



Acknowledgements

Baits containing Para-aminopropiophenone (PAPP) provide a new option for control of foxes and wild dogs.

The PAPP project has been a large team effort over many years. The end result is a thoroughly tested and well understood bait option for canid pest management.

While the team at ACTA and the IA-CRC have anchored the task for over a decade, this could not have been achieved without the initial financial support of AWI. Vital also were the selfless inputs of many pest managers and research staff in local, state and federal agencies who assisted with field testing. Inputs were also received under contract, from analytical groups and regulatory and environmental consultants who all helped generate data and documentation. Many private landowners and government land managers allowed the prototype products to be tested on their sites.

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Fox problems in Australia

Since their introduction into Victoria in the 1870's, foxes have adapted well to the Australian environment and now infest almost all habitats except the far tropical north of the continent. Their range and density may still be increasing.



Foxes are highly effective predators and thrive by killing a great number of Australian native animals. Small mammals and ground nesting native birds are at special risk. Many species have become extinct due to the relentless predation pressure from foxes.

Foxes are also responsible for major economic losses of newborn lambs and goat kids. These predation losses can reach more than 20% of lambs born, so effective

fox control programs commonly result in significant increases in marking rates.

Apart from their massive impact on wildlife and lamb production, foxes are known to spread weeds such as



blackberries and olives via their scats.

Perhaps even more importantly, foxes carry and spread parasites, bacteria and viruses that affect working and pet dogs as well as native wildlife (mange, worms, distemper, hepatitis and parvovirus). Foxes would transmit rabies, should this virus enter Australia.

Fox control is therefore an important aspect of environmental management and livestock production throughout Australia.



Background to PAPP

Since the middle of last century, Australia has largely relied on one very effective toxin for control of foxes and wild dogs. The toxin used is sodium fluoroacetate. It was the 1080th compound tested in a search for a new rodenticide, so its common name is '1080'.

While found to be unsuitable as a rodenticide, 1080 was highly toxic to foxes, rabbits and wild dogs but less toxic to native animals. It continues to be a proven effective tool in the battle against damaging pest animals in Australia.

PAPP is the short name given to para-amino propiophenone.

PAPP is a chemical toxin that is suitable for control of foxes and wild dogs (but not rabbits). It

has been developed as an additional tool and not as a replacement to 1080. Both chemicals have strengths and weaknesses that are useful in different pest management situations.

The development of PAPP arose from studies in the 1970's and 80's that assessed its ability to cause the formation of methaemoglobin in blood. When the toxicity of PAPP was tested in primates, rodents and dogs, the dogs were found to be much more susceptible than other species. The reason for the higher risk is that dogs and foxes metabolise PAPP by a different pathway that causes abnormally high concentrations of methaemoglobin in the blood.

Methaemoglobin contains oxidised iron Fe⁺⁺⁺ (or ferric) but normal haemoglobin is Fe⁺⁺ (or ferrous). Normal

haemoglobin carries oxygen very well, but methaemoglobin does not carry oxygen at all.

An animal that experiences high levels of methaemoglobin is unable to deliver oxygen to tissues such as the heart, brain and diaphragm. An affected animal will quickly become unconscious and



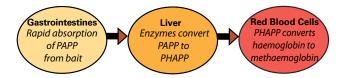
die, but an animal that suffers only a mild amount of methaemoglobin experiences temporary lethargy then recovers to normal within hours. The unusual metabolic pathway in canid animals (wild dogs and foxes) makes them highly susceptible to PAPP, so studies tested PAPP as a new poison that can be used to target these pests. It has taken some 10 years and several million dollars of industry funding to obtain registration of PAPP baits. As PAPP has not been used or registered for any other product, the regulatory authorities required a very extensive data and information package in order to be properly able to evaluate it's risks and benefits. In early 2016 final product labels were approved to allow PAPP to be used in baits to assist the targeted control efforts on foxes and wild dogs in Australia.

Though PAPP has many benefits that distinguish it from other pesticides, it also carries some risks that need to be understood and managed.

This booklet, supporting documents and advisory notes (see also www.animalcontol.com.au & www.pestsmart. org.au & industry publications) seek to give all users the correct understanding of PAPP and the right ways to use PAPP baits to achieve effective fox control, with minimal risk to domestic dogs, users and non-target wildlife.

Mode of action of PAPP

PAPP is absorbed rapidly from the gastrointestinal tract and is transported to the liver. Foxes and dogs have liver enzymes that convert PAPP to a hydroxylated version, PHAPP (Para hydroxyamino propiophenone). PHAPP is taken up by red blood cells where it causes the rapid conversion of haemoglobin to methaemoglobin.



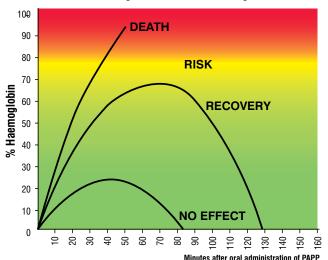
If levels of methaemoglobin in blood exceed about 80% the affected animal dies quietly from oxygen depletion. This is known as metabolic anoxaemia and is painless. Thus, PAPP poisoning is a very humane pest control technique. Metabolically the effect can be likened to carboxy haemoglobinaemia that is caused by carbon monoxide poisoning.



The process of absorption of PAPP, it's metabolic transformation to PHAPP and then action in the red blood cell is fast. Peak methaemoglobin concentrations occur about 30 - 60 minutes after peak PAPP levels. Typically, a fully dosed fox dies within 1-2 hours of ingesting a single FOXECUTE® bait . This is shorter than the time taken for 1080, which is approximately 4.5 hrs for a fox that receives a 3 mg 1080 fox bait.

While action of PAPP is fast, death only occurs if sufficient quantities of the toxin are eaten and absorbed quickly. The FOXECUTE® bait achieves this rapid delivery. However, if small amounts of bait are eaten slowly, this will allow time for detoxification mechanisms to work and haemoglobin levels will not reach lethal levels. An under-dosed or slowly dosed animal may become lethargic or may show symptoms like blue/grey (cyanotic) gums and tongue, but can recover without treatment and with no long-term effects.





Most animals possess a protective enzyme called *methaemoglobin reductase* that naturally reverses methaemoglobinaemia. This enzyme is a safety mechanism to convert methaemoglobin back into normal haemoglobin.

Features of the FOXECUTE® bait

PAPP is highly toxic to dogs and foxes but much less toxic to most other species (on a per kg liveweight basis). However, there are some species that are more susceptible to PAPP than to 1080. For example,1080 has very low toxicity for goannas but they are vulnerable to PAPP. For this reason the label recommends that PAPP baits are not used when goannas are most active (summer) and that PAPP baits are *not* approved for aerial application.

Quolls and bandicoots could also be vulnerable to baits containing PAPP, but studies have shown low uptake of buried manufactured baits by these native species. Independent environmental authorities have assessed that even if some individuals are lost during fox control programs, the impact on populations is low.

Removing the predators that otherwise prey on these native species or compete for their food, is a greater benefit than the risk, so the balance of acceptable risk is in favour of using baits to control introduced predators.

Risks to non-target animals are further reduced by the burying or covering baits, which reduces access to baits by birds and small native mammals, while not impeding uptake by foxes.

PAPP baits for foxes & wild dogs

The PAPP dose in FOXECUTE® baits is 400mg. This is ample to kill a fox weighing 5-7 kg, but may not be sufficient to kill a large dog. Moreover, because the effects are fast and the affected animal will feel lethargic, a larger dog that takes one fox bait is unlikely to have time to find additional fox bait(s) if baits are placed well apart. The dose used for the control of wild dogs in DOGABAIT is 1000mg/bait and this is a lethal dose for proven knockdown of any sized dog.

The lower dosing of FOXECUTE® baits for fox control creates a small margin of safety for some pets and working dogs. However, this is *not* absolute and small dogs would still be vulnerable to the fox dose, so normal protective measures are still required for pets and working dogs.

Restraining or muzzling working dogs while they are in baited areas is essential. If a dog has access to more than a single fox bait they will also be at high risk, so containers of PAPP baits must be stored securely.



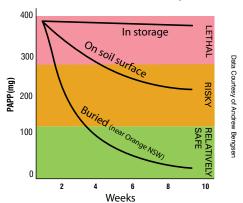
No long-term effects

PAPP does not bio-accumulate and it is metabolised and excreted quickly. Any animal that receives a sublethal exposure is able to quickly clear the toxin from the system and will have no long-term effects. Within a few hours a partially dosed animal will return to normal.

PAPP, like 1080, also degrades in the environment, though the breakdown rate for PAPP in baits is slower than for 1080 in baits. This is also dependent upon soil temperature and moisture content.

Indicative studies have shown that buried FOXECUTE® baits under field conditions retain lethal doses up to several weeks after deployment. This is longer than the typical 1 – 2 week period for which 1080 baits remain lethal in moist soil.

Bait breakdown after surface or buried placement



No risk of secondary poisoning

The levels of PAPP residue in a carcass are very low. Sufficient tissue could not be eaten quickly enough to lead to secondary poisoning of any scavenging animal.



A fox killed by a PAPP type bait will typically show a grey or blueish colour on the tongue and gums due to the loss of oxygen to tissues. If a pet or working dog is suspected of PAPP poisoning this discolouration of the tongue is a critical warning sign and indicates the need for quick intervention.



Blue Healer Antidote

Any compound, that converts methaemoglobin back to normal haemoglobin can reverse the effects of PAPP, even if an affected animal is close to death. Response to treatment is immediate.

A common antidote to methaemoglobinaemia is methylene blue, when injected intravenously. Sterile methylene blue solution is commercially available as a human medicine and vets can purchase this product. A ready-to-use product for dog owners is not yet available.

Advisory information about PAPP has been provided to all veterinarians and training is to be incorporated into new veterinary teaching programs.

Most large animal vets will already have supplies of methylene blue as it is used to treat nitrate/nitrite poisoning in cattle.



As PAPP acts quickly it is imperative to intervene as quickly as possible in an emergency.

It is necessary to get the affected non-target animal to a vet as soon as possible after ingesting a PAPP bait. During the early stages of toxicosis, dog owners can also induce vomiting via oral doses of salt water to an accidentally poisoned dog. Depending on how much bait has been



absorbed, the time to death will typically be 45-90 minutes. This means that it may not be possible to administer the antidote fast enough in remote areas.

We strongly recommend fitting muzzles to or chain restraints on working dogs and pets if they are near a baited area.

Marker beads now in baits

Another feature incorporated into PAPP baits by ACTA is the inclusion of small plastic marker beads. These remain in the stomach or gut of an animal that is killed and can even be found in a long-decayed carcass.





PAPP baits have yellow/orange beads

1080 baits have **red beads**

The marker beads used in PAPP baits are yellow/orange whereas those to be used in 1080 bait manufactured by ACTA are red. If a dog is presented to a veterinarian and it can be made to vomit, the nature of the poison can be immediately determined by the colour of the beads.







Moreover, dogs that have become ill for other reasons, such as snake bite (a common cause of death in farm dogs), will have no beads present. This increases the ability of veterinarians to diagnose the correct course of treatment and will help overcome some false claims that pets or other wildlife have been killed by baits when there is another cause of death.



Why PAPP baits are dearer than 1080 baits

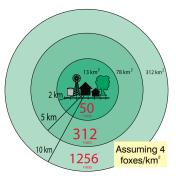
PAPP is synthesised from a precursor chemical called aniline, but its synthesis requires special conditions and releases corrosive by-products that can damage reaction equipment. Therefore PAPP is more expensive than 1080 to synthesise. Also, high doses of PAPP for dogs and foxes are required (400 or 1000mg PAPP per bait compared to 3 or 6 mg of 1080 respectively). Additionally the cost of gaining regulatory approval has been high. A royalty from sales will be returned to the IA-CRC and AWI to assist in further research into pest animal management.

Understanding the fox problem as a basis for action

An important first step is to understand the true size of the fox problem.

Fox numbers:

Most areas have between 1 and 4 foxes/Km². Some areas, such as swamps or some periurban areas, can harbour even greater local densities in excess of 10/Km².



At a density of 4 foxes/Km², there may be hundreds of foxes within a 10 Km radius. A common error of fox managers is to seriously underestimate fox numbers and to use too few baits or not run a baiting program for sufficient time to achieve good levels of control.



Home ranges:

Foxes have scent-marked home ranges where they spend most of their time. These can vary from 3 to 400 ha) but foxes are known to make sporadic transient forays of up to 10 Km outside their normal home ranges.

Foxes are excellent predators:

Foxes are agile, can climb reasonably well and can travel a kilometre in just a few minutes.

They have a diverse diet that includes meat and plant items including fruits. They can spread seeds of pest plants like blackberries and olives.





Foxes have great day and night vision, keen hearing and an excellent sense of smell. They are fast and have powerful jaws for inflicting major wounds with a single bite. Most small native wildlife or lambs are no match for this predator.



Blackberry seeds in fox scat.

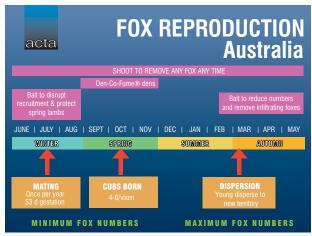


Olive seeds in fox scats.



Fox teeth and jaws are designed for killing.





Fox reproduction:

Foxes mate in late winter and give birth to about 4 cubs per female in spring, after a 5 week gestation. Fox cubs stay in natal dens for the first month or two of life then start to forage for food with parental assistance. In late summer the sub-adult cubs leave the parental location to establish their own territories. This is known as dispersal, when young foxes can move long distances to reinfiltrate any area of low fox abundance. Thus, control should be conducted on an annual basis, or more often if possible.

Fox production rate:

Fox density is estimated to be about 1 to 4 foxes/ Km². Therefore a state like Victoria (approx. 250,000 Km²) harbours up to 1 million foxes. Half are female and each female raises about 4 cubs/yr. The production rate is thus about 2 million new foxes per year.



Foxes have a high risk of failing in their first year of life. Only about half of the newborn foxes make it to one year old. The death rate continues at about 30% of each age group, each year, throughout the 5 year natural lifespan. Contrary to common opinion, most foxes are young and fewer than 10% of foxes reach 4 or 5 years old. All foxes can damage stock and wildlife. It is not just a "few old rogues" that need to be controlled.

Buried baiting works well for foxes:

Foxes naturally cache food and mark the sites of food caches by defecating or urinating nearby. This is not hiding of food, as other foxes can easily find and dig up the food. The buried baiting strategy simply mimics the natural behaviour of the fox. Even after a bait has been taken, other foxes will visit the site, so bait replacement during a program over several weeks is wise. A single bait round will not control all foxes in an area.

These facts about foxes inform the design of good control programs.



Foxes should be controlled annually or twice annually, in programs over several weeks.



Establish bait stations throughout an area, not just in rings around lambing paddocks. Foxes will investigate all parts of their range quickly. Localisation of baits will leave areas where foxes have no bait exposure.



Highest fox numbers are in Autumn so this is a good time to bait young foxes from the previous breeding to prevent recruitment of animals into the next generation. Baiting in winter and into early Spring can destroy breeding females, so that four fewer cubs are born for the following season. Therefore both Autumn and winter/spring baiting programs are desirable. These times also provide maximum protection at the times vulnerable lambs and goat kids are born.



Since foxes can move rapidly, it is not wise to place baits close together as a single fox can find and take several baits. This is a waste of baits. Do not set up bait stations closer than 200m apart.



Bait replacement at a baiting site where a bait has been taken is good practice, as not all foxes will be killed in a single baiting round.



Work with neighbours to achieve depletion zones that are as large as possible for maximum protection of stock





Availability and approvals for use

FOXECUTE® PAPP baits for foxes (and DOGABAIT PAPP baits for wild dogs) have been approved by APVMA. Legal instructions and restrictions for use are found on the approved product labels and must be followed. In addition, some constraints differ between States, so local instructions must also be followed. Approved labels



and MSDS sheets are available on the ACTA web site:

(www.animalcontrol.com.au).

Due the imposition of RESTRICTED S7 by the National Drugs & Poisons Scheduling Committee (NDPSC), only approved users can access PAPP bait products. Approvals and some constraints may differ between States, so local instructions must also be followed.

FOXECUTE® Baits, in pails of 10 or 40 baits, are available from traditional suppliers of 1080 baits in all states.

Notification:

Immediate neighbours must be notified 72 hours before PAPP baits are applied.

Storage Directions:

Baits must be kept out of reach of children and stored in a locked area.



Warning signs:

Signs must be put up at property entrances before the start and remain in place until 4 weeks after the end of approved programs, or until residual baits are recovered.



Reusable warning signs printed in UV resistant ink and on water resistant corflute are available from ACTA

Distance restrictions:

There are restrictive requirements for placement of baits. The national label restrictions are that baits must not be placed:

- · Within 150m of a dwelling
- Within 20m of a watercourse
- Within 5m from boundaries or roads

Safeguards for the environment

PAPP is stable in FOXECUTE® during storage but degrades in the environment. There are no long-term residues. At recommended rates the amount of PAPP applied is less than 80mg/ha for fox programs. There is no risk of contamination of the human food chain or crops from the proposed application as a toxic buried bait for control of foxes. PAPP is mixed throughout the bait, so a small animal nibbling at the bait would receive small quantities of toxin only.

Safeguards for users

PAPP is more toxic to canids than for most other animals, but it is still a poison. Large doses can kill any animal and the bait products are **poisonous if swallowed**. PAPP is not readily absorbed through skin. Contamination is easily removed by washing in soapy water.

Additional information

Poisons information line 13 11 26

ACTA web site:

www.animalcontrol.com.au

Pestsmart tool kit

www.pestsmart.org.au/pestanimal-species/wild-dog/ www.pestsmart.org.au/pestanimal-species/wild-dog/wilddogaction-step-1/)



How does PAPP

Sodium flouroacetate (1080) is a naturally occurring plant toxin. It is found in several plants but especially in Gastraolobium and some Acacia species. It is a simple molecule that is deceptively similar to normal acetate which is an essential intermediate in the breakdown of sugar into energy.

1080 works by blocking the action of a critical enzyme (aconitase), which is one of a series of enzymes responsible

for converting sugar into chemical energy in all animal cells. This enzyme sequence occurs in the mitochondria ("energy factories") of cells and is known as the Tri Carboxylic acid, or TCA cycle. 1080 works as a "spanner" in the gears of the energy factory, so all other biochemical processes that require energy cease, as metabolic energy is depleted.



differ from 1080?

Enzymes in some species are less able to be blocked by 1080, so reptiles are generally less susceptible than birds and birds are less susceptible than mammals. Even between mammals there are large differences in susceptibility. One reason for this is that 1080 occurs naturally in some toxic plants in Australia, so Australian native herbivores that eat such plants have been naturally selected for resistance.

Thus, 1080 can be used selectively to control introduced pest animals, since the introduced pests have not had the evolutionary time to adapt, while posing limited risk to the vast majority of native species.

Risks are further reduced by using baits that are preferred by the pests but not palatable to the non-target species and by using baiting techniques such as "buried baits", (where possible) that reduce the risk of non-target animals taking baits.

These practices have been well developed and tested over many decades and enable pest animals to be controlled while posing limited risk to non-targets.

However, 1080 is highly toxic not just for foxes and wild dogs but also for pets and working dogs. For this reason many landowners are reluctant to use this effective chemical as widely as is needed to manage the pest wild dogs and foxes.

While the action of 1080 is only to block an enzyme in the mitochondria, the resultant biochemical disruption of sugar metabolism, into carbon dioxide and energy,

causes a build-up of citrate in blood. Citrate binds up calcium ions that are necessary for normal muscle function and coordination. Therefore, during the last phases of poisoning with 1080, while the animal is unconscious, an affected animal exhibits muscle spasms that can be distressing for an owner to witness. Moreover, there is no proven antidote to poisoning with 1080 so most dogs that accidentally take a bait will succumb, even despite veterinary intervention.

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ACTA products for large-scale pest animal management available through agencies and/or leading rural merchant stores:



FOXOFF® Fox Bait

For the control of foxes

DEN-CO-FUME®

Fumigation Cartridges

For the control of foxes in natal dens



SLUGGOFF® Slug & Snail Bait

For the control of snails & slugs in the home garden



Fox Bait

Fish based bait for fox control



DOGGONE®

Wild Dog Bait For the control of wild doas



1080 Oat Bait For the control of rabbits



MOUSEOFF®

Zinc Phosphide Bait For the control of mice in crops



Bromadiolone Grain Bait For the control of rats and mice



RABBAIT®

Pindone Oat Bait

For the control of rabbits

RATTOFF®

Zinc Phosphide Bait Sachets

Reducing rat populations in sugarcane crops



MOUSEOFF®

Bromadiolone Rodent Block

For the control of mice and rats in domestic, commercial & industrial buildings



PIGOUT® Feral Pig Bait

For reductions in feral pig populations



FOXECUTE®

PAPP Fox Bait For the control of foxes



PAPP Wild Dog Bait

For the control of wild dogs



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