is a human food product, and is backed by an extensive existing toxicology profile, it is highly likely that the key data exists to facilitate the registration of the active by the United States Environmental Protection Agency.

As demonstrated by Campbell et al. (2006) and Campbell and Long (2007), PIGOUT baits are not species-specific in the USA and this is likely to hold true for HOG-GONE baits as well. As such, the oral delivery of toxicants to feral pigs in the U.S. will require innovative means to exclude nontarget species. Bait doses required to quickly euthanize a 50–100 kg pig will also
be lethal to nontarget species that are a fraction of this size. The Boar Buffet can greatly contribute to increasing the selectivity and efficiency in the way feral pigs are managed in the USA. With minor modifications to the bait hopper, the device could be used to deliver other bait matrices. Even if a pig-specific bait could be developed in the U.S., national parks and some landowners will likely be concerned about releasing a potent bait near nontarget wildlife and livestock. This is where we believe the Boar Buffet provides a safe, effective and easy-to-use alternative.

This paper details the steps involved in the development and potential registration of sodium nitrite as a new vertebrate pesticide. Readers are referred to Cowled et al. (2008b) for more information on the initial discovery process. New humane tools for feral pig management, as well as other species, are key priorities of the Australian Feral Pig Threat Abatement Plan, and the Australian Animal Welfare Strategy. Previously there has also been interest expressed at USA hog conferences into the use of a feral pig toxicant in the USA (M. Bodenchuck, 2008 National Conference on Feral Hogs, 15 April, St. Louis, Missouri, USA). The rapidly increasing range of feral pigs in the USA (Campbell et al. 2006), the humaneness of nitrite toxicosis and the predicted lack of residues, and the greatly improved cost-effectiveness of feral pig control using toxicants compared to shooting or trapping (Coblentz and Baber 1987) provide a unique opportunity for collaboration and partnership. The IA CRC and ACTA look forward to potentially working with U.S. authorities on this important wildlife damage management issue.

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