DESERT KNOWLEDGE CRC

A review of chemical, biological and fertility control options for the camel in Australia

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The Desert Knowledge Cooperative Research Centre is an unincorporated joint venture with 28 partners whose mission is to develop and disseminate an understanding of sustainable living in remote desert environments, deliver enduring regional economies and livelihoods based on Desert Knowledge, and create the networks to market this knowledge in other desert lands.

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List of shortened forms

CCE	Camel contagious ecthyma
CLOD	Coyote Lure Operative Device
DES	diethylstilbestrol
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FSH	follicle-stimulating hormone
GMO	Genetically modified organism
IA CRC	Invasive Animals Cooperative Research Centre
LD_{50}	Lethal dose for 50% of a population. The LD_{50} is the amount of a material, given all at once, that will cause death to 50% (one half) of a group of test animals.
LH	luteinising hormone
MGA	Melengestrol acetate
NRM	Natural
PAPP	para-aminopriophenone
PZP	Porcine Zona Pellucida
VCD	4-Vinylcyclohexene Diepoxide
VVIC	Virally Vectored ImmunoContraception

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Executive summary

In the last 160 years since their introduction to Australia, the one-humped camel, *Camelus dromedarius*, has gone from the colonist's companion to a conservationist's conundrum in the fragile arid ecosystems that dominate this country. The camel was brought to Australia for cartage purposes for exploration of the arid inland by early explorers, and was subsequently used to open up the inland through assisting in the development of towns and railways. From up to 20 000 ancestors introduced into Australia, potentially half of which may have been liberated in the 1940s, the feral population of camels is currently thought to number around one million individuals spread between Western Australia, Northern Territory, Queensland, and South Australia.

The species is ideally suited to inland Australia due to its low water requirement, opportunistic herbivorous diet, and stature that puts it above all other sympatric species in obtaining browse. And unlike in their natural range, the camel in Australia is virtually disease free, with melioidosis (in tropical areas only) and sarcoptic mange being the only two diseases of note. It is predicted that left unmanaged the species' population will double every eight years. Currently management techniques include aerial shooting and mustering for commercial use; however, they are failing to curb the current population growth.

In late 2007 the Desert Knowledge CRC approached the Invasive Animals CRC to undertaken a literature review of chemical, biological, and fertility control options for the camel as part of their larger Australian Government–funded 'Cross-jurisdictional management of feral camels to protect NRM and cultural values' project. The terms of reference included assessing the efficacy and appropriateness of known xenobiotics, diseases, and anti-fertility agents for managing feral camels.

Little is known about the lethality of most registered vertebrate pesticides in Australia to camels. A great deal more has been published on adverse drug reactions in camels used in agriculture and the racing industry. With the exception of sodium fluoroacetate, and potentially cyanide, most registered vertebrate pesticides were deemed inappropriate for camels due to their predicted high doses or welfare concerns. A promising xenobiotic is a nitrite salt that causes rapidly fatal methaemoglobinaemia in Artiodactyles (even-toed ungulates), particularly given the species' almost unique propensity to consume large volumes of salt. In addition, a combination of potassium chloride with a diuretic, with or without a nephrotoxic agent such as banamine or phenylbutazone, should be considered as a possible candidate for lethal control. Although almost uniquely toxic to camels in low doses, trypanocidal drugs and salinomycin or monensin are not recommended for further examination at this stage as the resulting death is unlikely to be quick or humane.

An examination of the literature on camel diseases that occur in the species' natural range – such as camelpox virus, contagious ecthyma, and papillomatosis – indicates that the infections do not generally result in high levels of mortality, and that they may not justify further examination in Australia. However, it has been indicated that as Australian camels are naïve to camelpox, a reportedly species-specific disease, mortality of greater than 50% of the entire population may occur, and as such it is worthy of further investigation. Additionally, *Aspergillus fumigatus*, a fungal mycotoxin, is the only fungal agent thus far associated with systemic disease and fatalities in camels, and may be worthy of further research.

As a long-lived species the camel is not ideally suited to fertility control. Notwithstanding, anti-fertility agents may have their place in preventing the re-establishment of camel populations once they have been reduced through mechanical, biological, or chemical means. Of the numerous anti-fertility agents currently being developed the immunocastration vaccines have the shortest developmental horizon, but due to intramuscular delivery their utility will always be very limited. For landscape-scale application an immunocontraceptive vaccine technology that holds the prospect of an orally active, species-

specific immunogen is particularly attractive. Such an approach is currently being investigated by a US researcher, and this potentially has utility for camels. The same principles of species specificity and oral activity also underpin the attractiveness of a product based on phage panned peptide technology. The Talwar protein, although not species specific, may well be orally active and a useful immunogen compared with alternative GnRH-based vaccines.

Delivery of any generic chemical or fertility agent will require a species-tailored pathway and an appropriate large-scale deployment method. The report suggests numerous avenues of investigation, in particular raised and offset feeding troughs or salt licks, and low concentration water delivery of short-lived xenobiotics given the large volumes of water that camels rapidly consume. Both techniques should be applied at natural camel congregation points, fresh water holes, and salt lakes to minimise the number of management sites and non-target species exposure.

Competing interests with camels, including bush food, commercial harvesters, animal rights groups, and land management agencies, will dictate that camel management in the future will very much be about people and perception management. The species has had over 70 years to colonise and prosper within Australia's rangelands, and it should not be expected that any one potential management tool discussed within this report will rapidly change the current overabundance situation. Notwithstanding, camel management within Australia requires improved broadscale management tools, and this report outlines some possibilities worth pursuing.

1. Introduction

Camelids originated in North America, where they are now extinct, and did not reach the Old World until about two million years ago (Dörges & Heucke 1997). Camels belong to the suborder Tylopoda of the Artiodactyles (even-toed ungulates, along with pigs). Within their current native range of north Africa and central and western Asia the one-humped camel or dromedary (*Camelus dromedarius*) is a highly revered species, used for food, fibre, and racing (Wilson 1984). The species reportedly has no known natural predators throughout this range. Australia is the only country in which camels have established a feral population, and is now the only location where the species lives in natural populations (Dörges & Heucke 1997).

Between 1840 and 1907 up to 20 000 camels (accurate estimates unknown) were imported from British India into Australia to serve in inland exploration ventures through providing cartage (Edwards et al. 2001). Later the species was used to pioneer the inland through their use in the construction and supply of towns and railways. The use of camels declined throughout the 1930s due to the increasing reliance on trucks, with potentially 5000 to 10 000 animals liberated during this time (Edwards, Saalfeld et al. 2004).

An estimated minimum of 300 000 feral camels (Edwards, Saalfeld et al. 2004), and a potential population exceeding one million (Desert Knowledge CRC 2007), currently roam over near 40% of the Australian mainland (Short et al. 1988). The species is already having significant impacts on Australia's fragile desert ecosystems (Edwards, Pople et al. 2004; Coventry et al. in press), with such damage only set to increase as the population grows (Edwards, Saalfeld et al. 2004). To curb the current population growth at least 10% of the entire population, or 100 000 individual camels, must be removed each year. Despite some significant effort this is not currently occurring, with commercial harvesting (~5000 animals per annum) and aerial and ground shooting falling significantly short. The only realistic solution to the current problem is species-specific (specific either in themselves or in the delivery method) and humane lethal chemical, fertility, or biological control agents.

1.1 Distribution and ecology

Feral camels are irregularly distributed throughout the arid rangelands of central Australia. They tend to live in remote areas away from habitation (Siebert & Newman 1989), in sand dune and spinifex (*Triodia* spp) country (Short et al. 1988). Edwards, Saalfeld et al. 2004) estimated the population of feral camels to be at least 90 000 in the southern regions of the Northern Territory and 270 000 in Central Australia. By comparing with previous surveys (Short et al. 1988), they concluded that in the absence of significant disease or predators camel numbers are increasing exponentially at the rate of 10% a year, so that the population doubles every eight years (Edwards, Saalfeld et al. 2004). The increasing feral camel numbers are a threat to the arid ecosystems of the interior (Edwards, Pople et al. 2004; Coventry et al. in press). High palatable flora, such as plum bush (*Santalum lanceolatum*), desert kurrajong (*Brachychiton gregorii*), curly-pod wattle (*Acacia sessiliceps*), wild potato (*Ipomoea costata*), desert poplar (*Codonocarpus cotinifolius*), bean tree (*Erythrina vespertilio*), quandong (*Santalum acuminatum*), and native pine (*Callitris glaucophylla*), are being selectively overgrazed, and natural water sources are being fouled. Camels are also increasingly causing infrastructure damage to artificial water sources, in particular in remote communities.

Feral camels occur across a range of land tenures throughout the Australian rangelands, including Aboriginal land, vacant crown land, parks and reserves, freehold land, and grazing leases (Figure 1). In summer they seek refuge from the heat in bushland and sandplain country, preferring more open salt lakes and marsh in winter. Over 80% of plant species occurring within the range of camels are utilised by the animals, with 98% of the camel diet consisting of shrubs and forbs with grasses generally only

consumed after rain (Dörges & Heucke 1997). The unique dexterity of the split upper lip does, however, mean that camels can browse selectively, up to a recorded height of 3.5 metres, and utilise thorny plants. Camels have a reported preference for high water and salt content plants, and have been recorded eating toxic plants avoided by other mammals (Dörges & Heucke 1997).

When forage is green following rainfall camels can meet their water requirements metabolically. In summer camels may drink every other day, usually at dawn. When dehydrated a camel can consume up to 200 litres of water in three minutes (Dörges & Heucke 1997), and during extended periods of drought up to 500 camels can be seen to congregate at water points.

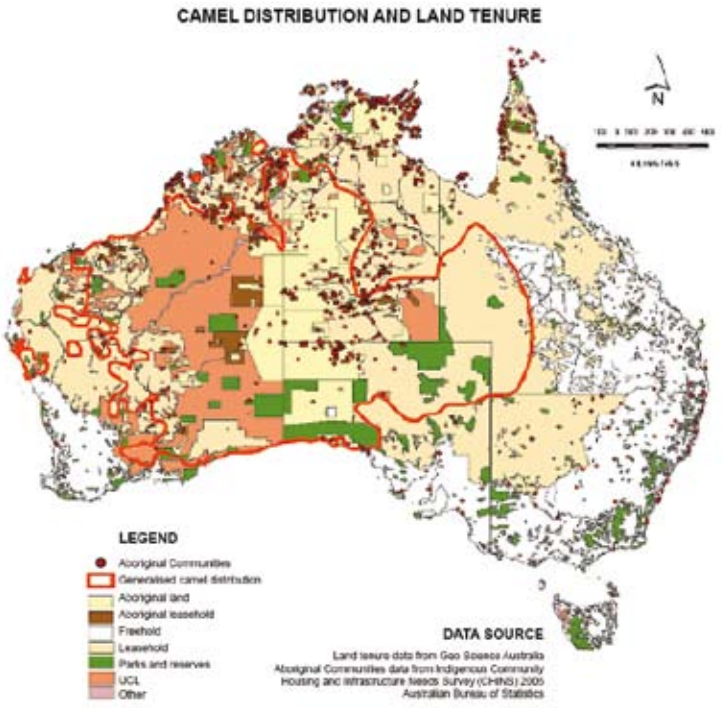

Figure 1: Camel distribution and land tenure in Australia
Source: Desert Knowledge CRC 2007

The camel is a social animal, living in non-territorial groups of three main kinds: year-round bachelor groups of bulls (males), summer groups of cows (females) and calves, and winter breeding groups that include a mature bull and several cows and their calves. Old bulls tend to be solitary. Herd size ranges from 2 to 45, with an average of 11 individuals, but larger herds may form in summer when groups congregate (Dörges & Heucke 1997). From May to October during the breeding season males have a herd of 20 or more cows, which they defend against advances from other bulls. Pregnancy lasts 12–13 months, and a cow gives birth to a single young, approximately 40 kg in mass, which is weaned at about 18 months. Feral camels can live for as long as 50 years and breed actively for 30 years.


Copied from http://www.ssn.flinders.edu.au/geog/Camels/

There are currently two published (Grigg et al. 1995, Edwards et al. 2001) and at least one current (Flinders University nd.) satellite radio tracking studies on feral camels in Australia. Grigg et al. (1995) followed the movements of two cows over a 17-month period. Both animals ranged over 1000 km during this time and had range radiuses of 125 km and 200 km. Long distance movements were, however, sporadic, often occurring after months with a relatively small range, and were thought to be the result

of rainfall events. Edwards et al. (2001) tracked a larger sample size of camels for longer (up to four years) but reported similar findings. Home ranges over a 12-month period varied from 449–4933 km^2 and were reportedly correlated with aridity. Both studies clearly indicate that appropriate management units for camels will need to be exceedingly large for effective population management to be sustained. Hopefully, the current camel genetic research being conducted at Murdoch University, Western Australia, will throw more light on this area of research (Spencer 2008).

1.2 General physiology

The Camelid family have evolved to form a multi-chambered forestomach akin to true ruminants. In keeping with this evolutionary heritage, camel physiology follows the general ruminant pattern (Manefield & Tinson 1997). However, due to the unique environmental selection pressures, elements of their physiology are worthy of note, particularly in the context of physiological adaptations and behaviours that promote or detract from efforts to manage their abundance.

The critical desert adaptations of camels relate to their tolerance of large diurnal temperature fluctuations, encompassing hot to very hot daytime temperatures, and their highly efficient use of water within the limits that permit cellular function. These two responses to strong environmental selection pressures have resulted in the following specialised physiologies:

- Coat type (hair/wool) and distribution that is short on the lateral and ventral aspects of the body and generally longer and denser over the dorsal surface to reduce the absorption of radiant heat, while dissipating heat from the shaded parts or the majority of the body surface area.
- Heat dissipation by adipose tissue localised in their hump and via their long legs, which facilitate ventilation and reduce exposure to ground-reflected heat.
- Normohydrated camels use sweating highly effectively because of the limited subcutaneous fat underlying the skin and the relatively short coat or lack of coat in areas rich in sweat glands. Dehydrated camels switch to respiratory evaporative cooling and conserve water through condensing it in the nasal cavity (Manefield & Tinson 1997).
- Specialist structuring of blood vessels within camels' legs which promote heat exchange during normal blood circulation (Wilson 1984).
- Myogenic vasoactive heat exchange to protect heat-sensitive brain tissue during heat stress (Elkhawad 1992).
- Sophisticated mechanisms to maintain plasma volume (2–4 times better at minimising plasma volume losses than humans, other ruminants, and temperate Camelids). This enables them to continue blood circulation to the skin for heat exchange during heat stress and dehydration (Manefield & Tinson 1997).
- Camels' appetites are maintained under conditions of up to 25% dehydration compared with 10% in cattle (Gauthier-Pilters & Dagg 1981).
- Camels are able to rehydrate rapidly without risk of osmotic imbalance due to highly specialised red blood cell architecture and function that enables them to expand and return to normal size without rupture, and the regulation of gut water osmolarity through the active transfer of sodium ions (Macfarlane 1968, Wilson 1984).
- Camelid maintenance energy requirement (~314 $KJ/kg^{0.75}$/day; Guerouabi & Filali 1992) is approximately two thirds of the requirement of beef cattle *(Bos taurus)* (National Research Council 1985).

- Whn food is scarce, Camelids are able to metabolise free fatty acids and ketone bodies effectively, whereas fasting in true ruminants induces breakdown of body tissue and generally causes a shift in the main energy-producing pathway (Trichloroacetic acid cycle, TCA-cycle) to increased formation of ketone bodies (hydroxybutyrate and acetoacetate) as a result of insufficient supply of oxaloacetate precursors.
- Camels produce relatively little urine (3–5 litres/day) in contrast to 20 litres/day for equivalently sized cattle, and can depress glomerular filtration rate and effective renal plasma flow by over 70% during heat stress and dehydration (Yagil 1993).
- Camels are extremely efficient at recycling urea, which in turn reduces urinary output and provides a source of nitrogen for protein synthesis.

Furthermore, two key behavioural physiology adaptations have aided in the successful establishment of camels in Australia:

- The relatively high water content of the browse plants on which they feed plays a significant part in their ability to abstain from drinking water, and it is estimated that camels may obtain up to 30 litres of water per day from green forage alone.
- The breeding behaviour of camels differs from sheep and cattle in two primary ways: males show strong seasonal activity (rut), while females are induced ovulators; that is, the act of mating stimulates ovulation. Males come into rut between May and October in the southern hemisphere.

The dromedary camel has a superb adaptive capability to withstand the extreme environmental conditions of the Australian rangelands due in part to its tolerance of severe dehydration. This tolerance stems from its capacity to reduce renal, respiratory, and alimentary water losses and replace strict evaporative homeothermia with daytime hyperthermia and physical cooling methods. Recycling of water and urea is salt-dependent and places the camel in a unique relationship with its environment, as forage and drinking water often contain high amounts of salt in the arid zone. These physiological changes are accompanied by anatomical and behavioural changes which also decrease water dependence. The net effect of the adaptations is lower energy expenditure and water requirement in maintaining body temperature, compared with sheep and cattle, which delivers the camel a wider browsing range from permanent water sources and less influence from natural waterhole tethering environmental pressures.

In summary, the general and specialised physiological adaptations of camels would, on the face of it, predispose them to chemicals that perturb renal function or blood osmolarity, such that salt-dependent urea and water recycling is adversely affected. The reproductive physiology of camels would also allow the effective – if not the practical – use of chemicals developed for other domesticated species that target the hypothalmic/pituitary axis or gonads.

1.3 Health and disease

The camel in Australia is relatively disease free, further adding to the species' population growth ability. Brown (2004) conducted a review of camel diseases based on several thousand camels from central Australia and reported few problems with the health status of the animals. Of note is that camels are free of bluetongue, and have previously not returned positive for brucellosis or tuberculosis (both no longer present in Australia). Although hydatidosis occurs in Australia, and can be fatal to camels, the tapeworm has never been detected in rangeland camels. Similarly, Johne's Disease is present in Australia, which camels are susceptible to, but has never been detected in the species. Two diseases that have caused camel deaths in Australia are melioidosis and sarcoptic mange. In 1990 seven out of 13 camels housed near Cooktown and Rockhampton died of melioidosis, caused by the bacterium *Burkholderia pseudomallei* (Bergin & Torenbeek 1991), with a further four incidents (one resulting in the death of 29 of 39 export camels) occurring in the Northern Territory. The disease only occurs in the wet tropics and generally only affects camels when they have been relocated from dry conditions.

Manefield and Tinson (1997) reported that sarcoptic mange (caused by *Sarcoptes scabei* var *cameli*) is the biggest killer of young feral camels in Australia, as it is highly contagious and spreads quickly through a herd. Unfortunately, no figures could be found on actual mortality rates.

1.4 Scope of review

This review aims to identify and compare all relevant published and potential chemical, fertility, and biological control agents for the camel in Australia. It also provides suggestions for possible landscape-scale delivery options for promising actives. In general, chemicals or diseases that are not specific to camels, or could not be delivered in a species-specific manner, have not been reviewed regardless of how lethal they are (i.e. anthrax and botulism). A review of current control methods – namely mustering, trapping, and shooting – has not been undertaken. Detailed suggestions into the biological modification of diseases for lethal or anti-fertility effects have also not been made. Furthermore, although many of the suggestions made in the review are based on the Achilles Heel principle of pest management (Marks 2001), whereby unique aspects of the pest species' biology in their 'new' environment are isolated and targeted for manipulation, this review focuses specifically on the manipulation agents themselves rather than the process of isolation. Readers are referred to Coventry et al. (in press) for a review of the more general Achilles Heel approach for the camel.

2. Chemical control

In the following section we outline the history, mode of action, and appropriateness of poisons or drugs for camel control. Firstly, we describe the key features of the existing non-anticoagulant vertebrate pesticides. Secondly, we describe the key features of the existing anticoagulant vertebrate pesticides. Thirdly, we examine the potential of two new candidate vertebrate pesticides, para-aminopriophenone (PAPP) and sodium nitrite, which are being developed for the control of canids and feral pigs respectively. Fourthly, drugs and toxins that camels might be especially susceptible to are considered. This is followed by an analysis of feasibility of poisoning and the relative merits of the compounds described below.

Lethal control of camels could potentially be achieved with established vertebrate pesticides, including those that are already used for pigs, foxes, rabbits, and rodents (see Table 1). Alternatively, drugs or other toxicants to which camels are particularly susceptible should be considered. Vertebrate pesticides are classified as:

1. anticoagulants, which include the indandiones pindone, diphacinone, and chlorophacinone, and the coumarins that include warfarin, coumatetralyl, difenacoum, bromadiolone, brodifacoum, flocoumafen, and difethalione
2. non-anticoagulant acute poisons, which include any substance that does not fall in the former category, such as strychnine, cyanide, zinc phosphide, sodium fluoroacetate (1080), cholecalciferol, and the new candidates para-aminopropiophenone and sodium nitrite.

None of these compounds have been previously tested in camels, hence the suggested likely acute toxicity of these agents are estimates extrapolated from values recorded in other mammals.

Table 1: Common and candidate vertebrate pesticides

Non–anticoagulant-established compounds	Non–anticoagulant-candidate compounds	Anticoagulants-indandiones	Anticoagulants-coumarins
1080	Para-aminopropiophenone	Pindone	Coumatetralyl
Cyanide	Sodium nitrite	Diphacinone	Bromodialone
Zinc phosphide		Chlorophacinone	Difenacoum
Strychnine			Flocoumafen
Cholecalciferol			Brodifacoum
			Difethialone

2.1 Chemical control options from existing non-anticoagulant vertebrate pesticides

This section focuses on acute poisons, such as cholecalciferol, strychnine, cyanide, zinc phosphide, and sodium fluoroacetate (1080). These compounds have different modes of action and different properties. The most commonly used of these in Australia is sodium fluoroacetate (1080).

2.1.1 1080

2.1.1.1 General information and history of use

Sodium fluoroacetate was first prepared in Belgium in 1896 but was not seriously investigated as a pesticide until the 1940s, when shortages of strychnine and red squill necessitated the development of other toxicants (Atzert 1971). 1080 has been developed as a poison to kill mammalian pests. Fluoroacetate also occurs naturally at lethal concentrations in poisonous plants (de Moraes-Moreau et al. 1995; Twigg et al. 1996a, 1996b). 1080 is currently registered in Australia as a vertebrate pesticide and is used in carrot, cereal, and meat baits. It has been used for pest control since the 1950s and is one of the only poisons that is registered for aerial control of pests. The use of this poison in Australia is a reflection of unique wildlife pest problems and the unwanted impacts of introduced species.

2.1.1.2 Mode of action

The period between the time fluoroacetate is consumed and the appearance of symptoms of poisoning in mammals is between 0.5 and 3 hours. Animals receiving a lethal dose mostly die within 24 hours. 1080 is converted to fluorocitrate, which inhibits energy production in the tricarboxylic acid (Krebs) cycle. This results in accumulation of citrate in the tissues and blood, energy deprivation, and death from heart or respiratory failure (Egeheze & Oehme 1979, Eason 2002). There is some debate about the humaneness of 1080 (Sherley 2007). While it is not as humane as PAPP or cyanide (Eason et al. 2008), it is considerably more humane than many other toxins, including strychnine or anticoagulant poisons.

2.1.1.3 Target species appropriateness and key features

No acute toxicity data exist for 1080 in camels; however, it is toxic to most animals (Table 2). The LD_{50} value for camels is likely to be in the range of 0.5–1 mg/kg (Eisler 1995), equivalent to a total dose of approximately 250–500 mg to kill an adult camel.

Table 2: Acute oral toxicity (LD_{50} mg/kg) for sodium fluoroacetate in selected species

Species	LD_{50} mg/kg
Pig	0.3
Sheep	0.4
Cow	0.4
Deer	0.5
Goat	0.6

Source: Ramell & Fleming 1978, Hone & Mulligan 1982, Eisler 1995

2.1.1.4 Summary of key features

- 1080 is the main poison currently used for fox, feral pig, and rabbit control, either in aerial application or ground-based operations.
- Since 1080 is highly water-soluble; it is readily dispersed in the environment by rain and degraded by soil microorganisms (Eason 2002).
- All animals are susceptible to 1080 poisoning, and camels would be likely to be killed by doses of 0.5–1 mg/kg.
- If an animal ingests a sub-lethal dose of 1080, toxin residues will not persist in meat, blood, the liver, or fat for more than one week (Eason et al. 1994; Eason, Wright & Meikle 1996). Unfortunately, carcasses retain the poison and there is a prolonged secondary poisoning risk (Meenken & Booth 1997).
- 1080 will kill non-target species unless baits or baiting strategies are designed to exclude them.

Table 3: Utility of 1080 for camel management in Australia

Advantages of 1080	Disadvantages of 1080
Highly effective for achieving a rapid reduction of pest species	Controversial, especially aerial operations
One of the only poisons available for aerial application	Secondary poison risk from carcasses (especially to dogs)
Cheap compared with most other poisons	No effective antidote
Biodegradable in the environment	Generates bait shyness if target animal gets sub-lethal dose
Registered in Australia for killing a number of vertebrate pest species	

2.1.1.5 Recommendation

1080 use for poisoning of camels would be controversial; nevertheless, it should at least be considered for the short list of candidates if poisoning is an option. The extensive experience that exists with this compound in Australia and its availability and registration status are all advantages. However, as a large amount of poison (approximately 500 mg) would be needed, a target-specific baiting technique would need to be developed, as discussed in section 5. Secondary poisoning risks would be prolonged, which would be a significant disadvantage.

2.1.2 Cyanide

2.1.2.1 General information and history of use

Cyanide is not currently registered as a vertebrate pesticide in Australia. It has been used experimentally for killing foxes (Marks & Gigliotti 1996). It is currently being researched as an alternative to 1080 for the control of over-abundant Bennett's wallabies in Tasmania. It has been used in New Zealand for several decades for killing possums, but has limited use elsewhere. Because of its fast action, cyanide is considered in a number of countries to be too hazardous for pest control. Cyanides are extensively used in the manufacture of synthetic fabric and plastics and metal-mining operations. Cyanogenic (cyanide-containing) compounds occur in plants and also in some fungi and bacteria. Some common sources for humans include cassava, sweet potatoes, yams, apricots, prunes, and plums. Like fluoroacetate, cyanogenic glycosides are considered to be a chemical plant-defence (Osweiler 1996a).

In New Zealand, pea-sized chunks of paste, coated with a little flour and icing sugar (or other lures such as cinnamon or eucalyptus oil), are placed on a rock, leaf, or stick for poisoning possums. Feratox® (a pea-sized encapsulated cyanide pellet) was developed to increase the effectiveness of cyanide and reduce the risk to operators of exposure to hydrogen cyanide gas. The pellets are placed in a bait station, either with similar-sized cereal feed pellets or in paste (Gregory et al. 1998).

2.1.2.2 Mode of action

Cyanide is potent and rapid-acting, producing unconsciousness within minutes in most animals (Eason et al. 2008). Of all the poisons currently used for vertebrate pest control, cyanide, when delivered in an optimised delivery system, is considered the most humane. Cyanide disrupts energy metabolism by preventing the use of oxygen in the production of energy. Cyanide's toxic effect is due to the formation of a stable cytochrome c oxidase – CN complex in the mitochondria, which blocks electron transfer from cytochrome oxidase to molecular oxygen, ceasing cellular respiration, and causing cytotoxic hypoxia in the presence of normal haemoglobin oxygenation. The combination of cytotoxic hypoxia with lactate acidosis depresses the central nervous system, the site most sensitive to anoxia, resulting in respiratory arrest and death (Osweiler et al. 1985).

2.1.2.3 Target species appropriateness and key features

Cyanide is a broad-spectrum toxin (Eisler 1991). The minimal lethal dose of HCN in humans is 0.5–3.5 mg/kg. Information on the LD_{50} values of specific species is detailed in Table 4 and is similar for a range of mammals and birds. There are no published LD_{50} values for camels, though the lethal dose is likely to be in the range of 2–5 mg/kg, equivalent to 2.5 gms for a 500 kg camel.

Table 4: Acute oral toxicity (LD_{50}mg/kg) of cyanide

Species	LD_{50} mg/kg
Duck	1.43
Cattle	2.00
Sheep	2.30
Deer	Approx. 3.5–4.5
Pig	Approx. 3.5–4.5
Goat	Approx. 3.5–4.5
Rabbit	Approx. 3.5–4.5

Source: Hone & Mulligan 1982, Marks & Gigliottti 1996

In New Zealand it is perceived that fewer land-bird species have been killed by cyanide than by trapping or 1080. Smaller numbers of individual birds have been killed by cyanide than caught in traps (Spurr 1991). The use of Feratox® baits for possums and improved delivery systems has limited non-target mortality. The risks of secondary poisoning are low (Eason et al. 2008).

2.1.2.4 Summary of key features

- Cyanide has been used since ancient times. It is used in New Zealand in a concentrated paste bait or pellet for controlling possums.
- Cyanide is a most humane poison when dose is optimised (Gregory et al. 1998).
- Naturally occurring cyanogenic compounds are a plant defence mechanism to deter browsing animals.
- Cyanide is a fast-acting broad-spectrum toxin, and in both birds and mammals it causes tissue anoxia through inactivation of cytochrome oxidase and death due to respiratory failure.

Cyanide biomagnification in food webs is most unlikely.

Table 5: Utility of cyanide for camel management in Australia

Advantages of cyanide	Disadvantages of cyanide
Cheap (1–2 cents per bait)	Hazardous to users
Humane (very rapid action)	Not registered in Australia
Low secondary poisoning risk	Limited experience with cyanide in Australia
Effective	Antidotes are available but have to be used quickly
Carcasses can be recovered	
Biodegradable in the environment	

2.1.2.5 Recommendation

While cyanide is a not ideal for poisoning of camels, because of its hazardous nature in large amounts, it should be included as one of the preferred options to consider, mainly because of its humaneness. As a large amount of poison would be needed, a target-specific delivery system (e.g. large Feratox®-style baits) and baiting technique would need to be developed to restrict non-target access.

2.1.3 Zinc phosphide

2.1.3.1 General information and history of use

Zinc phosphide was first synthesised in 1740 and first used as a rodenticide in 1911 in Italy. Zinc phosphide is an effective acute field rodenticide that has been in use for over 50 years, with very few non-target hazards. It was the most widely used rodenticide worldwide until the introduction of warfarin in the 1950s. It is still used as a rodenticide in the USA, as well as in Australia, China, and the Asia-Pacific region. In the USA it has been used to control rats, mice, voles, ground squirrels, prairie dogs, muskrats, feral rabbits, and gophers. In Australia it is used for rodent control. It found favour because of the comparatively low risk of secondary poisoning following its field use when compared with strychnine or 1080 (Hood 1972).

2.1.3.2 Mode of action

Zinc phosphide is a quick-acting compound with clinical signs first appearing from 15 minutes to 4 hours after consumption, and death after a lethal dose occurring generally in 3–12 hours. The oral toxicity of zinc phosphide is accounted for by the toxicity of the phosphine it produces when hydrolysed by the acid of the stomach. The emetic action of the zinc moiety reduces the toxicity of zinc phosphide. Rats lack a vomiting reflex; however, camels do have vomiting reflex, which may detract from its suitability. Death is from asphyxia but since zinc phosphide is known to cause ECG changes, and pulmonary oedema is associated with cardiac failure, it may be that death is mediated by a combination of cardiac failure and respiratory failure (Osweiler 1996b).

2.1.3.3 Target species appropriateness and key features

Zinc phosphide is a broad-spectrum toxin, but there are some marked differences in susceptibility (Table 6). The LD_{50} to rats (*Rattus norvegicus*) is around 40 mg/kg and it is similar in ground squirrels (36 mg/kg) (Freeman 1954). Some bird species are more susceptible to zinc phosphide (LD_{50} for the white-throated goose is 7–5 mg/kg). There are no published LD_{50} values for camels, though the lethal dose is likely to be in the range of 20–70 mg/kg, equivalent to 35 gm to kill a 500 kg camel.

Table 6: Acute oral toxicity (LD_{50} mg/kg) for zinc phosphide

Species	LD_{50} mg/kg
Sheep	60–70
Cow	50
Pig	20–40
Dog	20–40
Cat	40
Rat (Norway)	40
Rat (kiore)	23
Goose	7.5

Source: Hood 1972, Hone and Mulligan 1982

2.1.3.4 Summary of key features

- Zinc phosphide is registered as a rodenticide.
- Sub-lethal doses of zinc phosphide are unlikely to persist in meat or major organs.
- Risk of secondary poisoning is lower than that of 1080.

Table 7: Utility of zinc phosphide for camel management in Australia

Advantages of zinc phosphide	Disadvantages of zinc phosphide
Highly toxic to rodents	Lacks specificity, more toxic to birds than mammals
Inexpensive	No antidote
Alternative to 1080	
Non-persistent	
Comparatively low secondary poisoning risk	

2.1.3.5 Recommendation

Zinc phosphide is a not recommended for poisoning of camels as the large amounts needed would be a hazard to non-target species. It is difficult to conceive that a camel could be induced to ingest the 35 gm of active required, and sub-lethal poisoning of camel with zinc phosphide could be particularly inhumane.

2.1.4 Strychnine

2.1.4.1 General information and history of use

Strychnine is found in the seeds of *Strychnos nux-vomica,* a tree native to India, northern Australia, Vietnam, and Ceylon, where it is one of a number of different alkaloids. It has a long history as a rodenticide, being used first in Germany in the sixteenth century. The seeds have been used for killing cats, dogs, and birds since 1640 and the alkaloid has been used for rodent and vertebrate pest control since the mid-1800s (Schwartze 1922). In 1986, the US EPA suspended all above-ground registrations of strychnine, allowing only underground uses. The first recorded use of strychnine in Australia was in the 1880s. It is still used in Australia for wild dog control and mouse plagues, and in the USA to control several pests, including skunks, targeted for control using strychnine-injected eggs in rabies-infected areas.

2.1.4.2 Mode of action

Strychnine is a fast-acting poison that is readily absorbed into the circulatory system from the intestinal tract. Highest concentrations of strychnine are found in blood, liver, and kidney. It is a neurotoxin. Poisoned animals often die in less than an hour as a result of respiratory failure (asphyxia), but death may take 24 hours or longer. The typical signs of strychnine poisoning are restlessness and muscular twitching that progress to convulsive seizures and violent muscular spasms before death (Osweiler 1996b).

2.1.4.3 Target species appropriateness and key features

The LD_{50} to the Norway rat is 5–6 mg/kg (Prakash 1988). The oral LD_{90} for strychnine in mice is approximately 5 mg/kg (Mutze 1989; Table 8). There are no published LD_{50} values for camels, though the lethal dose is likely to be in the range of 0.5–1 mg/kg, the LD_{50} range for cows, if camel were more similar to cows than rodents. Hence it is probable that between 250–500 mg of strychnine would be needed to kill a 500 kg camel.

Table 8: Acute oral toxicity (LD_{50} mg/kg) of strychnine

Species	LD_{50} mg/kg
Rat	5-6
Mouse	5
Cow	0.5
Horse	0.5
Cat	0.75
Norway rat	6.8
Duck	2.9
Pigeon	2.1

Source: Hone and Mulligan 1982, Osweiler 1996b

2.1.4.4 Summary of key features

- Strychnine has been used as a poison for centuries.
- Its current use is limited.
- It is a most inhumane poison.
- Residues persist in carcasses.
- It causes secondary poisoning.

Table 9: Utility of strychnine for camel management in Australia

Advantages of strychnine	Disadvantages of strychnine
Highly toxic to rodents	Causes secondary poisoning.
Inexpensive	Inhumane

2.1.4.5 Recommendation

Strychnine is not recommended for poisoning camels under any circumstances; it would be most inhumane, hazardous, and would cause secondary poisoning.

2.1.5 Cholecalciferol

2.1.5.1 General information and history of use

Cholecalciferol (vitamin D_3) was developed in the 1980s as a rodenticide (Marshall 1984). In New Zealand it is registered as an alternative to 1080 for possum control because of the relative low risk of secondary poisoning of dogs (Eason 1991; Eason, Wickstrom et al. 2000). Inappropriate marketing of cholecalciferol-containing rodenticides in Australia in the late 1980s produced a spate of primary poisoning incidents of pets and a backlash against its use and it is no longer registered in Australia.

2.1.5.2 Mode of action

In order to gain biological and toxicological activity, cholecalciferol must undergo metabolic conversion to 25-hydroxycholecalciferol. It is metabolised to 25-hydroxycholecalciferol (25(OH)D). This metabolite is then transferred to the kidney and converted to 24, 25-, or 1,25-dihydroxycholecalciferol. The latter metabolite is the most biologically active form of the vitamin K (Keiver et al. 1988)

At toxic doses, this active metabolite mobilises calcium stores from bones into the bloodstream, and decreases calcium excretion by the kidneys. The net result is calcification in the cardiovascular system, kidneys, stomach, lungs, and muscles. Death from heart failure appears to be the mode of action of cholecalciferol in the possum, as in rodents, and takes 4–7 days. In other species, including cats and dogs, renal failure (caused by vessel blockage and nephrocalcinosis) and gastrointestinal haemorrhage appear more prominent (Dorman & Beasley 1989, Jolly et al. 1993).

Sub-lethal poisoning of target species can cause prolonged anorexia and wasting, which creates ethical and animal welfare concerns. Therefore, current baits are designed with the appropriate concentration of cholecalciferol to ensure maximum potency.

2.1.5.3 Target species appropriateness and key features

Species variation in response to cholecalciferol

The single-dose LD_{50} for cholecalciferol in Norway rats and house mice is very similar, but there is variation in susceptibility amongst other mammals and birds (Table 10). Possums and rabbits appear to be particularly sensitive to cholecalciferol (Jolly et al. 1995, Henderson & Eason 2000) and cholecalciferol has been explored for controlling rock squirrels, gophers, and ground squirrels (Beard et al. 1988, Tobin et al. 1993). Cats appear to be less susceptible than possums, but toxicity was less consistent with some cats surviving doses up to 200 mg/kg, while others died at 50 mg/kg (Eason 1991).

The relatively high LD_{50} in ducks suggests that cholecalciferol is less toxic to birds than the other toxins. When target species receive a lethal dose they lose their appetite. There are no LD_{50} data for cholecalciferol in camels. The minimum lethal dose might be anything in the range 10–100 mg/kg; hence between 5 and 50 gm would likely be needed to kill a camel.

Table 10: Acute oral toxicity (LD_{50} mg/kg) of cholecalciferol

Species	LD_{50} mg/kg
Rabbit	9.0
Possum	16.8 (reduced to 9.8 when administered with calcium)
Rat (Norway)	42.5
Mouse	43.6
Dog	80.0
Duck	2000.0

Source: Eason 1993, Eason et al. 1994, Jolly et al. 1995

2.1.5.4 Summary of key features

- Cholecalciferol was originally developed as a rodenticide.
- It is not currently registered in Australia.
- Rodents that receive a lethal dose of cholecalciferol usually die within 4–7 days.
- Possums, rats, and rabbits are particularly susceptible to cholecalciferol.
- It is converted to 25-hydroxycholecalciferol (25(OH)D).
- At high doses it causes tissue calcification.
- The risk of secondary poisoning is low (Eason, Murphy et al. 2000).

Table 11: Utility of cholecalciferol for camel management in Australia

Advantages of cholecalciferol	Disadvantages of cholecalciferol
Effective rodenticide	Expensive compared with 1080 and cyanide
Low risk of secondary poisoning	Not registered in Australia
Less toxic to birds than 1080	Treatment for accidental poisoning of pets is available, but is complex – use of secure bait stations is essential
A useful single-dose alternative to 1080	
No long-term residue risks in sub-lethally exposed animals	

2.1.5.5 Recommendation

Cholecalciferol is not recommended for poisoning camels under any circumstances as it would be most inhumane, and sub-lethal doses could cause prolonged sickness and anorexia.

2.2 Chemical control options from existing anticoagulant vertebrate pesticides

First-generation anticoagulant rodenticides (e.g., warfarin, pindone, diphacinone, and coumatetralyl), and second-generation anticoagulants (e.g., brodifacoum, flocoumafen, bromadiolone, and difethalione), all have the same mode of action, that is, interfering with the synthesis of blood clotting factors, which results in haemorrhaging and death. First-generation anticoagulant rodenticides were developed in the 1950s and '60s, and second-generation anticoagulants in the 1970s and '80s, partly to overcome resistance (Tasheva 1995). The second-generation anticoagulants such as brodifacoum are more toxic than first-generation anticoagulant rodenticides. The principal use of anticoagulants worldwide has been for control of commensal rodents, primarily Norway rats (*Rattus norvegicus*), ship rats (*Rattus rattus*), and house mice (*Mus musculus*).

The greater potency of second-generation anticoagulants, such as brodifacoum, and their greater potential to affect wildlife compared with first-generation anticoagulants, such as warfarin and pindone, is related to their greater affinity for vitamin K-epoxide reductase and subsequent accumulation and persistence in the liver and kidneys after absorption.

It is strongly recommended that none of the anticoagulant poisons are considered for camel control. Anticoagulants are extremely inhumane when used on species other than rodents (Littin et al. 2002), and should not be used on larger mammals. Nevertheless, for completeness key features of selected representative anticoagulants are briefly reviewed below.

2.2.1 First generation anticoagulants: pindone

2.2.1.1 General information and history of use

Pindone, like diphacinone, belongs to the indandione class of anticoagulants, which differ chemically from coumarin anticoagulants such as brodifacoum or warfarin. It was synthesised in 1937 (Beauregard et al. 1955) and developed as a pesticide in the early 1940s. Pindone has been used worldwide to control rodents, though its use for the control of rats and mice has decreased following the introduction of more potent anticoagulants such as brodifacoum. There are two other indandiones, diphacinone and chlorophacinone, which were synthesised in the 1950s and 1960s, and these two newer, more potent compounds have also contributed to a reduction in pindone use for rodent control. In Australia it has proved most effective for rabbit control (Eason & Jolly 1993).

2.2.1.2 Mode of action

Pindone acts like the other anticoagulant toxicants by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver. The weaker potency of first-generation anticoagulants such as pindone is related to a generally lower binding affinity when compared with second-generation compounds (Parmar et al. 1987, Huckel et al. 1988). As with all other anticoagulant compounds, clinical signs of toxicosis in animals will usually reflect some manifestation of haemorrhage (Osweiler 1996b).

2.2.1.3 Target species appropriateness and key features

There are limited acute toxicity data available on pindone, but even these data show marked species variation. For first-generation anticoagulants such as pindone, either very large single doses or repeated smaller doses are generally needed to induce death. A single dose of approximately 18 mg/kg is, however, sufficient to kill rabbits (Table 12). In rabbits the repeat dose (7 days) LD_{50} is 0.52 mg/kg/day.

By contrast, pindone doses of up to 12 mg/kg/day do not cause clinical or post-mortem haemorrhage in sheep. Possums appear to be even more resistant to pindone than sheep, with an LD_{50} of 51 mg/kg/day for 5 days calculated (Jolly et al. 1994).

Table 12: Acute oral toxicity (LD_{50}mg/kg) of pindone

Species	LD_{50} mg/kg
Rabbit	6–18
Dog	50
Norway rat	75–100
Sheep	approx. 100
Possum	>100

Source: Beauregard et al. 1955, Oliver & Wheeler 1978, Hone & Mulligan 1982, Eason & Jolly 1993

Non-target research conducted in Australia provides information on the susceptibility of horses, cattle, goats, chickens, dogs, and cats. All these species were less susceptible than rabbits. Daily doses of pindone, ranging from 0.3 to 2.5 mg/kg, were administered for 5 days. No mortalities occurred and susceptibility was assessed by using extension of prothrombin time as a biomarker of poisoning. Cattle and cats appeared most susceptible out of the six species tested, and horses least susceptible to pindone toxicity (Martin et al. 1991). No acute toxicity data exist for pindone in camels. It is probable that in excess of 1 gm of pindone would be required for several days.

2.2.1.4 Summary of key features

- Pindone rodenticidal properties were demonstrated in the 1940s.
- Pindone is a first-generation anticoagulant with relatively low potency.
- Pindone is moderately toxic to a range of species. Rabbits are most susceptible.
- It is effective for rabbit control.
- Pindone is less persistent than warfarin and considerably less persistent than brodifacoum.

Table 13: Utility of pindone for camel management in Australia

Advantages of pindone	Disadvantages of pindone
Effective for rodent control	Less potent than 2nd generation anticoagulants
Highly effective for rabbit control	Inhumane in larger animals
Antidote	
Less persistent than brodifacoum	

2.2.1.5 Recommendation

Pindone is not recommended for poisoning camels under any circumstances, as it would be most inhumane.

2.2.2 First generation anticoagulants: warfarin

2.2.2.1 General information and history of use

Warfarin, like pindone, is one of the earliest first-generation anticoagulant rodenticides. It has been used in a range of rodent baits since it was first introduced in 1947. In the ACT, baits containing warfarin are still used for control of feral pigs (O'Brien et al. 1987).

2.2.2.2 Mode of action

Warfarin, like the other anticoagulants, inhibits the synthesis of vitamin K-dependent clotting factors. In addition, warfarin is reported to induce capillary damage. Two different metabolites are thought to be responsible for these effects: 4-hydroxycoumarin inhibits the formulation of prothrombin and reduces the clotting power of the blood, and there is some evidence that, at sufficient dosage, benzalacetone produces capillary damage that exacerbates bleeding. In general the symptoms of poisoning do not appear suddenly, and will culminate in death in rats within 5–7 days of the initial ingestion of a lethal dose. There is a great deal of individual variation in the time it takes for pigs to die from warfarin poisoning, with some pigs dying before or soon after they have shown the initial symptoms of poisoning and others living up to 31 days, progressively weakening over time.

2.2.2.3 Target species appropriateness and key features

The toxicity of warfarin varies according to species and whether exposure was a single or multiple dose (Table 14). Rats can withstand single doses of 50 mg/kg, but are unable to survive doses of 1 mg/kg bodyweight when that dose is ingested for 5 successive days (Osweiler 1996b). No acute toxicity data exist for warfarin in camels. It is probable that in excess of 1 gm of warfarin would be required for several days.

Table 14: Acute oral toxicity (LD_{50}mg/kg) of warfarin

Species	Single dose (mg/kg)	Repeated dose (mg/kg)
Pig	3	0.5
Dog	50	5
Rat (unspecified)	50–100	1
Cat	50–100	1

Source: Osweiler 1996b

2.2.2.4 Summary

- Warfarin is a first-generation anticoagulant.
- For a lethal dose to be ingested, one large single dose or a small dose for several days in a row are needed.
- Because warfarin has a slow mode of action, bait shyness is not readily induced.
- It is not persistent when compared to brodifacoum.

Table 15: Utility of warfarin for camel management in Australia

Advantages of warfarin	Disadvantages of warfarin
Effective for rodent control	Less potent than 2nd generation anticoagulants
Antidote	Inhumane
Less persistent than brodifacoum	

2.2.2.5 Recommendation

Warfarin is not recommended for poisoning camels under any circumstances as it would be most inhumane.

2.2.3 Second generation anticoagulants: brodifacoum

2.2.3.1 General information and history of use

Brodifacoum is the most well-known and used rodenticide worldwide. Like the first generation anticoagulant warfarin it is structurally related to a naturally occurring coumarin that causes haemorrhagic syndrome in cattle eating improperly cured or mouldy sweet clover. The rodenticidal properties of brodifacoum were first described in the early 1970s (Hadler & Shadbolt 1975). It is a very potent anticoagulant active against rats and mice, including rodent strains resistant to warfarin and other anticoagulants (Rennison & Hadler 1975). A single ingestion of 1 mg/kg is usually sufficient to kill. Brodifacoum has been used successfully in recent rodent eradication programmes on offshore islands to protect populations of endangered indigenous birds. In addition to its use to control commensal rodents and eradicate rats from islands, it is used to control possums in New Zealand.

2.2.3.2 Mode of action

In rats the onset of symptoms and death usually occur within a week. Like other anticoagulant toxicants it acts by interfering with the normal synthesis of vitamin K-dependent clotting factors in the liver. In the liver cells the biologically inactive vitamin K1-2,3 epoxide is reduced by a microsomal enzyme into biologically active vitamin K, which is essential for the synthesis of prothrombin and other clotting factors (VII, IX, and X). Brodifacoum antagonism of the enzyme vitamin K1-epoxide reductase causes a gradual depletion of the active form of the vitamin, and consequently of vitamin K-dependent clotting factors, which results in an increase in blood-clotting time until the point where no clotting occurs.

The greater potency of second-generation anticoagulants such as brodifacoum compared with first-generation anticoagulants such as warfarin and pindone is related to their greater affinity for vitamin K-epoxide reductase and subsequent accumulation and persistence in the liver (Huckle et al. 1988, Parmar et al. 1987). Brodifacoum, like other second-generation anticoagulants, is not readily metabolised and the major route of excretion of unbound compound is through the faeces. The risk of secondary poisoning to non-target species is far greater from second-generation anticoagulants such as brodifacoum than from first-generation anticoagulants such as warfarin, because second-generation compounds are not substantially metabolised and excreted before death. Widespread wildlife contamination extends to native birds as well as to game species where there is field use of second-generation anticoagulants (Young & de Lai 1997; Eason, Wright & Batcheler 1996; Eason et al. 1999; Shore et al. 1999; Stone et al. 1999).

2.2.3.3 Target species appropriateness and key features

For second-generation anticoagulants like brodifacoum only a single dose is needed to induce death, if sufficient toxicant is ingested, and brodifacoum is extremely toxic in a number of animal species. The toxicity of brodifacoum varies between species (Table 16) but in most mammals LD_{50} values are 1 mg/kg or less. Some higher values are reported in sheep and dogs, but there is considerable variability in these reports (LD_{50} in sheep is 5–25 mg/kg, and in dogs is 0.25–3.56 mg/kg).

No acute toxicity data exist for brodifacoum in camels but it is likely to be <25 mg/kg and probably closer to 1 mg/kg.

Table 16: Acute oral toxicity (LD_{50}mg/kg) of brodifacoum for mammal species

Species	LD_{50} mg/kg
Pig	0.1
Possum	0.17
Rabbit	0.2
Cat	0.25–25
Dog	0.25–3.56
Rat	0.27
Mouse	0.4
Bennett's wallaby	1.3
Sheep	5–25

Source: Godfrey 1985, Eason and Spurr 1995

2.2.3.4 Summary

- Brodifacoum was developed approximately 30 years ago.
- It is a potent anticoagulant and toxic to mammals, birds, and reptiles.
- Brodifacoum is extremely persistent in the livers of lethally poisoned animals, and to a lesser extent in the meat of sub-lethally poisoned animals.
- Livestock must not be allowed access to brodifacoum baits as residues may persist in survivors of a sub-lethal dose for >9 months.
- Non-target effects on individual birds of a number of species have occurred after brodifacoum use for rodent control.

Table 17: Utility of brodifacoum for camel management in Australia

Advantages of brodifacoum	Disadvantages of brodifacoum
Generally available	High risk of secondary poisoning
Effective for rodent control	Persistent (>9 months) in liver
Antidote available	Expensive compared with 1080 or cyanide

2.2.3.5 Recommendation

Brodifacoum is not recommended for poisoning camels under any circumstances, as it would be extremely inhumane. Death would be likely to be prolonged with camels lame and unable to walk or support their weight.

2.3 Chemical control options from non-anticoagulant candidate compounds

In this section we examine the potential of two new candidate vertebrate pesticides, para-aminopropiophenone (PAPP) and sodium nitrite, which are being developed for the control of foxes and feral pigs respectively.

2.3.1 Para-aminopropiophenone (PAPP)

2.3.1.1 General information and history of use

Para-aminopropiophenone, or PAPP for short, was originally trialled in humans as a treatment for radiation poisoning in the 1970s in the UK. It is toxic to carnivores, with birds and humans being less sensitive (Fisher & O'Connor 2007, Murphy et al. 2007, Eason et al. 2008). The toxin is being developed as a humane, safer alternative to 1080 for the control of feral cats, foxes, and wild dogs in Australia (Fleming et al. 2006).

2.3.1.2 Mode of action

The toxic effects of PAPP are related to its ability to reduce the oxygen-carrying capacity of the red blood cell. The onset of symptoms is rapid and cats and foxes are usually unconscious within 30–45 minutes. The toxic effects of PAPP are related to the rapid formation of methaemoglobin in red blood cells. Once methaemoglobinemia has been induced the oxygen-carrying capacity of the blood is sharply reduced. This leads rapidly to unconsciousness and death due to respiratory failure. Animals initially become quiet and progress to being lethargic and slightly uncoordinated. An antidote, methylene blue, is available from veterinarians which will reverse the methaemoglobinaemia induced by PAPP (Eason et al. 2008).

2.3.1.3 Target species appropriateness and key features

Canids are more susceptible to PAPP than most other species (Table 18), with herbivores and omnivores being significantly less sensitive. There are no acute toxicity data for PAPP in camels or other large domestic stock. A lethal dose would be likely to exceed 200 mg/kg, in which case a dose of 100 gm or more might be needed to kill a camel.

Table 18: Acute oral toxicity (LD_{50}mg/kg) of PAPP for mammal species

Animal	LD_{50} (mg/kg)
Cat	5.6
Stoat	9.3
Fox	14.1
Ferret	29
Wallaby	89
Badger	100
Racoon	142
Mouse	223
Rat	221
Skunk	400
Possum	>500

Source: Savarie et al. 1983, O'Connor 2002

2.3.1.4 Summary of key features

- PAPP is being developed for fox, wild dog, and feral cat control in Australia.
- PAPP is a most humane poison.
- Large amounts would be needed to kill a camel unless camels showed some special sensitivity.

Table 19: Utility of PAPP for camel management in Australia

Advantages of PAPP	Disadvantages of PAPP
Simple antidote	Not yet registered in Australia
Humane (very rapid action and minimal distress)	Large amounts would be needed for camels
Low secondary poisoning risk	
Effective	

2.3.1.5 Recommendation

PAPP is not ideal for the poisoning of camels mainly because a large amount of poison would be likely needed. A target-specific delivery system and baiting technique would also need to be developed. An acute toxicity investigation could determine susceptibility. The possibility of using PAPP with another acute toxin, for example 1080, to make it more humane could be examined if poisoning is considered an option.

2.3.2 Sodium nitrite

2.3.2.1 General information and history of use

Sodium ($NaNO_2$; or potassium KNO_2) nitrite is a common salt that is variably toxic to most species. The chemical is currently under investigation at the Invasive Animals CRC (IA CRC) as an alternative feral pig toxicant, and a patent on bait-delivered nitrite for pest animal control has been secured (PCT/AU2008/000260). In feral pigs the chemical causes lethargy, dyspnoea, reduced consciousness and coordination, and death in approximately two hours depending on the delivery formulation (Cowled, Elsworth et al. 2008). The toxicology of sodium nitrite is well understood because of its past use as a preservative agent. The compound is already registered internationally as a human food product, as at low concentrations it is the most common meat preservative used worldwide. Information regarding the effect of nitrite on cattle and pigs is abundant and well understood due to naturally occurring nitrate/nitrite poisonings. Sodium nitrite is currently less expensive than other methaemoglobin-forming compounds such as PAPP. A further benefit of nitrite is that it is known to break down readily in the environment and has limited secondary poisoning risks.

2.3.2.2 Mode of action

The toxic effects of sodium nitrite, like PAPP, are related to its ability to reduce the oxygen-carrying capacity of the red blood cell. This leads to unconsciousness and death due to anoxia and heart failure. Animals initially become quiet and progress to being lethargic and slightly uncoordinated. As with PAPP, methylene blue is the recommended antidote.

2.3.2.3 Target species appropriateness and key features

Natural poisoning of cattle with nitrates, which are converted to nitrites in the body, is well understood. Nitrates may accumulate in bores, corn silage, sorghum, sudangrass, and sorghum-sudan crosses. Acute toxicity data are summarised in Table 20; however, no data exist for camels. The most relevant figures are likely to be those in pigs (same family) and cattle. A lethal dose would be likely to exceed 100 mg/kg, in which case a dose of 50 gms or more would be needed to kill a camel. Use of this poison is a distinct possibility as camels have a daily requirement for 55g salt/day (Farid 1989), will readily

consume over 250g NaCl/day in a 1% solution (hence potential for water delivery; Farid 1989), and are known to consume 100g of free salt/day in Australia given the opportunity (P. Gee 2008, Primary Industries and Resources, South Australia, pers. comm.).

Table 20: Acute oral toxicity (LD_{50}mg/kg) of sodium nitrite for mammal species

Animal	LD_{50} (mg/kg)
Pig	90-135
Rat	70-180
Mouse	215
Rabbit	87-124
Sheep	167 (10 gm/animal)
Cattle	67-110 (40-66 gm/animal)

Source: Cowled, Elsworth et al. 2008; Druckery et al. 1963; Riemann 1950; Smith & Layne 1969; Dollahite & Rowe 1974; Lewis 1950; Bartik & Piskac 1981

2.3.2.4 Summary of key features

- Sodium nitrite is being examined by the IA CRC as a quick-acting but reversible feral pig toxicant (Patent PCT/AU2008/000260).
- Sodium nitrite, like PAPP and cyanide, has the potential to be very humane.
- Large amounts would be needed to kill a camel unless camels showed some special sensitivity.

Table 21: Utility of sodium nitrite for camel management in Australia

Advantages of sodium nitrite	Disadvantages of sodium nitrite
Simple antidote	Not yet registered in Australia
Humane (very rapid action, with minimal distress)	Large amounts would be needed for camels
Low secondary-poisoning risk	
Effective	

2.3.2.5 Recommendation

Sodium or potassium nitrite has potential as a humane poison of camels due to their known daily requirement of large amounts of salt, and is therefore recommended for further investigation. Although currently undocumented, this may also mean that the species has biochemical safeguards against accidental nitrate/nitrite salt poisoning. Notwithstanding this, a target-specific delivery system and baiting technique would need to be developed (see section 5), which is certainly possible. An acute toxicity investigation should firstly determine the susceptibility of camels to nitrite (both sodium and potassium) via gavage in anesthetised animals to obtain proof-of-concept before the potential active is promoted.

2.4 Chemical control options from drugs and other toxins to which camel are known to be, or could be, particularly sensitive

In this section we examine the potential of drugs and toxins to which camels might be especially susceptible. The structure of the section is somewhat different to that of sections 2.1–2.3. In the earlier sections of our assessment of candidate poisons, we were reviewing well-established poisons which are supported by data on their acute toxicity and humaneness, or new candidate pesticides currently being researched by the IA CRC, among other organisations. In the following sections we consider the potential of xenobiotics or other compounds that have not previously been considered as vertebrate pesticides. Hence, much of the data required for a more comprehensive analysis are incomplete and our conclusions are more speculative. We have combined a physiological approach that might be exploited in a designer toxin, and we consider the comparative pharmacokinetics of drugs in the camel versus other species with links to poisoning incidents.

2.4.1 Unique dietary requirements, physiological characteristics, and species variation in pharmacokinetics that could be exploited by a designer drug

2.4.1.1 Dietary requirements and electrolyte imbalance

Camels will readily consume over 100 gm of salt (sodium chloride) per day and have unique physiological mechanisms for retaining Na/K electrolyte balance. Electrolyte imbalance can lead to heart failure. Substitution of salt with potassium chloride, coupled with a potent diuretic such as furosemide, may overcome the special ability of the camel to maintain electrolyte homeostasis, particularly if monensin were included. Accidental monensin toxicosis has been reported in sheep, and in a Bactrian camel. Animals died acutely although one was euthanased because of chronic hind limb paresis. Key observations of special interest were that severe, serum electrolyte disturbances, and haemoconcentration occurred with muscle damage (Miller et al. 1990).

Interference with camels' unique ability to conserve water and electrolytes is a potential target; however, this may be difficult. Unlike most species, furosemide-induced diuresis does not result in any significant changes in blood electrolyte balance of camels (Ali et al. 1997), probably because of the ability of these animals to preserve blood homeostasis despite severe loss of water or dehydration (Alquarawi & Ali 2000).

Camels are very prone to bloat, which is exacerbated by feeding alfalfa hay and over-feeding with grain. Deliberately feeding alfalfa hay might exacerbate electrolyte imbalance. Killing with bloat alone would, however, be painful (Wright 2002). Any attempt to overcome camels' ability to preserve electrolyte homeostasis would probably require more than one agent.

2.4.1.2. Kidney function

Drugs that are processed by the kidneys deserve special consideration. While the kidney of the camel is extremely efficient at conserving water, it is also very prone to damage by drugs that are potentially nephrotoxic such as banamine, phenylbutazone, some of the aminoglycoside antibiotics (Al-Dughaym et al. 1998), and, to a lesser extent, tetracyclines and sulfa drugs. This is principally due to the low glomerular filtration rate, long nephron, and low water turnover rate in the camel. There are reported cases of kidney failure in camels following a single dose of banamine. Finadyne™ is the trade name for flunixin meglumine. It comes in an injectable form for intravenous or intramuscular use. Of greater interest is that it can also be given orally in paste or granule forms. It is in the same category of drugs as aspirin and phenylbutazone (Burnett 2000). They are all nonsteroidal anti-inflammatory drugs with well-established nephrotoxicity and potential to cause lethal kidney failure in camels. Similarly, aminoglycosides can cause nephrotoxicity in doses as low as 1 mg/kg (Ali et al. 1996). Death by kidney failure through induced nephrotoxicity leading to electrolyte imbalance is predicted by the authors to be inhumane. Co-administration of furosemide and potassium chloride might be more effective and provide a more humane death.

2.4.1.3 Species variation in the pharmacokinetics of drugs

Dromedaries have lower hepatic mixed function oxidases and lower glomerular filtration rates than other mammals, all of which contribute to difference in the metabolism and excretion of drugs (Bahri et al. 1999). Pharmacokinetic data confirm that many drugs have longer absorption and elimination half-lifes and are poorly metabolised when compared with other animals (Ali et al. 1996, Alquarawi & Ali 2000). The anatomical, biochemical, and physiological peculiarities that differentiate the camel from other ruminants may influence the disposition of drugs and their pharmacodynamic activity (Kadire et al. 1997). Paracetamol metabolism has been compared in camels and goats, and large differences

were found. The clearance was two-fold slower in the camel, which may link to lower glutathione S-transferase activity and might increase their susceptibility to paracetamol overdosing (Alquarawi & Ali 2000). Unfortunately, we could find no further information on the toxicity of paracetamol to camels.

2.4.2 Other compounds shown to be toxic to camels

2.4.2.1 Copper

Camels have been indicated as being sensitive to copper poising (Manefield & Tinson 1997). The major uses of copper sulphate are in agriculture as a fungicide, a growth stimulant for fattening pigs and broiler chickens, and as a molluscicide for the destruction of slugs and snails, particularly the snail host of the liver fluke. We could not identify any publication where copper sulphate was used as a vertebrate pesticide.

After ingestion, more than 99% of copper is excreted in the faeces. However, it is also strongly bioaccumulated. Examinations of copper sulphate–poisoned animals showed signs of injury to the brain, liver, kidneys, and gastrointestinal tract. Some of the signs of poisoning are pain and intense nausea, repeated vomiting, diarrhoea, anorexia, headache, sweating, shock, and discontinued urination leading to yellowing of the skin. Injury to the brain, liver, kidneys, and stomach and intestinal linings may also occur in copper sulphate poisoning.

The oral LD_{50} is 472 mg/kg in rats. Two camels receiving 200 mg/kg/day orally died within 8 days, while three camels given 2 mg/kg intravenously died after 4, 95, and 138 (euthanased) days. Post-mortem histopathology revealed damage to the liver, kidneys, and the heart (Damir et al. 1993; Manefield & Tinson 1997). Camels, however, are not uniquely susceptible. We would therefore not recommend copper sulphate for camel control as it would be inhumane and non-specific.

2.4.2.2 Trypanocidal drugs

Trypanocidal drugs that are well tolerated by domesticated species can cause severe toxic reactions in camels (Ali 1988, Al-Dughaym et al. 1998). These drugs have been developed to treat parasitic infections and have a variety of modes of action. For example, a furazolidine nitrofuran derivative with antiprotozoal and antibacterial activity acts by gradual inhibition of monoamine oxidase. Furazolidine at high doses of 160 mg/kg and 320 mg/kg does not cause toxicity in mice (Zhang 1982) but causes overt toxicity in camels, including trembling and recumbency (Ali et al. 1996). Similarly, diaminazine aceturate (Berenil) at 10 or 20 mg/kg was toxic in camel (Leach 1961, Homeida et al. 1981) but not in mice (El Amin et al. 1984). Symptoms included salivation, frequent urination, defecation, sweating, recumbency, regurgitation, and convulsions. Histology revealed haemorrhages in the heart, liver, kidneys, urinary bladder, and brain (Homeidia et al. 1981; Al-Dughaym et al. 1998). Isometamidium chloride is another antitrypanocidal drug that has been reported to be ineffective but toxic to camels (Ali et al. 1984; Ali et al. 1996). The reason for the susceptibility is not readily apparent, although the transformation of the drugs into toxic metabolites in the camel is likely responsible. Research into the metabolites may provide a low-dose camel toxicant.

Although camels appear to be more susceptible to the toxic effects of some trypanocidal drugs than other species (Ali 1988), the clinical signs reported suggest that these drugs would not induce a particularly humane death. Exposure to 200 mg/kg has killed a camel, but they show no species susceptibility. We recommend that trypanocidal drugs themselves should not be considered as first choice poisons for camel despite camels being particularly susceptible to the side effects of these drugs. They would not induce a humane death.

2.4.2.3 Salinomycin

The ionophoric coccidiostat salinomycin is widely used in chicken feed and is closely related to monensin. In some countries, salinomycin is added to the feed given to ruminants to improve their

absorption of nutrients. For a mouse, an oral LD_{50} dose of 50 mg/kg, or an intraperitoneal dose of 7 mg/kg, the antibiotic is considered to be very toxic, and may be fatal if swallowed, inhaled, or absorbed through the skin. Recently Koenig (2007) reported on the death of at least 2000 camels where salinomycin in fodder was the cause. Unfortunately, Koenig (2007) did not report on the symptoms or time to death in camels. Plumlee et al. (1995) reported on acute salinomycin toxicosis in pigs, stating death occurred in 24 hours following severe skeletal muscle (more pronounced) and cardiac muscle myodegradation. Clinical signs included myoglobinuria, progressive weakness, and dyspnea. Concurrent administration of the antibiotic tiamulin was reported to increase toxicity by interfering with the metabolism and excretion of salinomycin. Manefield and Tinson (1997) also reported on the high toxicity of monensin to camels, with 80% of treated animals suffering severe muscular dystrophy and death. However, Cowled, Elsworth et al. (2008) recently tested the monensin-tiamulin antibiotic combination (20/40 mg/kg and 80/160 mg/kg respectively) on feral pigs as a potential new toxicant and found that although the high dose combination was lethal, it was a protracted (time to death 342 ± 96 min; S.D. n=3) and visually distressing death and the trial was terminated on humaneness grounds. Histopathology showed lesions primarily on the intestinal mucosa and skeletal muscles. As such, salinomycin or monensin are not recommended as a potential camel toxicants.

2.4.2.4 Ivermectin

Ivermectin is a broad-spectrum antiparasitic medication, traditionally used against worms (except tapeworms), but more recently found to be effective against most mites and some lice too. The main concern when using ivermectin as a treatment is neurotoxicity, which in most mammalian species may manifest as central nervous system depression and consequent ataxia (Hayes & Laws 1991).

Although highly poisonous to insects, mammals should not generally be adversely affected by normal use of ivermectin pesticide formulations. However, pure – as opposed to the diluted – formulations are both highly toxic to insects and mammals. The LD_{50} for rats is 10 mg/kg. The toxicity of ivermectin has been studied in camels, and while repeated monthly injections of ivermectin at 0.6 mg/kg had no adverse effects, and single doses of 5 mg/kg had no severe effects, doses of 10 mg/kg caused severe depression, ataxia, and death within 24 hours (Bahri et al. 1999). Bahri et al. (1999) implied that camels have been shown to be particularly susceptible to the acute toxic effects of ivermectin; however, the LD_{50} for rats is similar. Nevertheless, ivermectin could be considered further if poisoning is deemed an option. The extensive database and experience that exists with this compound in Australia and its availability and registration status are all advantages. However, as a large amount of poison (approx. 5g) would be needed a targeted specific-baiting technique is required. Oral toxicity and humaneness would also need to be established.

2.4.2.5 Diminazene

Diminazene aceturate is commonly used to treat trypanosomiasis. The recommended dose for cattle is 3.5 mg/kg injected subcutaneously or intramuscularly. Deaths have been reported in camels dosed at 3.5–7.5 mg/kg, whereas cattle will tolerate 21 mg/kg (Bahri et al. 1999). There are few acute toxicity data available with diminazene in the usual laboratory species and minimal data on oral toxicity. What little data exist indicate poor oral toxicity; for example, in a study in mice an oral dose of 1 500 mg/kg to 3 males and 3 females resulted in a single death (IPCS Inchem 2008). Lack of oral toxicity would prevent this compound being effective and useful.

2.4.2.6 Nitroxynil

Nitroxynil is an anithelmintic agent that is well tolerated in camels at doses of 40 mg/kg when given by sub-cutaneous injection. However, it has shown to be fatal at 50 mg/kg (Bahri et al. 1999). As with diminazene, lack of oral toxicity would prevent this compound being effective and useful.

3. Biological control

Biological control is classically defined as the reduction of a pest animal or plant population through the use of natural enemies. It generally involves either predation, parasitism, herbivory, or other natural mechanisms, and typically involves an active human role. Australia is well versed in the practice of biological control, with some notable successes being rabbit myxomatosis and haemorrhagic disease, but also some devastating failures, such as cane toads. Generally, biological control is of three basic types: conservation, classical biological control, and augmentation. Conservation biological control relates to conserving the natural enemy of the target organism where one occurs. Classical biological control, a practice more familiar in Australia, involves introducing the natural enemy of the target species, which is often an invasive species that has been introduced by humans without a pathogen or predator that keeps the species in check in its native range. Augmentation consists of the propagation and supplemental release of natural enemies, a practice most commonly used in agriculture. Brown (2004) recently reviewed the disease of camels in central Australia, and as no diseases were found to cause significant morbidity or mortality of camels within their Australian range, a suitable biological control agent would require introduction and would therefore fall under the classical banner.

This section takes a broad view of potential forms of biological control and includes poisonous plants, as they have caused the demise of camels in their natural range. Conversely, the review has not focussed on potential camel diseases or pathogens that have no species specificity and/or would cause serious economic consequences if they were introduced. Examples include camel trypanosomosis (*Surra*), anthrax, botulism, brucellosis, tuberculosis, tetanus, foot-and-mouth disease, rift valley fever, and rinderpest. Interestingly, McGrane and Higgins (1985), Wernery and Kaaden (2004), and Abbas and Omer (2005) report that while the latter three are a serious threat to cattle, they are of little consequence in camels. Camel trypanosomosis, or *Surra*, is a significant killer of camels throughout much of their range (30% morbidity and around 3% mortality; Enwezor & Sackey 2005). *Surra* is transmitted non-cyclically by haematophagus flies and is endemic in Africa, Asia, and South America. In addition to camels, other species of domesticated livestock are seriously affected, and as such it was not considered further in this review. Readers are referred to Losos (1980) or the recent review by Enwezor and Sackey (2005) for further information.

3.1 Plants poisonings

Camels have a reputed ability to avoid or digest (due to the thorough mixing of forestomach digesta) poisonous plants within their range, and are generally only poisoned when moved to unfamiliar areas (Manefield & Tinson 1997, Coventry et al. in press). Australian plant species that have been reported to cause camel deaths include ironwood (*Erythrophloeum chlorostachys*, alkaloid esters of diterpenoid acid active that killed 5 out of 50 camels near Cairns), desert poison bush (*Gastrolobium grandiflorum*, fluroacetate active, see 1080), camel poison/sandhill corkbark (*Gyrostemon ramulosus*, no active identified), emu poison bush (*Duboisia hopwoodii*, pyridine alkaloid active), and poison peach (*Trema tormentosa*, uncharacterised glycoside active) (Trueman & Powell 1991; Manefield & Tinson 1997). Unfortunately, reports of plant poisonings are often not supported with pathology results, so potential doses, symptoms, and times to death are unreported. Because of this it is difficult to assess the appropriateness of any plant-based chemicals (besides those discussed previously) for development as a camel toxicant.


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Within the camel's native range in Africa the most significant poison plant is *Capparis tomentosa*, the magico medicinal plant (also known as woolly caper-bush, see inset). This spiny scrambler or small tree grows up to 10

m tall and when consumed by camels causes neck distortion, muscular tremors, limb weakness, then stiffening, incoordination, dyspnoea, and convulsions. Death results with 24 hours, and post-mortem findings include various oedemas (Manefield & Tinson 1997). As such, it is unlikely to be a humane camel toxicant.

3.2 Fungal mycotoxins

Aspergillus fumigatus, a common feed contaminant particularly ubiquitous in conserved forages, produces several mycotoxins that can affect the health of animals and is the only fungal agent thus far associated with systemic disease in camels (Abbas & Omer 2005; Boudra & Morgavi 2005). *A. fumigatus* was the cause of an outbreak of bronchopneumonia and gastroenteritis that killed 40 of 70 racing camels (57%) in the Emirates. The brief illness was characterised by pyrexia, lachrymation, oedema of throat, and diarrhoea. Nervous signs and vomiting preceded death. Pneumonia and haemorrhages in the heart, pleura, mediastenal lymph nodes, and omasal and abomasal mucosa were reported post mortem (El-Khouly et al. 1992, Abbas & Omer 2005). Further information on *A. fumigatus* in the camel, such as species specificity, lethal dose units, and time to death could not be found, but may be worthy of further investigation.

3.3 Camelpox

Camelpox (*Orthopoxvirus cameli*) is the most common viral disease of camels and the most devastating. It occurs throughout the range of camels with the notable exception of Australia (Manefield & Tinson 1997). Camelpox virus, a true pox virus, has been shown to be strongly related to the human *O. variola* smallpox virus. This has led to numerous authors to question whether the disease could be zoonotic (Kriz 1982, Jezek et al. 1983, Abbas & Omer 2005); however, current findings indicate that it is clearly not.

Camelpox is an acute dermatitis that starts as a mild fever and develops into papules then pustules and scabs around the eyes, lips, neck, and thighs (Figure 2), although scabs can occur anywhere on the body. The disease occurs in epizootics that last 2–5 months, with higher prevalence in the winter, and is spread mainly by direct contact between sick and susceptible animals, particularly at waterholes or feeding sites. The average duration of illness is 16 days (range 10–30 days) (Kriz 1982). Most camels will recover from the disease over two to four weeks. Jezek et al. (1983) describe two distinctive types of the disease: the severe, generalised form normally occurring in younger animals, and the milder, localised form occurring in older camels. While morbidity rates can reach 100% in some camel herds, mortality rates range between 0% and 2% in the mild form and 28% to 40% during severe outbreaks (Abbas & Omer 2005). Mortality is generally the result of severe and mutilating labial lesions, pneumonia, haemorrhagic gastroenteritis, and generalised adenopathy (swollen lymph nodes).

Figure 2: Camelpox virus is one of the most devastating diseases of the camel
Source: McFadden 2005

In Somalia camelpox most commonly occurs in younger camels aged up to three years, with 18% of cases in camels aged up to one year, 30%

in 1–2 year olds, and 16% in 2–3 year olds (mean case age 2.7 years, Kriz 1982). Kriz (1982) further reported the respective mortality rates of 44%, 31%, and 13%, indicating that older camels are more likely to recover from the disease, likely a result of earlier challenges and subsequent seroconversion. Khalafalla (1998) reported slightly different findings in Sudan, with 31% of mortalities occurring 0–1 year olds and 63% 1–2 year olds. Kriz (1982) and Jezek et al. (1983) also described a high incidence of illness and a twice higher case fatality rate in male camels. This finding detracts from the potential use of camelpox as a biological control agent, as the male-biased population reduction will not slow the current population growth to the same effect as an unbiased or female-biased form of control.

A prophylactic vaccine for camelpox already exists to protect domestic livestock and pets, which increases the possibility of introducing a biological control to manage feral camels. As camels are used throughout Australia in the tourism industry, and have become somewhat of an icon of the Australian outback, this will likely be essential. Wernery and Zachariah (1999) report that a single dose of Durapox™ at age 1 can protect camels from camelpox for at least five years.

Although rates of mortality from camelpox are generally low throughout much of the species range, they are still significant. Furthermore, Manefield and Tinson (1997) suggest that adult camels that naïve to camelpox are equally as susceptible to the disease as the young, and as such mortality rates of 50% in all age groups could occur within Australia. However, it must be noted that the above reports are based on pastoral camels only (wild herds do not exist), and it is unknown to what extend the husbandry techniques of camel herders contribute to the prevalence of disease. Moreover, it is highly likely that the natural movements of free-living camels may limit the effectiveness of the technique.

Due to its species specificity and potential effectiveness the use of camelpox as a biological control agent in Australia should be investigated further. However, the humaneness of the disease is questionable, and, before proceeding to such an investigation, public, animal welfare groups, and Australian Pesticide and Veterinary Medicine Authority engagement should occur to ensure that the agent would be publicly and regulatory acceptable. If this step is foregone a great deal of time and money could be spent on unnecessary and expensive contained clinical trials without any hope of the virus being released.

3.4 Camel contagious ecthyma

Camel contagious ecthyma (CCE) is caused by a *Parapox* genus virus with the disease predominantly affecting calves less than one year of age (Abbas & Omer 2005). The disease has been reported to occur in Mongolia, Kazakhstan, Kenya, Somalia, and Sudan (Abbas & Omer 2005). CCE is clinically characterised by nodules appearing on the lips followed in most cases with swelling of the face and sometimes the neck (Figure 3). Transmissions occur through direct and indirect contacts, often at waterholes, and can be exacerbated through lip abrasions caused by browsing prickle plants (Khalafalla 2000). Papules and vesicles appear later and develop into thick scabs and fissured crusts within a few days (Figure 4). CCE legions are confined to the head, in particular the lips, nostrils, and eyes, with the fissured crusts differentiating the disease from camelpox or papillomatosis. Healing generally occurs within 20–30 days, although can take up to 3 months (Khalafalla 1998). In Sudan the disease re-appears every year in the early rainy season (July–August) affecting camel calves in their first autumn of grazing.

Figure 3: Camel contagious ecthyma: Acutely affected young camel showing swelling of the head and upper part of the neck

Source: Khalafalla 1998

Figure 4: Camel contagious ecthyma: A close-up view of face affected camel showing scabby lesions around the lips, nostrils and eyes

Note: The lower lip is pendulous Source: Khalafalla 1998

Morbidity and mortality associated with CCE can be highly variable, with contract rates of 60–100% and mortality rates from 0% to 75% (Figure 5; Khalafalla 2000). More commonly an outbreak will cause morbidity rates of 18% and mortality rates of 7% (38% case mortality rate, Khalafalla et al. 1994). Khalafalla (2000) reported that 27% of CCE cases in eastern Sudan occurred in animals 0–6 months, and 71% in animals 7–12 months of age. The remaining 2% of cases occurred in camels up to three years of age. Case fatality rates of 24% in 0–6-month-old calves and 11% of 7–12-month-old animals have also been reported (Khalafalla 1998). CCE mortality is caused due to starvation resulting from the inability of affected animals to graze or suckle. As such, the disease must be considered inhumane and should not be considered as a potential form of biological control.

Table I

Cases of camel contagious ecthyma recorded in Herd 1, Kassalla area (1987-1996)

Year	Total num. of calves*	Num. of calves affected with CCE	Num. of calves dead	Mortality rate %
1987	6	6	0	0
1988	7	5	0	0
1989	10	7	0	0
1990	12	10	1	8
1991	10	7	2	20
1992	4	4	0	0
1993	6	6	0	0
1994	9	7	0	0
1995	12	10	0	0
1996	14	12	0	0
Total	90	74	3	3.3

* Camel calves less than one year old

Table II

Cases of camel contagious ecthyma recorded in Herd 2, Southern Butana area (1987-1996)

Year	Total num. of calves*	Num. of calves affected with CCE	Num. of calves dead	Mortality rate %
1987	4	4	1	25
1988	9	9	0	0
1989	8	7	0	0
1990	10	10	5	50
1991	3	3	2	67
1992	3	3	1	33
1993	7	6	2	29
1994	8	8	1	13
1995	6	6	1	17
1996	8	8	0	0
Total	66	64	13	20

* Camel calves less than one year old

Table III

Cases of camel contagious ecthyma recorded in Herd 3, Blue Nile area (1987-1996)

Year	Total num. of calves*	Num. of calves affected with CCE	Num. of calves dead	Mortality rate %
1987	12	12	4	33
1988	14	14	6	43
1989	14	14	2	14
1990	15	14	9	60
1991	8	8	6	75
1992	9	9	3	33
1993	11	11	4	36
1994	13	11	5	38
1995	11	10	3	27
1996	13	13	3	23
Total	120	116	45	38

* Camel calves less than one year old

Figure 5: Sudan morbidity and mortality rates of camel contagious ecthyma indicate that the disease can be highly variable between years and locations

Source: Khalafalla 2000

3.5 Camel papillomatosis

Camel papillomatosis is the fourth most widespread viral disease of camels, along with camel pox, echthyma, and rabies. Papillomas, or warts, are most commonly seen on younger animals 3–14 months old (Figure 6; Khalafalla 1998). The disease appears as round cauliflower-like horny masses mainly on the skin on the lips and submandibular area. The warts are generally self-limiting and disappear between 8–12 weeks

Figure 6: Camel papillomatosis: Advanced stage of the wart growth on the upper and lower lips and the submandibular area

Source: Khalafalla 1998

(Manefield & Tinson 1997). Khalafalla (1998) reported morbidity rates of 3.3% in Sudan, but no mortality. The disease is spread through direct contact between affected and susceptible animals. The major concern with camel papillomatosis is that the clinical signs are often indistinguishable from camel pox, and that the disease can often occur with or follow CCE. As camel papillomatosis does not result in mortality it is of little interest as a potential form of biological control.

3.6 Helminths

Within their natural range, as well as within their range in Australia, camels are unlikely to suffer from helminth infestations as they are somewhat protected by the dry conditions they inhabit. Manefield and Tinson (1997) do, however, report that camels kept on the east coast of Australia can suffer heavy infestations leading to parasitic gastroenteritis, diarrhoea, and anaemia. Similarly Agab and Abbas (1998) reported that helminth infection was the leading cause of death for pastoral camels in Sudan, accounting for 36% of deaths (71/199 deaths), particularly in autumn. Unfortunately, Agab and Abbas (1998) did not report the helminths involved in these high mortality rates.

Brown (2004) reported that the whipworm *Trichuris* spp is common in Australian rangeland camels, and may lead to some diarrhoea and weight loss. Another helminth that is common in camels overseas, but has not been detected in 4915 inspected camels in Australia, is the hydatid tapeworm *Echinococcus granulosis* (Brown 2004). It is unknown whether this is because a hydatid cycle is absent from the Australian range of camels (as reported for the Northern Territory, Brown 2004), or whether the browsing feeding habit of camels means they are unlikely to encounter eggs (Manefield & Tinson 1997). Regardless, the seeding of hydatids would be an unacceptable and inefficient form of camel population reduction.

El Bihari (1985), in a review of camel helminths, reported that systematic studies of the disease conditions caused by helminths in the camel are few, and that most infections did not precipitate frank clinical disease. The exception to this is *Haemonchus longistipes*, a camel stomach nematode that can be highly prevalent (up to 89% herd infection rate) and individually debilitating (500 worms per animal reported), and has lead to death. *Haemonchus contortus* has been found in Australian camels occupying desert fringes. Regardless, mortality rates are low and biological control using helminths is unlikely to be successful.

3.7 Digestive system diseases

Mehta et al. (2003) reported that digestive system diseases were the major cause of death in farmed camels in India. Unspecified digestive system diseases accounted for 49% of all deaths, or 5% of a herd of 1824 camels over a five-year period. Agab and Abbas (1998) reported a similar finding for pastoral camels in eastern Sudan, with calf diarrhoea accounting for 39% of deaths in summer, although this figure declined in autumn when helminth infections were the main killing disease. Kaufmann (2003) also reported that diarrhoea was the most common cause of calf loss in eastern Africa, but goes on to suggest that it is likely related to calf husbandry, in particular the practice of withholding colostrum. As such, the high incidence of digestive system diseases in farmed camels is likely an artefact of the circumstance and of little relevance to controlling wild camel populations.

4. Fertility control

4.1 Principles and feasibility of fertility control to manage camel populations

The feasibility of successfully managing wildlife populations using fertility is only now coming into focus as our awareness of the extent to which manipulating fertility can affect population dynamics (Bomford 1990, Hone 1992, Barlow et al. 1997, Davis & Pech 2002, Sibley & Hone 2002) coincides with the development of appropriate biotechnologies. This, along with the perceived humaneness of fertility control (Oogjies 1997) compared to lethal controls, has reinforced its application in future integrated management of wildlife.

Manipulating camel fertility can be achieved immunologically, chemically, or through novel technologies; however, whether fertility control is biologically feasible for this particular species in Australia will depend on whether populations are open or closed, population sizes, sex ratios, age structure, their estimated rate of increase and mortality (Curtis et al. 1998, Nielsen et al. 1997, Fagerstone et al. 2006), an estimate of the proportion of the population that will require treatment and for how long (Dolbeer 1998), and the relative efficiencies of the fertility control approach.

Overlay these with the unique biology of an animal that has enormous home range size, and a relatively low requirement for water, and achieving wild camel population management using fertility control is a huge challenge. Notwithstanding this challenge, this section presents a review of the current suite of fertility control options that are (1) currently the focus of research, (2) in development, or (3) are commercially available, and examines their suitability for camel population management on a landscape scale.

4.2 Fertility control management options

4.2.1 Immunological fertility control

Fertility control via immunological means works on the premise that immune tolerance to 'self-antigens' can be overridden or broken so that the immune system recognises 'self proteins/peptides' as foreign once immunised. In this context immunological fertility control can take many forms depending on the approach taken to control fertility (immunocastration, immunocontraception, or immune interference with the maintenance of pregnancy), the reproductive target (steroid hormone, reproductively critical proteins, or gamete), and the administration (injection, oral, self disseminating routes) of the vaccine.

4.2.1.1 Immunocastration vaccines

This class of vaccines targets the hypothalmic/pituitary axis and in so doing inhibits the reproductive physiology of both sexes through generating antibodies that bind and sequester gonadotrophin-releasing hormone, or GnRH, hampering its bioavailability to the pituitary. Gonadotropin-releasing hormone is an endogenous decapeptide neurohormone with an obligatory role in reproduction. This down regulates the subsequent release of gonadotropic hormones, leading to atrophy of the gonads and concomitant infertility akin to the effects of castration. GnRH vaccines have been evaluated as immunocastration agents in pets (Ladd et al. 1994), cattle (Robertson 1982, Adams & Adams 1990), horses (Rabb et al. 1990), sheep (Schanbacher 1982), and swine (Meloen et al. 1994; Miller, Talwar et al. 2006). The utility of GnRH vaccines has also been investigated in wildlife, with 100% of immunised male and female Norway rats infertile (Miller et al. 1997), and an 86% reduction in white-tailed deer fawning during active immunisation and a 74% reduction over five years (Miller et al. 2000). GnRH vaccines are not species specific and appear effective in reducing fertility in most mammals for at least 1–2 years

without boosting. Eventually titre concentrations fall and animals return to pre-treatment reproductive status. GnRH vaccines also affect reproductive/social behaviours by reducing the sexual activity of both sexes. Because of this GnRH vaccine treatment may be a useful technique where sexual activity contributes to human–camel conflicts.

4.2.1.2 Commercially available GnRH/LHRH vaccines

Vaccines against GnRH (Vaxstrate™ and Improvac™) and LHRH (Equity™) have been registered for control of libido, sex steroid production, and increased growth of livestock such as pigs, cattle, and sheep (Ferro & Mordini 2004; Delves & Roit 2005), and behavioural modification in mares (Pfizer Animal Health Australia 2008) in Australia. These vaccines tend to be relatively expensive (Equity™ retails >AUD $300) and at least Vaxstrate™ is no longer registered in Australia due to insufficient efficacy. GnRH vaccines are presently available only in injectable form and generally require an initial injection and booster injections for a prolonged effect exceeding one year. Annual boosters to maintain antibody titres and their contraceptive effect are required.

GonaCon™, although not yet commercially available, is a GnRH vaccine that has been developed by the National Wildlife Research Centre, United States Department of Agriculture and is currently undergoing its final pivotal trials before a registration application is filed with the United States Environmental Protection Agency. Trials using this vaccine have proven it effective for the 100% depression of reproductive capacity in Australian wildlife (male and female Tammar Wallaby) over the past 18 months and the vaccine would be available for additional studies in Australian landscapes. Critically, this vaccine carries the promise of single shot effectiveness for periods of greater than 2–3 years for a majority of the species tested to date (Fagerstone et.al. 2006). This characteristic is particularly valuable when considering its application for the control of free-ranging camels.

Table 22: Utility of GnRH/LHRH vaccines for camel management in Australia

Advantages of GnRH/LHRH vaccines	Disadvantages of GnRH/LHRH vaccines
Registered in Australia	Injectable administration
Single shot	Not yet tested in Camelids
Non-target risk and environmental risks negligible	Expensive
Low risk of trade implications	Undesirable adjuvant characteristics
	No reduction in environmental impact

Recommendation

Commercially available GnRH/LHRH vaccines are a viable technology and product for the control of camel fertility at small scales or for localised management of discrete populations (if any occur in Australia). The technology also has further developmental potential. However, its application even if a single shot generates long-term (>5 years) infertility, is impractical at the scale required to effect widespread camel population control across the Australian landscape.

4.2.1.3 Immunocontraception vaccines

Immunocontraceptive vaccines (Talwar & Gaur 1987, Turner & Kirkpatrick 1991, Miller et al. 2001, Bradley et al. 1999, Kirkpatrick & Frank 2005) target other proteins essential for reproduction that do not depress the reproductive axis at the level of gonadotrophin release as do immunocastration vaccines. As a result they do not affect reproductive behaviour to the same degree. The reproductive targets are highly varied and range from sperm antigens that bar penetration of the egg zona pellucida, to zona pellucida proteins that affect oocyte viability, fertilisation, or implantation, to tropic hormones/proteins important for implantation and development of the fertilised egg, embryo, or reproductive tissue development.

To date, the greatest demonstration of immunocontraceptive vaccine utility has been the porcine zona pellucida–based technologies. Zona pellucida is an acellular glycoprotein layer located between the oocyte and the granulosa cells on the outer surface of the egg. Antibodies to this glycoprotein layer result in infertility either by blocking the sperm from binding to and penetrating the zona pellucida layer or by interference with oocyte maturation, leading to the death of the developing oocyte (Dunbar & Schwoebel 1988). The zona pellucida vaccine in use today comes from the pig ovary: Porcine Zona Pellucida (PZP). As an injected protein broken down in the body, PZP does not enter the food chain and its effects are reversible after short-term use. PZP vaccine has been used to produce immunocontraception in numerous species, including dogs (Mahi-Brown et al. 1985), baboons (Dunbar 1989), coyotes (Deliberto et al. 1998; Miller, Bynum et al. 2006), and burros (*Equus asinus*) (Turner et al. 1996), but the focus of much of this research has been on wild horses (Kirkpatrick et al. 1995, Garrott et al. 1992) and white-tailed deer (Turner et al. 1992, 1996; Miller et al. 1999). Results in receptive species are very positive, with Miller et al. (1999) achieving an 89% reduction in fawning during two years of active immunisation and 76% reduction in fawning over a seven-year study in white-tailed deer. However, the longevity of the contraceptive effect is highly species specific and titre dependent (Miller et al. 1999), as is the potential complication of injection site reactions due to the choice of adjuvant, which may affect the perceived humaneness of the technology. The PZP vaccine also induces multi-oestrus in female deer and feral horses, which is an effect that could carry over into Camelids. This result may have unexpected behavioural consequences and also late season births if antibody titers drop below a critical threshold. The currently available zona pellucida contraceptive vaccines are relatively expensive (approx USD$50 per dose), which is exacerbated by a requirement of an initial dose, a subsequent booster dose to achieve adequate initial contraceptive effect, and annual booster inoculations to maintain this effect. To put the total cost into perspective, a New York control program for 300 white-tailed deer cost approximately $80 000 per year to undertake (Nielsen et al. 1997).

Currently these vaccines must be injected by hand or using a biobullet/dart gun, and because of US Food and Drug Administrators concerns about the safety of the adjuvant, huntable animals must be ear-tagged with a ‘Do Not Consume’ notice. This has particular implications for the management of camels in Australia, which are also harvested as a commercial resource.

In addition to GonaCon™, the National Wildlife Research Center and Pennsylvania State University has demonstrated that a single-shot PZP vaccine incorporating a newly developed adjuvant (SpayVac™) delivered to deer by dart or biobullet can effectively cause infertility in deer for multiple years. The new adjuvant also may eliminate the requirement that vaccinated animals be ear-tagged, making immunocontraception using PZP a more feasible approach depending on the aim of the management regime. Although SpayVac™ represents a step in the right direction for immunocontraceptive products, a field study conducted to determine the feasibility of using contraceptive vaccines to regulate numbers of free-ranging deer in Irondequoit (Nielsen et al. 1997, Rudolph et al. 2000) indicated that, at least for deer, it will be extremely expensive to treat enough individuals to regulate population growth as long as fertility control agents need to be delivered by dart-gun to individual animals.

Table 23: Utility of immunocontraception vaccines for camel management in Australia

Advantages of immunocontraception vaccines	Disadvantages of immunocontraception vaccines
Non-target risk and environmental risks negligible	Injectable administration
Reversible	Not yet extensively tested in Camelids
Low risk of trade implications	Expensive
	Not registered in Australia or overseas
	Multiple shots required

Recommendation

PZP technology requires a minimum of two administrations and additional multiple administrations to effect reproductive suppression approaching or equivalent to GnRH vaccines and confers no advantages over the GnRH vaccine technologies. As such it is not recommended for camel fertility control at landscape scales.

4.2.1.4 Species-specific immunocontraception

While immunisation can be an effective means of reproduction control, its major obstacle is the possibility of affecting other species, particularly when the antigen is deployed remotely and designed to be orally active. The two principal antigenic epitopes previously described (three proteins comprising the mammalian zona pellucida and the LHRH molecule) are highly conserved in mammals (Delves & Roitt 2005, Litscher & Wassarman 2007) and even with sophisticated delivery to target camels, non-target risks will remain. Clearly the prospect of an oral immunocontraceptive using an immunogen that generates a species-specific immune response is very attractive. One research group is conducting research that holds this promise for the camel. This research is very new and confidential. Accordingly, the principal of the concept is described, but additional detail will only be available under the terms of a confidential disclosure agreement.

The research has uncovered reproductively critical proteins in a limited number of mammals (in the superorder Laurasiatheria, including ruminants, horses, pigs, carnivores, and, most probably, camels. To date, these proteins have been identified as products of the endometrium in sheep, goats, cattle, pigs, and water buffalo, but genes for homologous proteins are) that are not present in a majority of Australian non-targets. Furthermore, there is considerable species diversity between the amino acid sequence of the proteins that provides an opportunity to generate immunogens that will be species specific. Should camels also express these similar reproductively critical proteins then these may prove effective targets for manipulating their fertility immunologically. Crucially, evidence of significant heterology between species opens the door to the prospect of an immunocontraceptive vaccine for camels being highly species specific or a vaccine that can be used to control other feral animals in concert.

Table 24: Utility of species-specific immunocontraception for camel management in Australia

Advantages of species-specific immunocontraception	Disadvantages of species-specific immunocontraception
Non-target risk and environmental risks potentially negligible	Very new technology
Reversible	Not yet researched in Camelids
Oral administration	
Low risk of trade implications	
Small amounts of active required	

Recommendation

This is a potentially powerful and uniquely targeted technology and approach to inducing immunological fertility control. The approach will require additional research to develop the technology for Camelids; however, the proposed research timeframes may be considerably shorter than for the development of other fertility control options. As a consequence this research warrants particular consideration for funding in the short-term and is highly recommended as a camel fertility control.

4.2.1.5 Virally Vectored ImmunoContraception (VVIC)

The utility of biotechnology to rapidly advance the progression of technologies within this research field is demonstrated in the use of genetically modified viral vectors to produce anti-fertility biological control agents. This technology makes it possible to insert a reproductively attractive target gene into a replication competent virus host that can be selected based on the susceptibility of the target species. The transformed viral host effectively acts as a sophisticated adjuvant that expresses the reproductive

immunogen on its coat along with other antigenic viral coat proteins. The combination of a live attenuated virus expressing reproductively important self-antigens is designed to induce an autoimmune response which breaks self-tolerance and induces infertility. This approach can be used to generate a non-disseminating virus that can be directly administered to the target species, or the more powerful tool, which is a self-disseminating virus that can potentially contracept/sterilise multiple animals as it cycles through populations (Williams 1997).

To date VVIC has only been tested as a concept in the laboratory and although it could be used to sterilise mice that were directly inoculated (Jackson et al. 1998, Redwood et al. 2005), antibody titres and reproductive efficiency of mice co-housed with the inoculated mouse were unaffected, indicating that the genetic manipulation of the virus may be adversely affecting its pathogenicity (Redwood et al. 2007). The success of this technique is highly dependent on the choice of vector and the reproductive epitope in order for the host virus to retain its infectivity and transmissibility, while also eliciting an immune response sufficiently robust to impair reproduction. To date the technology has proven effective when mice were directly inoculated (injection/oral administration) in laboratory tests (Lloyd et al. 2003, Redwood et al. 2005). Application of this technology to induce infertility in laboratory-housed rabbits showed a transient depression in fecundity (MacKenzie et al. 2006) but the transmissibility of the virus construct used was not tested. Although VVIC was also considered for fox fertility control the lack of a suitably species-specific vector resulted in the move towards a bait-delivered species-specific immunogen (Hardy & Braid 2007, McLeod et al. 2007). Thus a platform of research exists from which we are now able to make better-informed decisions that balance the potential benefits, risks, and resources required to achieve an outcome using this approach to immunological manipulation of fertility as a means of population control.

Table 25: Utility of VVIC for camel management in Australia

Advantages of VVIC	Disadvantages of VVIC
Low non-target and environmental risks	Cost of development
Rapid population effects – disseminating host	Release of a GMO
	May not be species specific
	Risk to domestic Camelids
	Not yet extensively tested in Camelids
	Not registered in Australia or overseas
	Zero control over treated animals (GMOs) once released
	High probability of trade implications

Recommendation

VVIC is a powerful technology and approach to inducing immunological fertility control. It will require considerably more resources to develop this technology for Camelids, and the timeframes involved warrant serious consideration before committing to this technology in favour of options that require less research, development, public consultation, and government regulation to deliver.

This approach is currently contraindicated for camel fertility control given the level of knowledge regarding camel physiology/immunology, the existence of suitable species-specific vectors, and the appropriate species-specific target epitopes. Getting to this point will require significant resources, let alone the resources required to prove the effectiveness of any given approach, however promising. Taking this approach to control camel populations in Australia also carries a high probability that there will be trade implications in its implementation because of the higher value placed on camels in other areas of the world, including key trading partners.

4.2.2 Chemical fertility control

4.2.2.1 Synthetic steroids

Chemical contraception through the use of synthetic steroids, oestrogens, and progestins was investigated widely during the 1960s and 1970s in many species, such as coyotes (Balser 1964, Brusman et al. 1968), pigeons (*Columba livia*, Woulfe 1970), red-winged blackbirds (*Agelaius phoeniceus*, Guarino & Schafer 1973), rats (Gartison & Johns 1975), coturnix quail (*Coturnix coturnir*, Schafer et al. 1977) and deer (Matschke 1977a, 1977b, 1980; Roughton 1979). More recently, androgens have also been tested for use in male rodents and wolves (Asa 1997) and the cholesterol competitive mimic (DiazaCon) has been used in prairie dogs (Nash et al. 2007). These steroid hormones act by interfering with sex steroid production, ovulation, or implantation of the egg in females and by impairing spermatogenesis in males.

Specific examples of more commonly used steroids are discussed below:

- Mestranol is an orally active oestrogen tested for rodent, rabbit, and bird control. The half-life of mestranol is less than 6 hours, so accumulation in food chains is not a problem (Sturtevant 1970, 1971), but it has caused bait aversion.
- Norgestomet (FDA approved for use in cattle oestrus synchronisation, Darling 1993): Black-tailed deer (*Odocoileus hemionus*) administered with Norgestomet using a biobullet (n=10, Jacobsen et al. 1995) failed to exhibit oestrous behaviour, and two treated bucks exhibited no sexual behaviour for one year. Additional studies with white-tailed deer (DeNicola et al. 1997) confirmed the contraceptive effect of the implant.
- Progesterone is the main hormone involved in maintaining pregnancy, and progesterone antagonists – which can be given orally – competitively inhibit progesterone binding to its cellular receptors. Progesterone antagonists (which are metabolised less readily than progesterone) can be administered as infrequently as monthly as contraceptives, or once in early pregnancy to interrupt pregnancy for seasonal breeders. Their mechanism of action disrupts the preparation of the uterine lining, which prevents implantation (Gao & Short 1994). Lutalyse™, produced by Upjohn (prostaglandin PGF2), is routinely used in feedlot cattle during the first 100 days of gestation and will cause abortion within 35 days of injection. DeNicola et al. (1996) and Waddell et al. (2001) reduced fertility in white-tailed deer by injecting Lutalyse™. Depending on the gestational time of administration, the technology could be considered either contragestive or abortifacient. Lutalyse™ is, however, only available in an injectable form. Several other synthetic progestins (which prevent ovulation in female mammals and inhibit testicular activity in males) have been identified as potential wildlife infertility agents. Levonorgestrel (norgestrel) is the active component of the Norplanta implant, approved for human use as a contraceptive implant by the FDA (McCauley & Geller 1992). It has been used in zoos and in Australian wildlife to reasonable effect (Nave et al. 2002) but was not effective in deer (Plotka & Seal 1989, White et al. 1994).
- Norethindron acetate is used in combination with ethynylestradiol as an oral contraceptive in humans but has not been effective in suppressing oestrus in heifers (Kesler 1997).
- Medroxyprogesterone acetate (Proveram™) has been used in zoos. Melengestrol acetate (MGA) is the steroidal compound most widely tested in wildlife and is approved by the FDA for use in cattle as a daily administration (Zimbelman & Smith 1966) for suppression or synchronization of oestrus, increased weight gain, and improved feed efficiency (Bennett 1993). It inhibited reproduction in white-tailed deer when ingested daily (Roughton 1979) or implanted (Bell & Peterle 1975, Plotka & Seal 1989). MGA implants have been used by zoos for about 20 years, but recent findings of uterine pathology in felids have raised concerns about their use (Kazensky et al. 1998).

- Some steroid hormone preparations target males rather than females (Asa 1997). Bisdiamine is a compound that selectively interferes with spermatogenesis but not testosterone production. When administered daily in ground meat to gray wolves it suppressed spermatogenesis without affecting mating behaviour. Indenopyridine also blocks sperm production, but has been tested only in rodents. Alphachlorohydrin (Epibloca), a male chemosterilant, was approved by the EPA for use as a rat control agent in 1982 (Bowerman & Brooks 1971, Ericsson 1982, Andrews & Belknap 1983), but is no longer marketed.

Steroids have the advantage that they can be fed orally or implanted, and they have been shown to be effective for some species. However, none of these steroids has proven practical as a wildlife management tool for various reasons. Orally, they are effective for only a short period and need repetitive applications, making them costly and impractical in most field situations. Furthermore, some of the steroids, such as diethylstilbestrol (DES), persist in tissue and in the food chain, making them unsatisfactory from an environmental point of view. They can also have deleterious health effects on treated animals and potentially on predators that eat treated animals (discussed earlier under health effects).

Table 26: Utility of synthetic steroids for camel management in Australia

Advantages of synthetic steroids	Disadvantages of synthetic steroids
Orally active	Non-target risk and environmental risks
Reversible	Not yet extensively tested in Camelids
	Transient response
	Continuous exposure required
	Longevity increased
	Not all orally active
	Long-term use potentially a health risk
	Large amount of active required

Recommendation

This class of fertility control actives are not recommended for camel control in the Australian landscape due to the need for continual or accurate temporal exposure and the risk to the environment. Chemical means of inducing fertility control are also contraindicated because the size of camels is prohibitive when considering the risks in deploying sufficient active into the environment, even if very species-specific delivery mechanisms were in effect. Moreover, camels are induced ovulators and the rut can last from May to October in Australia, necessitating prolonged treatment time frames and environmental/non-target exposure.

4.2.2.2 Plant extracts

The livestock industry has been concerned for some time about naturally occurring plant compounds that can result in lowered reproductive rates in production settings (James et al. 1994). Phytoestrogens naturally occur in over 300 plant species (Shemesh & Shore 1994). A constant source of oestrogen interferes with normal oestrous cycles in most animals, and phytoestrogens exert many of the same effects as oestrogen, even though their chemical structure is quite different.

Another source of reproductive loss in cattle is endophyte-infected tall fescue. Ergot peptide alkaloids produced by the endophyte are suggested as the primary cause of the reduced reproduction (Porter & Thompson 1992). Vasoconstrictive effects and neurohormonal imbalances are thought to be the principal mechanisms for the reproductive losses (Browning et al. 1998).

Bromocriptine (cabergoline) is a derivative of the alkaloid ergot family that acts as an enzyme inhibitor of prolactin. The lactation-blocking effects have been tested on kangaroos (Hinds & Tyndale-Biscoe 1994), and its anti-fertility effects investigated in foxes by injection into lactating females (Marks et al. 2001) and coyotes (DeLiberto et al. 2002).

Table 27: Utility of plant extracts for camel management in Australia

Advantages of plant extracts	Disadvantages of plant extracts
Orally active	Non-target risk and environmental risks
Reversible	Not yet extensively tested in Camelids
Relatively cheap	Not registered in Australia or overseas
	Transient response
	Continuous exposure required
	Longevity increased
	Long-term use potentially a health risk
	Large amount of active required

Recommendation

This class of fertility control actives are not recommended for camel control in the Australian landscape due to the need for continual or accurate temporal exposure, the potential risk to the environment, and the lack of testing in Camelids. Chemical means of inducing fertility control are also contraindicated because the size of camels is prohibitive when considering the risks in deploying sufficient active into the environment, even with very species-specific delivery mechanisms in effect.

4.2.2.3 Gonadotrophin Releasing Hormone (GnRH) Agonists

GnRH stimulates the pituitary gonadotroph cells to release follicle-stimulating hormone (FSH) and luteinising hormone (LH), which regulate functioning of the ovaries in the female and the testes in the male. Numerous superactive analogs of GnRH (agonists) have been synthesised (Rivier et al. 1983) that are routinely used to clinically suppress the pituitary-gonadal axis and include leuprolide, buserelin, nafarelin, and histrelin. These analogues are 15–200 times more active than naturally occurring GnRH (Conn & Crowley 1991). Pituitary gonadotrophs can be made unresponsive to GnRH by administering an agonist of GnRH in a continuous manner. Prolonged, continuous infusion of a GnRH agonist, especially at high concentrations, results in desensitisation and suppression of gonadotropin secretion and loss of gonadal function (Clayton et al. 1979). However, when administration of the GnRH agonist is discontinued, fertility returns. The practicality of this approach is therefore dependent on the development of a long-acting, slow-release formulation that can be delivered remotely. Slow release formulations of GnRH agonist have been commercially available for some time (Ovuplant™, Suprelorin™) and are effective in suppressing gonadal function for up to 12 months in some species. Continuous treatment with a GnRH agonist will inhibit ovulation in females of several species (Nett et al. 1981, Adams & Adams 1986, D'Occhio et al. 1989), including dogs (Vickery et al. 1989), cattle (Herschler & Vickery 1981), sheep (McNeilly & Fraser 1987), horses (Montovan et al. 1990), and stumptailed monkeys (Fraser 1983). Similar studies for wild ungulates are more limited. Leuprolide administered as a subdermal implant was effective in suppressing LH secretion and pregnancy for one breeding season in female mule deer (Baker et al. 2004) and elk (Baker et al. 2005). As with the immunocastration vaccines, these technologies generally suppress reproductive behaviour.

Table 28: Utility of GnRH agonists for camel management in Australia

Advantages of GnRH agonists	Disadvantages of GnRH agonists
Registered in Australia	Implant
Reversible	Not yet extensively tested in Camelids
Negligible non-target risk and environmental risks	Transient response
	Potential health implications

Recommendation

This class of fertility control actives is not recommended for camel control in the Australian landscape due to the need to implant camels most probably 2–3 times per year to effect continued contraception. As previously stated, chemical means of inducing fertility control are also contraindicated because the size of camels is prohibitive when considering the risks in deploying sufficient active into the environment, even with very species-specific delivery mechanisms in effect.

4.2.3 Novel approaches to fertility control

4.2.3.1 Talwar protein

Miller, Talwar et al. (2006) have begun researching the potential of a single chimeric protein manufactured using recombinant DNA techniques that consists of GnRH peptides interdispersed among several highly antigenic epitopes derived from *Plasmodium falciparum*, tetanus toxin, the respiratory synctical, and measles viruses. This chimeric protein has the potential to elicit powerful immune responses to GnRH by proxy, via adjacent antigenic epitopes. Theoretically, this protein could be delivered appropriately via the nasopharyngeal route or orally. The target protein for this vaccine is GnRH; it is therefore considered non-specific and will require sophisticated delivery mechanisms to limit non-target exposure.

Table 29: Utility of Talwar protein for camel management in Australia

Advantages of Talwar protein	Disadvantages of Talwar protein
Orally active	Not tested in any species
Small dose required	Non-target risks
Long term effect	Specific delivery mechanism required

Recommendation

This is a potentially powerful technology and approach to inducing immunological fertility control. It is recommended that this technology warrants additional research to accelerate studies examining its potential as a fertility control agent for camel population control. It is additionally recommended that research examining species-specific deployment methodologies are accelerated to ensure non-target risks posed by this technology are minimised.

4.2.3.2 Phage-panned peptides

Bacteriophage, or phage for short, are bacterial viruses that are amenable to the introduction of genetic material that because of very short generation times is subjected to a multitude of random mutations. The introduced genetic material is expressed by the phage on its coat surface and can be used to identify proteins that bind with high avidity to target cell receptors, proteins, glycoproteins, and the like. Aitken (2006) targeted ovarian granulosa cells via F-pilus attachment peptides expressed by phage using a similar technique developed to target peptides to sperm membranes (Eidne et al. 2000). The technology generates vast peptide libraries that can be screened against target cell surface epitopes for their relative avidity. For example, phage binding to granulosa cells in culture with high avidity can then be treated

to successive rounds of panning using successively more stringent conditions to further enhance avidity and enrich for the especially avid clones. This technology has been used with cultured murine granulosa cells to generate phage clones and peptides that exhibit remarkable species specificity and, moreover, cell specificity. Preparations of these phage clones or phage peptides administered peritoneally to mice have successfully depleted mouse ovaries of the majority of their primordial follicles (Aitken 2006). Oral delivery of phage-panned peptides is also a reality as they are relatively small, and enteric formulations are commercially available that can aid in the translocation of peptides across the gut epithelium (Mahato et al. 2003, Hamman et al. 2005). Accordingly, this technology exhibits all the necessary traits required for a field-practical oral fertility product that could be used for camel fertility control – exquisite species specificity coupled with oral activity, readily biodegradable, and environmentally benign. The qualities of this platform technology are very enticing, but the panning process must be repeated for each target species and as yet the technique has not been tested outside of mice.

Table 30: Utility of phage-panned peptides for camel management in Australia

Advantages of phage-panned peptides	Disadvantages of phage-panned peptides
Orally active	Not tested in Camelids
Small dose required	Specific delivery mechanism required
Long-term effect	
Target species specific	
Negligible non-target and environmental risks	

Recommendation

This is a further potentially powerful technology and approach to inducing immunological fertility control. It is recommended that this technology warrants additional research to accelerate studies examining its potential as a fertility control agent for camel population control.

4.2.3.3 GnRH cytotoxin

The selective depletion of cells critical for reproduction, be they in the brain or ovary, is a strategy being pursued by several research groups around the world. Qi et al. (2004) and Ball et al. (2006) are attempting to sterilise animals through the generation of gonadotrophin releasing hormone (GnRH) and/or GnRH superactive analogues coupled to cytotoxins that after systemic administration (injection or ingestion) bind only to cells expressing GnRH receptors, to achieve highly specific gonadotroph depletion. This renders the pituitary unable to respond to GnRH, depresses follicle stimulating hormone (FSH)/luteinising hormone (LH) release, and effectively dislocates the reproductive axis to effect long-term contraception or sterility (Sabuer et al. 2003, Yang et al. 2003, Ball et al. 2006) in both sexes and numerous vertebrate species. At present, clinical trials are being conducted with dogs, cats, sheep, mule deer, and elk to evaluate the effectiveness of ribosome-inhibiting proteins extracted from plants as toxins for permanently deactivating pituitary gonadotroph cells. Results to date in female mule deer indicate that a GnRH-toxin conjugate will suppress LH secretion for up to six months (Baker et al. 1999). Safety studies have not been reported. Since there are GnRH receptors in other sites in the body, toxicity could be a potential problem with this technique.

Table 31: Utility of GnRH cytotoxin for camel management in Australia

Advantages of GnRH cytotoxin	Disadvantages of GnRH cytotoxin
Orally active	Not tested in Camelids
Small dose required	Non-target and environmental risks
Long-term effect	Specific delivery mechanism required for oral administration
	Potential safety concerns

Recommendation

Again, this is a potentially powerful technology and approach to inducing immunological fertility control. It is recommend that a watching brief over this technology is kept so that research results (especially sterility induction and safety studies in additional species) can be used to inform camel management research priorities in Australia. It is additionally recommended that research examining species-specific deployment methodologies are accelerated to ensure non-target risks posed by this technology are minimised.

4.2.3.4 4-Vinylcyclohexene Diepoxide (VCD)

Hoyer et al. (2001) and Mayer et al. (2002), in developing a rodent model of human menopause, characterised a chemical active (4-vinylcyclohexene diepoxide, VCD) that appears selectively toxic to primordial follicles as they are less competent at metabolising VCD to non-toxic forms (Flaws et al. 1994). This chemical, when repeatedly injected or ingested over a period of approximately two weeks, causes apoptosis of the squamous epithelial cells, which are critical to primordial follicle viability. This in turn accelerates the rate at which ovarian senescence occurs and ultimately results in sterility. This has been demonstrated in mice, rats, and dogs using systemic administration. Recent work has focused on preparing and testing orally active formulations in rats and characterising the various isomer composition of the active preparation to determine isomers that may have a preferable toxicity and efficacy profiles. Overlaying this, the active must be formulated to achieve sterility with fewer exposures (preferably only one), and this will be challenging via the oral route.

Table 32: Utility of VCD for camel management in Australia

Advantages of VCD	Disadvantages of VCD
Orally active	Not tested in Camelids
Potential to sterilise offspring	Non-target and environmental risks
Long-term effect	Specific delivery mechanism required for oral administration
	Potential safety concerns
	Large amount required for sterility

Recommendation

Chemical means of inducing fertility control are contraindicated because the size of camels is prohibitive when considering the risks in deploying sufficient active into the environment, even with very species-specific delivery mechanisms in effect. This is countered by the potential of this active to ablate neonate primordial follicles in utero (at very low doses) providing the means to sterilise all female offspring of a female camel consuming an effective dose at the critical time during ovarian development. Therefore, it is not recommended for camel control until more is understood regarding target and non-target safety and recommended dosage.

4.2.3.5 Antigen delivery systems

New Zealand researchers are leading an international consortium that is investigating the potential of transgenic plants (Cowan et al. 1999) and bacterial ghosts (Szostak et al. 1996, Jalava 2002) as vaccine delivery systems for the delivery of possum reproductive antigens. The principle of delivering antigens via these systems has been developed, and antibodies to a model protein expressed in transgenic plants (Mason et al. 1998, Tacket et al. 1998) have been detected in the general circulation and uterine secretions of treated possums. Additionally, zona pellucida 3 protein attached to the inner cell membrane of bacterial ghosts by specific anchor sequences, and/or through the use of self-assembling S-layer proteins (Eko et al. 1999) demonstrated inherent adjuvant properties that induced humoral and cellular immune responses, which reduced the fertility of possums in breeding studies (Duckworth & Cui 2004). These technologies have the advantage of being designed specifically for target species and

for efficient oral delivery from the outset, compared with those that require sophisticated formulation to aid passage through the gut and translocation across gut epithelium. Both of these model systems have the potential to facilitate the delivery of sufficient antigens to camels, although the mechanisms would need to be tested in the target species to ensure cross-species applicability.

Table 33: Utility of antigen delivery systems for camel management in Australia

Advantages of antigen delivery systems	Disadvantages of antigen delivery systems
Orally active	Not tested in Camelids
Small dose required	Delivery system required
Potentially long-term effect	
Highly target species specific	
Negligible non-target and environmental risks	

Recommendation

This is an innovative technology and approach to inducing immunological fertility control. It is recommend that a watching brief be kept over this technology so that research results (especially sterility induction and safety studies in additional species) can be used to inform camel management research priorities in Australia.

5. Delivery systems

Delivery of non-species–specific toxic chemical, biological, or fertility control agents to camels in Australia will require a tailored delivery system. This will also be essential to facilitate product registration and to reduce the risks for regulators and operators alike. Tailoring chemical delivery requires an understanding of the target species' ecology and niche, particularly in complex communities or between similar species. Once understood, niche separation has many aspects, all of which can be capitalised on. Habitat (generalist/specialist, terrestrial/arboreal/fossorial), diet (generalist/ specialist, omnivore/carnivore/herbivore), morphology as compared with conspecifics (large/small, musculature, dentition, bite force, mouth dexterity, problem solving ability), sensory perception (relative importance of vision, smell and taste when foraging), and physiology (water requirements, digestion/agitation) are all characteristics that help identify a species niche (Humphrys & Lapidge 2008). Defining each of these at the outset of the development process is a useful practice in an initial attempt to tailor delivery systems.

Although many baits currently used to deliver chemicals are to a large degree generic, such as grains or meat, the process of species tailoring is not new. O'Brien (1986) proposed a framework for developing a feral pig bait based on many of the above attributes. This framework formed the basis of the subsequent PIGOUT® project that began in January 2004, with aim of developing and registering a manufactured 1080 feral pig bait (Cowled, Gifford et al. 2006). The manufactured bait had to be highly attractive to pigs, cheap, target-specific, and easy to use. Extensive field testing of the product has shown it to be near target specific (Cowled, Lapidge et al. 2006), except in America (Campbell et al. 2006), and potentially suitable for delivery of disease vaccines or contraceptives (Campbell et al. 2006; Cowled, Lapidge et al. 2008). For some species the tailoring process has already occurred, such as with the M-44 mechanical ejector and Coyote Lure Operative Device (CLOD) for selectively targeting canids (Busana et al. 1998, Berentsen et al. 2006). Further levels of selection can be provided through the use of target species attractants/non-target repellents, or mechanical bait delivery devices.

Perhaps more complex than bait or delivery device development is developing an appropriate baiting strategy. For orally-delivered chemical products aimed at reducing overall population levels of open, free-ranging species, working with whole populations is critical. Cowled, Aldenhoven et al. (2008) recently demonstrated the large scale over which some genetically contiguous feral pig populations can occur in the Australian rangelands. A similar study is now being undertaken with camels at Murdoch University (P. Spencer 2008, Murdoch University, pers. comm.). Targeting only a small proportion of the population with a control technique will likely result in no overall effect due to reinvasion and breeding compensation. Added to the scale complexity are questions regarding timing (temporal variation in bait uptake), placement (where in the environment – spatial variation in bait uptake), and distribution (bait density and grouping). Frequency of bait re-application is also critical, all of which should be tested empirically. Moreover, what is appropriate for one habitat may not work in another, when a different suite of non-target species and environmental conditions are present.

Although the species tailoring process can be complex, it is greatly aided when the target species is unique within its range with respect to a number of characteristics that can be exploited. Such is the case with the camel in Australia, with only domestic cattle being of a similar weight and size. Unfortunately, due to the camels' generalist browse herbivore diet, a traditional bait approach is unlikely to be highly accepted and even less likely to be species specific. Notwithstanding, camels have a number of unique traits that can be targeted for isolation and species-specific delivery. Table 34 highlights nine such unique characteristics that could be capitalised on, but no doubt others exist. One uniqueness is that the camel can tolerate body water losses of 25% of their body weight, where 15% losses are fatal in most other mammals. As a consequence camels can consume up to 200 litres of water in three minutes

without risking osmotic imbalance, whereas rangeland cattle, for example, consume one-third to a half of this volume throughout the day. Such a behaviour could be used to deliver water-soluble toxins, such as 1080 or nitrite, at very low concentrations in water troughs from which camels are known to drink. Although dose compliance would need to be critically assessed, it is theoretically possible that no other species could physically consume enough water in a short enough time period to receive a toxic dose. This method of delivery should not, however, be used for toxins that are not rapidly metabolised, as bioaccumulation and debilitation could result in smaller species.

As with many rangeland species camels naturally congregate at waterholes in summer or during drought. Such an opportunity logically provides a catalyst for greater control effort, as the control area requiring treatment, and in turn the environment exposed, is greatly reduced. Interestingly, due to the camels' high salt requirement, the species also congregates at salt lakes in summer (Coventry et al. in press), which is somewhat unique for a large mammal. Hence, providing fresh water–delivered xenobiotics at salt lakes or conversely salt-delivered actives at fresh water lakes may be the best approach for camels in Australia. Furthermore, Ali et al. (1996) reported the increased effectiveness of xenobiotics when camels are dehydrated, and as such the delivery of actives in summer should lead to increased efficacy.

Table 34: Unique characteristics of camels in the Australian landscape that could aid in species-specific delivery

Anatomical, physiological, or ecological feature	Delivery system feature
1. Height of camel, reach of neck	**Elevate/offset delivery system, such as feeder platforms/poles**
2. Shape/strength/morphometrics of camels	**More easily targeted with selective access devices and Machine Vision Technology**
3. Tongue length	Potential to use grills over chemicals
4. Single event water consumption ability: 30–40 L day and up to 200 L in 3 min when water not readily available	**Deliver low concentration actives via water i.e. non-target species could not drink enough water to receive an effective dose**
5. Salt intake: up to 200g a day	**Deliver toxic salts or other actives in salt lick formulations**
6. Congregation at limited desert water points or salt lakes	**Provides focus for management activities**
7. Large home range	**Minimises the number of management sites and non-target exposure**
8. Browse/shrub diet	Delivery of actives on high browse or within the crown of low trees
9. Natural dehydration in summer	**Many xenobiotics work more effectively in summer when camels are naturally dehydrated (Ali et al. 1996)**

Note: Bold characteristics are deemed the most promising

A delivery device that could capitalise on the species height and neck length, nomadic but congregational behaviour, and natural requirement for salt is depicted in Figure 8. The 'Camel Canteen' would require the height and neck length of a camel to gain access to the hopper. The active would be contained within the feed trough to minimise environmental exposure, to maximise stability, and to avoid environmental contamination/soil resides. Non-target bird and mammal species would be excluded from the device through metal flaps over the feeding trough, which could be easily lifted by a camel's snout. Standard salt could be initially placed in the bed of the trailer to promote camel feeding, and air holes high in the sides of the hopper could advertise the presence of salt, either as NaCl as a delivery medium or $NaNO_2$ (sodium nitrite) as the active itself. Such a device could carry several hundred kilograms of active for long-term remote deployment and low maintenance. Mounted on a trailer or similar it could be towed (or airlifted in more remote areas) into place in summer where required. A simpler version of this is depicted in Figure 9. The raised camel salt licks ('Pop-salt-cles') could consist of a salt-formulated active, which camels are naturally attracted to, particularly at sources of fresh water where salt deprivation may occur. Such a delivery technique may be more appropriate for anti-fertility actives that often require multiple exposures.

The above outline is a brief summary of the species-tailoring process, including a few initial suggestions, much of which is ultimately refined through trial and error. Regardless of the specific order of steps taken in the process, before attempting registration of a non-specific active each of the following needs to be demonstrated:

1. field efficacy and target specificity in a variety of habitats in which the final product will be used
2. shelf and field stability of the bait and active under varying environmental conditions
3. product cost, scale, and consistency of production must be amenable to commercialisation
4. the logistical benefit and operator safety must be appropriate for the end user.

*Figure 7: A delivery system such as the '**Camel Canteen**' would require the height and neck length of a camel to gain access to the 'bait' hopper*

Figure 8: The 'Camel Canteen' or 'Pop-salt-cles' would be best deployed in summer in areas where camels are known to congregate

6. Discussion

Any form of large-scale camel control in Australia will no doubt be controversial, and substantial public education will be required prior to implementation. The species has gained a special place in the hearts and minds of many Australians and tourists, and is now seen as an icon of the outback and tourism (Figure 10). Furthermore, very few Australians would have first-hand experience with the damage that camels can cause, and as such public empathy for the management of the population will likely be minimal. Notwithstanding, management of the ever-increasing camel population should be undertaken to reduce the species' environmental, economic, and social impacts on the Australian landscape and remote communities. Unfortunately eradication of camels from the Australian mainland will be virtually impossible, and for many highly undesirable.

Figure 9: Camel mural at Adelaide Airport
Note: camels have become an icon of the outback and tourism industry in Australia

Camel control with poisons will be the most controversial of the control methods discussed and should not be considered as an immediate first choice or as a single means of control. If poisons are advanced it should be as part of an integrated package of control tools, and research would be needed to verify the humaneness, target specificity, and effectiveness of a short list of candidates outlined above. Out of all the conventional anticoagulant and non-anticoagulant poisons currently registered in Australia there are only two that could be considered as potential candidates: 1080 and cyanide. Should 1080 or cyanide be advanced, new baits would need to be developed that deliver a rapid bolus of toxin to the camel in a species-specific fashion. However, as a dedicated browser camels are unlikely to take ground-laid baits, and more novel forms of delivery will likely be required.

Sodium nitrite and PAPP are two new toxicants currently under development for the humane destruction of feral pigs and foxes, feral cats and dogs respectively. Of these two the toxicity of sodium nitrite is better understood in larger animals such as livestock and pigs, and it should be considered as a prime candidate. Natural nitrate/nitrite poisoning of livestock occurs throughout Australia, due to bore-water and feed contamination, and as such this form of poisoning may be more publicly acceptable with an appropriate education campaign. Although large volumes (>50g) of nitrite will be required to euthanase camels, the volume is well within the species' necessary daily intake of salt. The symptomatology of nitrite toxicosis, including lethargy, laboured breathing, reduced consciousness and coordination, and death within three hours (generally 80 min of symptoms) is unlikely to be different in the camel as this process has been described for every species studied to date. The low cost and chemical scheduling of the active (Schedule 5 to 6, depending on presentation), its registration as a human food product, its relative operation safety (large doses are also required in humans) and low residues, and the existence of a commonly available antidote all support the further investigation of the active for camels.

Pharmacokinetic data indicate that many drugs have longer absorption and elimination half-lives in camels and are poorly metabolised when compared with other animals. This is in part responsible for the species' susceptibility to nephrotoxins, as well as the coccidiostat salinomycin. Although salinomycin is highly toxic to camels, and Koenig's 2007 report in *Science* (death of 2000 camels due to salinomycin poisoning) was greeted with a good deal of interest in Australia, the death is likely to be protracted and

inhumane as it was observed to be in feral pigs (S. Lapidge pers. obs.). Unfortunately, none of the drugs or compounds that camels have been accidentally poisoned with in the past would be likely to provide as humane a death as sodium nitrite, cyanide, or even 1080. Several drugs are inappropriate because to cause death they need to be administered by injection. However, they should not all be discounted at this stage. Ivermectin is an exception. It is orally active and potentially lethal by this route. Paracetamol or toxic metabolites of isometamidium chloride (trypanocidal drug) may have similar properties. Small-scale testing of a short list of chemical candidates administered alone and in combination is the logical next step. The short list should include 1080, sodium and potassium nitrite alone and with a low dose of 1080, and a sodium nitrite/potassium chloride combination. In addition, a combination of potassium chloride with a diuretic with and without a nephrotoxic agent such as banamine and/or phenylbutazone should be considered as principal candidates. As a rule the use of drug combinations should be avoided for registration purposes; however, real welfare benefits may come from such a combination and they are therefore worthy of investigation.

As Australia is the only country potentially interested in the control of camels through biological means, little is published in this area of research. Furthermore, what is published generally relates to diseases of domestic camels, where inappropriate animal husbandry techniques are often promoting morbidity and mortality. Although there are many diseases that affect camels, such as anthrax, surra, botulism, and brucellosis, the majority are inappropriate for introduction or proliferation within Australia due to their effect on other species. Out of the four main viruses of camels, camelpox virus, camel contagious ecthyma, camel papillomatosis, and rabies, camelpox is the only virus that warrants further investigation as it is species specific, has a prophylactic vaccine, and may cause up to 50% mortality within a naïve population. However, with the average illness taking 16 days, and death resulting from severe and mutilating facial lesions, pneumonia, and haemorrhagic gastroenteritis, the humaneness of the disease in camels would obviously have to be questioned.

The only other form of biological control that showed some promise, perhaps through the lack of information rather than the clarity of the information garnered, was the fungal mycotoxin *Aspergillus fumigatus*. The fungal agent was responsible for the rapid death of 40 out of 70 camels in the Emirates through bronchopneumonia and gastroenteritis. Although worthy of further investigation, delivery of the fungus to camels would be difficult and the mycotoxin should be seen as a secondary option.

Delayed sexual maturity and longevity of camels preclude fertility control, however successful, from impacting significantly on the damage caused by the species immediately or in the short term. For this reason alone fertility control cannot be considered in isolation, but must be integrated into a comprehensive management plan that will necessarily include harvesting and other lethal measures. The greatest benefit fertility control may convey to future camel management is the capacity to minimise additional lethal incursions in our attempts to manage camels in the Australian rangelands. This outcome is highly desirable and because of this we have examined the benefits and risks of all existing fertility control technologies. We have also considered a range of technologies currently being developed that may be useful in controlling camel fertility in the future (near and far). Considering the options available or likely to become available has highlighted four key principles in assessing the applicability of a fertility control technology for camels. These are:

1. The physical size of camels means that manipulating fertility using pharmacological intervention (hormones, VCD, plant extract), however efficacious, will in every case translate into a concomitant large amount of ‘drug’ being introduced into a fragile environment that also has a significant non-target risk. This is an unacceptable outcome.
2. The use of actives that have a contraceptive (synthetic hormones, contraceptive vaccines) or transient effect, as opposed to a sterilisation effect, will require repeated administration, consumption, or exposure. This will not be a practical, cost-effective, long-term management practice for managing camel fertility at landscape scales.

3. Four novel technologies (GnRH-cytotoxins, phage-panned peptides, the Talwar protein, and antigen delivery systems) are currently being developed that hold great prospects for effective fertility management in a range of species including camels. The phage-panned peptides confer the advantage of a uniquely species-specific and potentially sterilising practicality. The Talwar protein may be an acceptable immunogen that may provide long-term contraception (>5 yrs) but at least has the potential to be orally delivered. GnRH-cytotoxins offer the promise of sterility from a single exposure, but these are unlikely to ever be species specific and oral delivery may prove difficult. The antigen delivery systems are an enticing possibility as they offer an oral delivery system that can be manipulated to express a number of antigenic epitopes such that fertility control could be coupled with disease management. However, the inherent risk of unexpected and adverse results in this developmental research impacting on a successful outcome remains high at this stage. Despite this high risk, research accelerating the potential application of phage-panned peptides and the Talwar protein should be considered, while a watching brief of the antigen presenting systems and the GnRH cytotoxins would be prudent.
4. Immunomodulation of fertility using species-specific immunogens or deployment that targets camels presents by a significant amount the least risk from an environmental (little amount of active required, readily biodegraded), non-target (little cross reactivity, reduced exposure), technology development (technique has been proven in many different species over time), and international relations perspective, while retaining many of the benefits of long-term contraception.

One vaccination target may, based on the available evidence, provide a species specific immunogen that depending on the management prerogative gives an outcome ranging from good to great. For example, at its most selective, this technology may result in camel-specific fertility control over a long period (>5 yrs with a single exposure). As the cross-reactivity of the epitope increases (by design) the same camel oral vaccine may concomitantly reduce the fertility of feral camels, feral pigs, feral horses, feral donkeys, and feral water buffalo, without affecting other species (marsupials, birds, reptiles, and other mammals). However, as the cross-reactivity of the epitope increases so too does the risk that sheep and cattle fertility might be similarly impacted. Hence this exciting research deserves special attention and an international collaboration should be sought with this research group as soon as possible to advance the assessment of this technology for camel fertility control. The confidentiality of the work currently prevents additional detail being disclosed in the context of this review; however, the information can be reviewed with the execution of confidentiality agreements.

The remaining immunomodulatory options are the Talwar protein and virally-vectored immunocontraception. The Talwar protein is as yet untested in most species as sufficient amounts of the protein are only now becoming available for inclusion into vaccines. To date no-one has demonstrated oral or mucosal delivery and efficacy of this immunogen, and research is focused on proving its effectiveness via systemic administration. VVIC certainly can also not be ruled out as a viable technology, especially from the perspective of providing a cost-effective landscape-scale population reduction or maintenance of low populations in the future. However, before this could ever become a reality a concerted international political consultative and research effort would be needed to negotiate a developmental path that was acceptable globally, prior to resourcing the elucidation of camel-specific reproductive immunogenic targets and suitable vectors.

The challenge is now to apply these principles to select the most appropriate fertility control option that can be applied cost-effectively at a landscape scale to maintain low camel populations in Australia. The immunocastration vaccines could be registered in Australia for use in camels within 24–30 months from registration application. The more practical options have a longer time horizon before application at the scale sought is possible, but will vastly improve cost effectiveness. Finally, advancing a majority of the technologies that carry this promise will require a cross-discipline approach encompassing ecological, active formulation, active presentation/delivery, reproductive physiology, immunophysiology, and biotechnology inputs.

Camels are a somewhat unique species in the Australian landscape, and as such they should be able to be selectively targeted for oral delivery of chemical, biological (mycotoxins), or anti-fertility actives. Outlined above are a few simple approaches, which are often the best in terms of cost and usability. More elaborate chemical or mechanical approaches are certainly possible, such as using machine vision technology (Finch et al. 2006); however, the added cost and complexity can lead to reduced uptake by land managers. All considered, the most promising techniques are a camel-specific feeding trough ('Camel Canteen'), raised salt licks containing either chemical (nitrite) or anti-fertility actives, and low concentration water delivery of acute xenobiotics.

The human dimensions of camel management will forever mean that there is no simple path forward. Competing interests, including those of conservationists, harvesters, politicians, and the public, will need to be taken into account at the earliest possible stage to ensure a stable research and development platform can be agreed upon at the outset. The species has had over 70 years to colonise and prosper in Australia's rangelands, and it should not be expected that any one potential management tool discussed in this report will rapidly change the current overabundance situation. Notwithstanding, camel management in Australia requires improved broadscale control tools, and this report outlines some possibilities worth pursing.

7. Recommendations

In summary, it is the opinion of the authors that the following techniques should be investigated further, at least initially with camel stakeholder groups, animal welfare groups, the Australian Pesticide and Veterinary Medicine Authority, and the Australian public:

1. Low concentration delivery of nitrite or 1080 in raised water troughs. This may be made more specific if delivered at salt lakes where fresh water is more desirable for camels and species diversity is lower.
2. Delivery of sodium or potassium nitrite via a camel-specific feeding trough or raised salt lick at natural congregation points. Potassium chloride or 1080 may act synergistically with nitrite, which would lower the dose required and shorten the time to death.
3. A combination of potassium chloride with a diuretic, with and without a nephrotoxic agent such as banamine or phenylbutazone, should be examined further as it may prove uniquely toxic to camels.
4. Camelpox is worthy of further investigation, particularly in reference to its spread in more natural nomadic camel populations within the species range and the humaneness of the virus. Regardless, camelpox is unlikely to be the 'calicivirus' of camels in Australia, and would be principally introduced to limit population recruitment.
5. An immunocontraceptive vaccine technology that is orally active and has a species-specific immunogen is favoured for fertility control. Research into a feral pig anti-fertility vaccine that can be used as a platform from which to undertake similar research in Camelids holds the greatest hope of this in the immediate future, but requires funding for the extension of the work into camels.
6. Three other novel approaches to manipulating fertility warrant attention: phage-panned peptide technology, the Talwar protein, and antigen delivery systems such as bacterial ghosts.

The authors recommend that a balanced research and development approach is undertaken rather than risking what will likely be limited future funding resources on a single management tool. Furthermore, any future research program should have short-, medium-, and long-term deliverables so incremental improvements can be made in managing the camel population in Australia. Finally, at the heart of future research program decisions must remain the public acceptability and animal welfare aspects of each management technique.

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