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Pesticides used in the Management of Vertebrate Pests in Australia: A Review

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Introduction

The management of Australia's vertebrate pests such as rabbits, foxes and wild dogs has historically relied heavily on the use of a variety of pesticides. In 1982, Hone and Mulligan[1] published their book *Vertebrate Pesticides* to bring together the considerable scientific information on the pesticides in use at the time, and make it more readily available to researchers and end users.

Thirty years on, although vertebrate pest management still relies on a variety of pesticides their use has come under increasing scrutiny, with a growing attention to ethics, efficacy, environmental safety and best practices within Australia. At the same time there has been a growing public demand for more effective management of the impacts of vertebrate pests.

Many of the pesticides included in Hone and Mulligan (1982) are no longer registered or endorsed for use in Australia and several new pesticides have been introduced. These changes and the increase in scientific knowledge of many of these compounds made it timely to produce an updated and relevant source of information on vertebrate pesticides currently or about to be registered in Australia.

The information presented includes the basic physical and chemical properties of the pesticide, along with physiological and toxicological data. Included is information on the mode of action, acute and chronic symptoms, antidote, and treatment. This guide details the environmental and non-target risks, including potential primary and secondary poisoning, and user safety information.

The use of vertebrate pesticides has come under increasing public scrutiny and it is hoped that this publication will provide a significant contribution to the public accountability of vertebrate pest management by demonstrating the depth of knowledge that applies to the registration and use patterns of vertebrate pesticides in Australia.

The listing of any pesticide or trade name of any pesticide does not constitute or imply endorsement of that pesticide by the authors or the publisher. The approved use of pesticides is dependent on State and Federal legislation which may vary across location and time.

Structure of the review

The pesticides are referred to by their common names as recommended in Australian Standards AS 1719-1994 or, if not published in this reference, by the International Organisation for Standardisation. The pesticides are grouped according to their mode of action and chemical structures as acute poisons, anticoagulants and fumigants. The information collected for each pesticide is outlined below:

Chemical name	The full chemical name for the pesticide; may be the same as the common name.
Synonyms	Other names, or numbers, used to describe a pesticide. Trade names are not included.
Source	The biological or chemical source of the pesticide.
Formula	The chemical formula for the pesticide.
Molecular wt	The sum of the atomic weights of all the atoms contained in a molecule.
Physical form	The state of the chemical at room temperature, either solid (powder, crystals), liquid or gas.
Colour	The colour of the chemical. This may depend on the purity of the compound.
Taste	The taste of the chemical.

[1] Hone, J., and Mulligan, H. (1982). *Vertebrate Pesticides*. Science Bulletin 89, NSW Department of Agriculture, Sydney. ISBN 07240 2101 9.

Odour	The odour of the chemical.
Melting point	The temperature (degrees celsius - oC) at which the chemical changes from a solid to a liquid.
Solubility	A qualitative statement of the solubility of the chemical in water and various other solvents.
Stability	The effect on the chemical of environmental factors such as temperature, light and moisture.
History	A brief history of the use of this chemical as a vertebrate pesticide.
Uses in Australia	A summary of how the pesticide is currently used in Australia. As regulations may change frequently, the reader should always check current legislation.
Poison Schedule	The classification according to the Australian Poisons Schedules using the criteria in the Standard for the Uniform Scheduling of drugs and Poisons. See Appendix 1 for a general description of these Schedules. In addition the Australian Pesticide and Veterinary Medicines Authority (APVMA) may declare certain chemical products to be 'restricted chemical products' if special training, and/or other requirements are needed to be able to handle or use the chemical. These designated products can only be used by an 'Authorised Person', who is determined by the relevant State of Territory authority.
Formulation types	Formulations of the pesticide available in Australia.
Absorption	The route(s) by which the pesticide can be absorbed into an animal.
Mode of action	A description of the physiological or biochemical effect of the pesticide on animals.
Latent period	The time between an animal receiving a dose of a pesticide and the first appearance of symptoms.
Symptoms	A description of the changes in an animal's behaviour and/or metabolism caused by exposure to the pesticide.
Time to death	The time taken between an animal receiving a dose of the pesticide and death.
Detoxification and excretion of sub-lethal doses	A description of the breakdown and removal from the body of the pesticide and pesticide metabolites.
Accumulation of sub-lethal doses	The storage of a pesticide in tissues of the body.
Long term effects of sub-lethal doses	Metabolic and/or behavioural effects on an animal exposed over a period of time to a pesticide in non-lethal or chronic quantities.
Tolerance	The decreased susceptibility of an animal to a pesticide as a result of a history of exposure or some other conditioning stimulus.
Resistance	The inherited ability of an animal to survive and reproduce following exposure to a pesticide dose that would normally be lethal to the majority of individuals of that species. This implies some type of genetic difference and selection.
Aversion	The avoidance of a pesticide usually associated with an unpleasant or painful stimulus (for example smell). If the pesticide is used in

	association with a bait material this is often referred to as bait shyness.
Antidote	A substance or number of substances reported to alleviate or overcome the effects of the pesticide.
Treatment	A list of therapies and management that may be used to alleviate the symptoms and restore health following exposure to the pesticide.
User safety	A list of procedures required for the safe handling of the pesticide.
Decay time in soils	The fate of the pesticide or its metabolites in the soil.
Aquatic systems	The fate of the pesticide in water.
Atmosphere	The fate of the pesticide in the atmosphere (if relevant).
Effect on plants	The uptake and effect of the pesticide or metabolites on plant life.
Effects on microorganisms	The known effects of the pesticide on bacteria, fungi, algae and other forms of microorganisms.
Acute toxicity to vertebrate species	Information on the hazard presented by the pesticide to vertebrate animals is discussed and compared for a range of indicator species (introduced and native), in most cases using the oral median lethal dose (LD_{50}). This LD_{50} value should be viewed only as a guide to the sensitivity of a species to a pesticide with many experimental factors affecting its determination such as age, health, seasonal and environmental conditions as well as the method of administration and method of calculation. The LD_{50} is only part of the information required to determine the potential hazard of a pesticide in the field. The actual amount of pesticide present should also be considered. The total amount of pesticide required to be consumed for the death of an average size animal is calculated to provide an alternate comparison. For aquatic species and fumigants the toxicity is reported as either the median lethal concentration (LC_{50}) or the median effective concentration (EC_{50}). This is usually reported for a known exposure time. When oral LD_{50} values were not available, alternative values have been reported.
Toxicity to invertebrate species	Information on the hazard presented by the pesticide to invertebrate animals is discussed and compared, using either the oral median lethal dose (LD_{50}) or the median lethal concentration (LC_{50}). See above for discussion of these measurements.
Non-target primary risk profile	Research and reported occurrences from Australia and overseas of non-target species' direct deaths after the use of the pesticide.
Non-target secondary poisoning risk profile	Research and reported occurrences from Australia and overseas of non-target species' deaths after exposure to the pesticide through an indirect route (e.g., the consumption of prey that had been poisoned by the pesticide).

References A list of all literature cited in the text for each pesticide. As information has been summarised for this guide, these publications will be valuable for the reader to seek more detailed information where required.

Acute toxins

4-aminopyridine

Chemical name: 4-aminopyridine

Synonyms: pyridine-4-amine, 4AP, DRC-1327, Phillips 1861

Source: 4-aminopyridine is prepared by the decarbonylation of pyridine-4-carboxamide using sodium hypochlorite (Shimizu et al. 2007).

Physical chemistry:

Formula	$C_5H_6N_2$
Molecular wt	94.1
Physical form	Solid
Colour	Colourless
Melting point	158^{o}C
Solubility	Moderately soluble in water
Stability	Stable to light

Applications:

History	First synthesised in Germany by Koenigs in 1924 but not used for bird control until the 1960s (Goodhue and Baumgartner 1965). Although toxic in sufficient amounts, also used as a repellent with vocal symptoms of sub-lethal dosed birds used to repel other individuals.
Uses in Australia	Control of nuisance birds: pigeon (*Columba livia*), sparrows (*Passer domesticus*, *P. montanus*), starlings (*Sturnus vulgaris*) and Indian myna (*Acridotheres tristis*).
Poison Schedule	Australia: Schedule 7 poison Restricted chemical product
Formulation types	Granular bait (ready to use)

Toxicology:

Absorption	Absorbed through the gastro-intestinal tract, skin and respiratory tract (Beasley 1997).
Mode of action	Blocks potassium channels and enhances release of some neurotransmitters. High dose may affect heart action (Beasley 1997).
Latent period	Initial effects as short as four minutes but 7-15 minutes common (Swindle 1992).
Symptoms	Symptoms include hyperexcitability, salivation, disorientation, loss of coordination, tremors, seizures, cardiac arrhythmias, rapid heart beat, increased blood pressure, vocalisations caused by involuntary contractions of the diaphragm and respiratory arrest (Sobek et al. 1968, Schafer et al. 1973a).

Time to death	Death often occurs 0.25-4 hours after dosing (Schafer et al. 1973a)
Detoxification and excretion of sub-lethal doses	Rapidly metabolised by birds (Schafer et al. 1974), detoxified in the liver and excreted in the urine. In humans initial tissue distribution is very rapid and elimination almost exclusively in the urine (Uges et al. 1982).
Accumulation of sub-lethal doses	No evidence of cumulative toxicity, although repeated exposure can become lethal if the time between doses is less than the time required to detoxify and excrete the toxin (Schafer and Marking 1975).
Long term effects of sub-lethal doses	No effects noted on birds fed multiple sub-lethal doses over an extended period of time (Schafer et al. 1975, Schafer and Marking 1975).
Tolerance	No evidence of tolerance to this pesticide has been reported.
Resistance	No evidence of resistance to this pesticide has been reported.
Aversion	There have been no reports of aversion to this pesticide.
Antidote	No specific antidote has been documented.
Treatment	Ingested material should be removed by vomiting or gastric lavage, activated charcoal and saline cathartic. Seizures should be treated with appropriate medication, alternatively animals can be sedated. Any disturbance of the heart rhythm should also be treated with appropriate medication (Beasley 1997).
User safety	User should wear gloves, protective clothing and a dust mask. Contaminated skin should be washed thoroughly with soap and water. Protective clothes should be washed after each day's use.

Environmental fate:

Decay time in soils	4-aminopyridine is readily absorbed by soil and relatively unavailable for root absorption or leaching (Starr and Cunningham 1974).
Effects on plants	No visible phytotoxic effects on corn and sorghum plants reported (Starr and Cunningham 1974).

Acute toxicity to vertebrate species:

Very toxic to all vertebrates (see Schafer et al. 1973a). Fish become increasingly sensitive with increasing exposure, and decreasing water temperatures (see Schafer and Marking 1975).

Table 1. The sensitivity to 4-aminopyridine for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of 4-aminopyridine is calculated using the average male body weights derived from McIlroy (1984), Strahan (1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Brown rat, *Rattus norvegicus* (lab. strain)	28-32	0.32	9.0-10.2	(Goodhue and Baumgartner 1965, Deichmann and Gerade 1969)
Pig, *Sus scrofa*	18	70	1260	(Deichmann and Gerade 1969)
Dog, *Canis lupus familiaris*	4	16.0	64	(Deichmann and Gerade 1969)
Birds				

English sparrow, *Passer domesticus*	3.6-7.5	0.03	0.10-0.22	(Goodhue and Baumgartner 1965, Schafer 1972, Schafer et al. 1973b)
Chicken, *Gallus domesticus* (chicks)	15	2.8	42	(Deichmann and Gerade 1969)
Mallard duck, *Anas platyrhynchos*	4.2	1.2	5.0	(Schafer 1972)
Pigeon, *Columba livia*	6-7.5	0.27	1.6-2.0	(Goodhue and Baumgartner 1965, Schafer et al. 1973a)
Ring-necked pheasant, *Phasianus colchicus*	5.6-7.5	1.2	6.7-9.0	(Schafer 1972, Schafer et al. 1973a)
Starling, *Sturnus vulgaris*	4.9-6	0.07	0.3-0.4	(Goodhue and Baumgartner 1965, Schafer 1972, Schafer et al. 1973a)

Table 2. The sensitivity to 4-aminopyridine for a range of aquatic vertebrate species expressed as the median lethal concentration (LC_{50}) in milligrams per litre of water, where 50% mortality occurred within the specified time frame. Results are from static water tests.

Species	LC_{50} (mg/L)	Time (hours)	Water temp. (^{o}C)	Reference
Fish				
Channel catfish, *Ictalurus punctatus*	8.74 4.00 9.35 5.80	24 96 24 96	12 12 22 22	(Schafer and Marking 1975)
Bluegill, *Lepomis macrochirus*	11.2 4.41 12.3 7.56	24 96 24 96	12 12 22 22	(Schafer and Marking 1975)

Toxicity to invertebrate species:

No information was found on the toxicity of this pesticide to invertebrates.

Non-target primary risk profile:

Although highly toxic the primary hazard depends mainly upon the method of exposure to target species. There are reports of deaths of small numbers of non-target wildlife after control programs; however, the risk is considered very low, especially to livestock, if used correctly (Goodhue and Baumgartner 1965).

Non-target secondary poisoning risk profile:

This pesticide is rapidly metabolised by birds and under laboratory conditions thought to pose minimal secondary hazards (Schafer et al. 1974). However in field use there have been deaths in scavenger bird species and there is a potential risk to predatory species from unabsorbed toxin in the GI tract of affected or dead birds (Holler and Schafer 1982).

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Alpha-chloralose

Chemical name: (R)-1,2-*O*-(2,2,2-trichloroethylidene)-α-D-glucofuranose

Synonyms: chloralose, α-chloralose, α-dextrochloralose, glucochloralose, alphamonoglucochloralose, chloroalosane

Source: Chloralose is formed by condensing chloral with glucose. Two isomers are extracted but only the alpha form possesses anaesthetic properties (Ridpath et al. 1961, Murton et al. 1965, Lees 1972).

Physical chemistry:

Formula	$C_8H_{11}Cl_3O_6$
Molecular wt	309.54
Physical form	Crystalline powder
Colour	White
Taste	Bitter taste
Odour	Odourless
Melting point	187^{o}C (beta-form 227-230 ^{o}C)
Solubility	Alpha isomer is not soluble in water or ethanol. Soluble in alcohols, diethyl ether and glacial acetic acid. Sparingly soluble in chloroform. Practically insoluble in petroleum ether. The beta-form less soluble than alpha-form in water, ethanol and diethyl ether (Williams 1966).
Stability	Alpha isomer stable in sunlight (Williams 1966).

Applications:

History	Alpha-chloralose has been used as an anaesthetic in experimental animals due to its minimal depressant action on autonomic features (Balis and Monroe 1964, Thomas et al. 1988). It is marketed as a rodenticide (Alphakil) in West Germany and England, and is used as an avian control agent (both for stunning and lethal baiting) with research conducted in France, then England and United States (Thearle 1960, Murton 1962, Williams 1966) (Caithness 1968).
Uses in Australia	Registered for use as bird control agent against pigeons (*Columba livia*) and sparrows (*Passer domesticus* and *P. montanus*). A number of minor use permits are current for a variety of nuisance or exotic bird species in different states and territories. Also registered for indoor use against mice (*Mus* sp.) by authorised personnel.
Poison Schedule	Australia – Schedule 6 poison Restricted chemical product
Formulation types	Bait powder concentrate and bait blocks

Toxicology:

Absorption	Absorbed through the gastrointestinal tract.
Mode of action	Alpha-chloralose acts primarily a depressant of the central nervous system, although in some species it may have a stimulant action, causing involuntary

	muscle twitching and convulsions (Balis and Monroe 1964). This toxin metabolises in the body to chloral, which in turn is converted largely to trichloroethanol which anesthetises the cortical centres of the brain; retarding metabolic processes, reducing blood pressure, lowering the body temperature, and rendering the dosed animal immobile and in coma-like state. The hypothermic effect is more marked on smaller animals due to their greater body surface to volume ratio. Recovery is possible for sub-lethally dosed animals, but over-dosage results in death. It is primarily effective below 15.6^{o}C (Cornwell and Bull 1967, Lees 1972). Alpha-chloralose may also cause hyperexcitability, producing muscle tremors and convulsions. The severity of these symptoms is species specific, but also depends on the concentration of the toxin, and the mode of administration (Balis and Monroe 1964). In humans there are reports that chloralose is not metabolised in the body but excreted mainly unchanged, and the features of over-dosage include generalised convulsions and coma (Thomas et al. 1988).
Latent period	Time to narcosis in birds is dependant on dose rate but usually 7-30 minutes (Ridpath et al. 1961, Murton et al. 1963, Williams 1966, Crider and McDaniel 1967, Caithness 1968, Cline and Greenwood 1972, Cyr 1977). In mice (*Mus* sp.) the latent period is dependent on dosage and bait presentation occurring from 5-25 minutes (Greaves et al. 1968).
Symptoms	In birds the first symptoms include cessation of activity, uncoordinated and sluggish reflexes, slightly drooping wings and ruffled feathers (though still capable of flight) and slowly blinking eyes. Some species also display wing shuddering, muscle twitching and slight convulsive movements. Deepening anaesthesia develops gradually and after about an hour affected birds stand in a hunched position or sink to rest on their breasts. Frequent periods of dozing move to a more deep sleep with head drooped and eyes closed. Birds generally remain still except for occasional periods of wing and tail flapping. Time to full anaesthesia (sleep) varies with species and dose, and if overdosed the affected bird will remain motionless, even when touched, and die without regaining consciousness (Williams 1966, Crider and McDaniel 1967, Caithness 1968, McGinnis et al. 1972, Cyr 1977). In cats (*Felis catus*) and dogs (*Canis lupus familiaris*) symptoms include hyper-excitement, uncoordinated movements especially in the hind legs, followed by drowsiness. Most animals recovered within 12 hours (Balis and Monroe 1964, Stopforth 1970).
Time to death	Dependent on dose. High dose, relatively quick with no disturbance (Caithness 1968)
Detoxification and excretion of sub-lethal doses	This toxin is metabolised to chloral, then converted largely to trichloroethanol which combines with glucuronic acid in the liver to form inactive urochloralic acid. This is readily excreted in the urine (Murton 1963, Lees 1972).
Accumulation of sub-lethal doses	Alpha-chloralose is rapidly metabolised and does not accumulate.
Long term effects of sub-lethal doses	In the short term sub-lethal doses can stimulate mucus secretions and can cause dehydration. However if intoxicated birds are allowed to recover and are released in good condition then no further ill effects on health and breeding potential have been recorded (Murton et al. 1963, Williams 1966). The time to recovery is dependent on dose, species and age of bird (Cline and Greenwood 1972, Hofman and Weaver 1980, Holbrook and Vaughan 1985).

	Liver and kidney disorders may develop following repeated administration (Schafer 1981).
Tolerance	No tolerance reported in mice (*Mus* sp.); within days of eating a series of sub-lethal doses, they were still fully susceptible to alpha-chloralose (Cornwell and Bull 1967).
Resistance	No evidence of resistance to this pesticide has been reported.
Aversion	No development of bait shyness in birds has been observed. The affected birds emitted no distress call that warned other individuals (Crider and McDaniel 1967, Caithness 1968, Cyr 1977).
Antidote	There is no specific antidote for alpha-chloralose (Lees 1972).
Treatment	The principles of treatment are the removal of unabsorbed poison and the support of vital functions. Evacuation of the stomach by administering emetic, or gastric lavage will prevent further absorption. Sufficient warmth should be applied if required. Animals may need to be restrained to prevent injury when hyperexcited or administered antagonist drugs for convulsions if required. Artificial ventilation may be required in severe cases (Lees 1972, Thomas et al. 1988).
User safety	When preparing baits users are advised to wear elbow-length PVC gloves and protective clothing which should be washed after use. If skin is exposed wash thoroughly with soap and water.

Environmental fate**:**

Decay time in soils	Baits normally disappear within one week, but can persist longer, up to a maximum of 31 days. Settlement in soil seems to account for the disappearance (Murton et al. 1963).

Acute toxicity to vertebrate species:

The oral acute toxicity for a range of species is compared in Table 3. Different species of birds are more sensitive than others and it is thought this is partially due to anatomy of their digestive system, in particular possession of crop (Murton 1962, Murton et al. 1963, 1965). The toxicity is effected by the mode of administration, for example the LD_{50} for chickens (*Gallus gallus domesticus*) when injected is 80 mg/kg whereas the oral LD_{50} is much higher at around 300 mg/kg (McGinnis et al. 1972). There is no information available for reptiles and amphibians.

A concentration of 5 ppm was reported to have no effect on adult rainbow trout, (*Oncorhynchus mykiss*) and bluegill sunfish (*Lepomis macrochirus*) or larvae of sea lamprey (*Petromyzon marinus*) after 24 hours (Applegate et al. 1957).

The lethal dose in adult humans is considered to be around 1g/kg (20mg/kg in infants), although death is more likely due to complications of coma rather than a direct toxic effect of this toxin (Thomas et al. 1988).

Table 3. The sensitivity to alphachloralose for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of alphachloralose is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	300	0.02	6.0	(Cornwell 1969)
Brown rat, *Rattus norvegicus*	400	0.32	128	(Cornwell 1969)
Cat, *Felis catus*	100[a]	5.0	500 [a]	(Cornwell 1969)

Dog, *Canis lupus familiaris*	600-1000 [a]	16.0	9600-16000[a]	(Cornwell 1969)
Human, *Homo sapiens*	>1000 [a]	70	70000 [a]	(Thomas et al. 1988)
Introduced birds				
English sparrow, *Passer domesticus*	42	0.03	1.2	(Schafer 1972)
Chicken, *Gallus gallus domesticus*	300	2.8	840	(Loibl et al. 1988)
Mallard duck, *Anas platyrhynchos*	34-55	1.2	40.8-66	(Cline and Greenwood 1972, Schafer 1972, Woronecki et al. 1992)
Pigeon, *Columba livia*	131-215	0.27	35.4-58.1	(Thearle 1960, Ridpath et al. 1961, Schafer 1972, Woronecki et al. 1992)
Ring-necked pheasant, *Phasianus colchicus*	>100	1.2	>120	(Schafer 1972)
Starling, *Sturnus vulgaris*	75	0.07	5.3	(Schafer 1972)

[a] minimum lethal dose

Toxicity to invertebrate species:

No information was found on the toxicity of alpha-chloralose to invertebrates.

Non-target primary risk profile:

There have been reports of non-targets being killed (Table 4), primarily other species of birds but also small mammals, such as hedgehogs (Erinaceidae) and Koi goldfish (*Cyprinus* sp.). Larger bird species and mammals, such as cats (*Felis catus*) and dogs (*Canis lupus familiaris*) that are affected tend to recover fully (Copestake 1967, Caithness 1968, Snow and Sheppard 1968, Cyr 1977, Woronecki et al. 1990).

The risk can be reduced by best practice baiting practices including the collection of non-targets which can then be allowed to recover under suitable conditions (Ridpath et al. 1961, Murton 1962, Murton et al. 1963, Cyr 1977, Holbrook and Vaughan 1985, Woronecki et al. 1990). Recovery can be increased by irrigation or removal of stomach/crop contents of birds and keeping the victim warm (Williams 1966, Cyr 1977). Recovery of non-targets is not possible if the initial dose was too large.

Table 4. Reports of non-target primary poisoning after alphachloralose baiting.

Targeted Species	Bait presentation	Non-target Risk	Reference
Black-backed gull, *Larus dominicanus*	Bread spread with beef dripping – high dose 200mg	All non-targets (mallard ducks , rook, skylark, starling, sparrow & hedgehog) died except 3 cats who recovered.	(Caithness 1968)
Corvidae	Eggs	Hedgehog deaths from eating poisoned eggs	(van Nie 1975)
Starling *Sturnus vulgaris*, red-winged blackbird *Agelaius phoeniceus*, common grackle *Quiscalus quiscula* & cowbird *Molothrus ater*	Oat and corn baits scattered across fields	12 other species of birds including 9 protected species were caught. The smaller birds such as sparrows suffered the highest mortality, whilst larger birds recovered.	(Cyr 1977)
Mallard ducks *Anas platyrhynchos* and coots *Fulica americana*	Bread bait - golf course including pond	Sparrows, geese, other species of waterbird and Koi goldfish. The smaller birds such as sparrows suffered the highest mortality, whilst larger birds recovered. All affected fish died.	(Woronecki et al. 1990)
Canada geese *Branta canadensis*	Bread bait in park area	Four California gulls *Larus californicus* died	(Woronecki et al. 1990)

Non-target secondary poisoning risk profile:

Secondary poisoning from mice (*Mus* sp.) baiting programs is considered unlikely due to the rapid rate of detoxification, and the very small amount necessary to kill a mouse (Cornwell and Bull 1967). Overseas, buzzards (*Buteo buteo*) have been reported dying following bird control programs (Knapp and Russell 1973, van Nie 1975); however, the risk from poisoned birds is considered negligible for mammalian predators such as the fox (*Vulpes* sp.) as they would need to eat many bird carcasses including the crop contents before being affected (Murton 1963).

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Cholecalciferol

Chemical name: (3β,5Z,7E)-9,10-secocholesta-5,7,10(19)-trien-3-ol

Synonyms: Vitamin D_3, activated 7-dehydrocholesterol, toxiferol, calciol.

Source: Cholecalciferol is produced industrially for use in vitamin supplements and to fortify foods by the ultraviolet irradiation of 7-dehydrocholesterol extracted from lanolin found in sheep's wool or also from lichens (Wang et al. 2001).

Physical chemistry: (Marshall 1984, Pelfrene 2010)

Molecular wt	384.62
Formula	$C_{27}H_{44}O$
Physical form	Crystalline solid, forms tiny needles
Colour	White to light brown, amber
Melting point	84-86^{o}C
Solubility	Practically insoluble in water, soluble in acetone, chloroform and fatty oils
Stability	Very sensitive to UV radiation and will rapidly break down when exposed. Oxidised and inactivated by moist air within a few days.

Applications:

History	Developed in the 1970s as a commensal rodenticide either in combination with warfarin or by itself (Lund 1977, Marshall 1984, Brown and Marshall 1988). In the 1990s also used against field rodents in the US (Tobin et al. 1993, Witmer et al. 1995). Registered in 1995 in New Zealand for brushtail possum (*Trichosurus vulpecula*) control (Eason and Wickstrom 2001).
Uses in Australia	Control of rats (*Rattus* sp.) and mice (*Mus* sp.), particularly anticoagulant-resistant individuals. It can be deployed in and around buildings and also for perimeter baiting along fence-lines around buildings.
Poison Schedule	Australia: Schedule 7 poison
Formulation types	Grain and block bait

Toxicology:

Absorption	Absorbed through the gastrointestinal tract. Oral doses partially degraded in intestinal tract of rats so require larger dose than by intravenous injection (Frolick and Deluca 1973).
Mode of action	Results in an increase in circulating vitamin D metabolites, which disrupts calcium metabolism and produces hypercalcemia by promoting the resorption of calcium from bones and the intestinal absorption of calcium as well as decreasing calcium excretion by the kidneys (Jolly et al. 1993; Beasley et al. 1997). Calcium salts are deposited in blood vessels, soft tissues and organs. Death can be due to any of the following causes or a combination: kidney, heart or respiratory failure, or haemorrhaging from the calcification of blood vessels and internal organs (Dorman and Beasley 1989, Peterson et al. 1991).
Latent period	The onset of clinical signs of acute poisoning with cholecalciferol can appear within 14 hours, but usually takes 18 - 48 hours (Gunther et al. 1988, Dorman

	and Beasley 1989, Hatch and Laflamme 1989).
Symptoms	There is a gradual onset of symptoms which increases in severity over time. Clinical signs include depression, anorexia, vomiting, constipation, increased thirst and urination, hypertension, muscle weakness, gastrointestinal and pulmonary haemorrhages (Dorman and Beasley 1989). Poisoned rodents become lethargic, cease eating and grooming, become weak, dehydrated, and anorexic. They take on a hunched posture, show signs of severe discomfort, and very often became blind (Lund 1974). In mice (*Mus* sp.) this is followed by tremors, coma and death or gradual recovery (Hatch and Laflamme 1989). Rabbits (*Oryctolagus cuniculus*) lose appetite and weight (Eason 1993). Dogs (*Canis lupus familiaris*) become less active, lethargic, weak, anorexic, develop bloody vomit and faeces, become recumbent after 60 hours and can go into shock (Dale et al. 1932, Gunther et al. 1988).
Time to death	Time to death is dependent on the dose received. Death in rats (*Rattus* sp.) usually takes 2-6 days, although periods of up to 11 days have been recorded (Greaves et al. 1974, Lund 1974). Mice (*Mus* sp.) die within 3-21 days, (Hatch and Laflamme 1989), dogs (*Canis lupus familiaris*) within 65-77 hours (Gunther et al. 1988), rabbits (*Oryctolagus cuniculus*) within 4-8 days (Eason 1993) and brushtail possums (*Trichosurus vulpecula*) up to two weeks after dosing (Jolly et al. 1995).
Detoxification and excretion of sub-lethal doses	Metabolised in the liver to calcifediol (25-hydroxycholecalciferol) which is further metabolised in the kidney to produce calcitriol, the most active hormone of vitamin D_3, active in enhancing bone resorption and intestinal calcium transport. (Dorman and Beasley 1989, Brouwer et al. 1998).
Accumulation of sub-lethal doses	Death can occur after a single large dose, or smaller sub-lethal multiple doses which accumulate if time between repeated doses is less than time for metabolism. Sub-lethal doses of cholecalciferol and its metabolites can persist in adipose tissue (half-lives in rats 81 days) and are only released slowly in periods of energy balance (Brouwer et al. 1998).
Long term effects of sub-lethal doses	Sub-lethally dosed rodents can recover but are likely to be ill and anorexic for a period of several days to two weeks. There were no adverse effects on reproduction noted in rats (*Rattus* sp.), however female rabbits (*Oryctolagus cuniculus*) exhibited weight loss and there was an increase in resorption rate and neonatal mortality as well as deformed foetuses (McClain et al. 1980). Rabbits that survived doses regained appetite, weight and overall condition within 2 weeks of dosing, after some weight loss during the first week (Eason 1993). Suppression of appetite lasting 7-15 days in brushtail possums (*Trichosurus vulpecula*) (Morgan and Milne 2002). Reduced feed intake and leg abnormalities were apparent in chronically dosed sheep (*Ovis aries*) and were most pronounced in the aged ewes (Thomas et al. 1981).
Tolerance	No reports of tolerance to cholecalciferol were found.
Resistance	There is no evidence of resistance to this pesticide.
Aversion	No aversion has been reported in rodents (Greaves et al. 1974) (Lund 1977, Marshall 1984). Some bait shyness was reported in rats (*Rattus* sp.) after being fed sub-lethal doses, however the response was thought to be towards the bait carrier

	rather than the toxin itself (Rennison 1977, Prescott et al. 1992). Some aversion has been shown in rabbits (*Oryctolagus cuniculus*) (Henderson and Eason 2000). 20% of brushtail possums (*Trichosurus vulpecula*) tested developed bait shyness when feed sub-lethal baits of this toxin despite inducing toxicoses at a relative slow rate (>24 hours) and this was strongly influenced by dose with higher doses resulting in greater shyness. The persistence of this bait shyness has not been tested (Morgan and Milne 2002, Morgan et al. 2002).
Antidote	No specific antidote has been recorded, however sodium- or magnesium sulphate appears to have some effect (Lund 1977). Also treatment with Na_4EDTA or cytochrome P-450 inhibitors metyrapone or chloramphenicol has reduced mortality and increased survival time in mice (Hatch and Laflamme 1989).
Treatment	Aims are to decrease absorption (emesis, gastric lavage activated charcoal), correct fluid and electrolyte imbalances and initiate specific therapy to reduce hypercalcemic state (diuresis by use of furosemide and administration of corticosteroids). Seizure control and other symptomatic therapies may be required. Regime should be maintained for at least two weeks, along with a low calcium diet (Gunther et al. 1988, Dorman and Beasley 1989, Fooshee and Forrester 1990).
User safety	Users should wear protective clothing and gloves which should be washed after use. If skin is exposed wash thoroughly with soap and water.

Environmental fate:

There is no published data on the fate of cholecalciferol in soil and water. However studies on the fate of baits vary, with Greaves et al. (1974) reporting that in rodent baits this toxin tends to decompose in the presence of air and moisture and toxicity of damp baits deceases significantly within a week. In possum baits both Booth et al. (1999) and Morgan (2004) found that there was little decline in cholecalciferol levels in baits exposed to rain, with small quantities of the toxin found in the soil underneath the baits.

Acute toxicity to vertebrate species:

The acute oral toxicity varies between species and between sexes within species (Table 5). Brushtail possums (*Trichosurus vulpecula*) and rabbits (*Oryctolagus cuniculus*) are particularly sensitive (Eason 1991, 1993, Jolly et al. 1995). Black rats (*Rattus rattus*) are more susceptible than brown (*R. norvegicus*) (Bai et al. 1978). Cats (*Felis catus*) are less susceptible and toxicity less consistent with some individuals surviving doses up to 200 mg/kg while others died after doses of 50 mg/kg (Eason 1991). Some fish-eating marine mammals such as seals are quite tolerant as they have a faster metabolism and high capacity to store Vitamin D in blubber mass (Keiver et al. 1988).

Birds are not so sensitive (Marshall 1984). Three out of four chickens (*Gallus domesticus*) and one out of four canaries (*Serinus canaria domestica*) died when given 2000mg/kg, while all mallard ducks (*Anas platyrhynchos*) survived (Eason et al. 2000).

Table 5. The sensitivity to cholecalciferol for a range of species expressed as the single dose oral median lethal dose (LD_{50}). The amount of cholecalciferol is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	42.5-136.4	0.02	0.85-2.7	(Marshall 1984) (Hatch and Laflamme 1989)
Brown rat, *Rattus norvegicus* (lab. strain)	43.6	0.32	14.0	(Marshall 1984)

Rabbit, *Oryctolagus cuniculus*	4-9	1.6	6.4-14.4	(Eason 1993, Henderson and Eason 2000)
Cat, *Felis catus*	50-200	5.0	250-1000	(Eason 1991)
Dog, *Canis lupus familiaris*	88[a]	16.0	1408	(Marshall 1984)
Native mammals				
Brushtail possum, *Trichosurus vulpecula*	15-30	3.5	52.5-105	(Eason 1991) (Jolly et al. 1995)
Birds				
Mallard duck, *Anas platyrhynchos*	>2000	1.2	>2400	(Eason et al. 2000) (Marshall 1984)

[a] LD_{50} reported in literature, however several other authors have reported deaths to doses between 3-20 mg/kg (Gunther et al. 1988, Dorman and Beasley 1989, Talcott et al. 1991).

Toxicity to invertebrate species:

No insecticidal effects were recorded when fed to weta (Eason et al. 2000). There are no other reports of the effect of this toxin on invertebrates.

Non-target animals are at risk during a baiting campaign using this toxin. Short-term population declines were recorded in three rodent species, squirrels, voles and chipmunks after field baiting for Pocket gophers (*Thomomys* sp.), however there were no long term changes (Rizor et al. 2006).

There have been dog (*Canis lupus familiaris*) deaths (Fooshee and Forrester 1990, Talcott et al. 1991), while others have recovered with treatment. There are also reports of cat (*Felis catus*) deaths (Peterson et al. 1991), although many poisoned cats have recovered as they are less likely to consume large quantities of bait (Moore et al. 1988).

Non-target secondary poisoning risk profile:

Although cholecalciferol is relatively persistent in brushtail possums (*Trichosurus vulpecula*) and rats (*Rattus* sp.) (Eason et al 1996, Brouwer et al. 1998) the risk of secondary poisoning is considered low. Research in rats has shown this toxin is partially degraded in the intestinal tract (Frolick and Deluca 1973), and hence not all cholecalciferol present would be bioavailable to animals eating the poisoned carcasses. In a trial no dog (*Canis lupus familiaris*) deaths were reported after being fed poisoned rats (Marshall 1984).

There is no data on persistence in brushtail possums (Eason et al. 2000), although cats (*Felis catus*) fed poisoned possums over six days showed no changes in behaviour, appetite or body weight (Eason et al. 1996). Dogs (*Canis familiaris*), however, did show signs of kidney damage, and although no deaths were recorded there is a slight risk to these animals if they repeated ate poisoned carcasses (Eason et al. 2000).

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Cyanide

Cyanides are defined as organic and inorganic compounds that contain the –C≡N grouping. In pest control only the simple cyanides or alkali water-soluble salts such as potassium cyanide (KCN) and sodium cyanide (NaCN) are used. In all cases, the primary toxic agent is free cyanide (i.e. the sum of the molecular hydrogen cyanide (HCN) and the anion CN^-), which is produced when these salts react with acids in the stomach and oral mucosa.

Chemical name: cyanide

Synonyms: hydrocyanic acid, prussic acid

Source: Cyanide and its compounds occur naturally, but can also be synthesised. There are over 130 species of Australian plants that contain cyanogenic glycosides (Everist 1981).

Physical chemistry: (Towill et al. 1978, Eisler 1991)

	Hydrogen cyanide	Potassium cyanide	Sodium cyanide
Formula	HCN	KCN	NaCN
Molecular wt	27.13	65.12	49.01
Physical form	Gas or liquid	Solid	Solid
Colour	Colourless	White	White
Odour	Similar to 'bitter almonds' (only detected by 20-40% of humans)		
Melting point	-13.2 ^oC	635 ^oC	564 ^oC
Solubility	Extremely soluble in water	Soluble in water	Soluble in water, slightly soluble in alcohol
Stability	Free HCN is very reactive	Reacts with acid to form HCN	Reacts with acid to form HCN

Applications:

History

Natural occurring sources of cyanide, such as 'bitter almonds' and cherry laurel leaves, have been known for their toxic properties for thousands of years. It was first synthesised in 1782 by the Swedish chemist Scheele, although it was not recognised as the same compound found naturally until 19 years later (Sykes 1981). Cyanide has been used as a vertebrate poison against many species of mammals including rodents, possums, wallabies and predators such as coyotes and foxes.

Uses in Australia

Neither potassium or sodium cyanide are currently registered for use against pest animals in Australia, although potassium cyanide can be used under special permit in Queensland for the control of brushtail possums (*Trichosurus vulpecula*) on the Keppel Islands.

Both these cyanide compounds have previously been granted permits for particular research projects. They have been used to sample red fox (*Vulpes vulpes*) and pig (*Sus scrofa*) populations, and are being investigated for use in free-ranging dog (*Canis* sp.) and fox trapping, and in association with mechanical ejectors.

Poison Schedule

Australia: Schedule 7 poison

Formulation types

potassium or sodium cyanide salts

Toxicology:

Absorption	Cyanide is rapidly absorbed through inhalation, ingestion or skin contact (Egekeze and Oehme 1980, Ballantyne 1984).
Mode of action	Cyanide produces acute anoxia of the central nervous system and disrupts energy metabolism by inactivating the cytochrome oxidase enzyme preventing the transfer of oxygen in cellular respiration (Kreb's cycle). Acute toxicity is the result of rapid suffocation as the body is deprived of oxygen, although other mechanisms may also be involved (Solomonson 1981).
Latent period	Onset of symptoms is rapid, within 15 seconds up to 10 minutes (Gettler and Baine 1938, Sterner 1979, Ballantyne 1984, Wiemeyer et al. 1986, Gregory et al. 1998).
Symptoms	Symptoms after mild exposure are variable and can include headaches, giddiness, salivation, nausea, vomiting, breathing difficulties, weakness, lethargic, loss of coordination and irritation of the eyes, nose and throat. Severe poisoning may result in convulsions, paralysis, loss of consciousness, cessation of respiration and cardiac arrest (Humphreys 1978, Wiemeyer et al. 1986, Yen et al. 1995, Marks and Gigliotti 1996, Gregory et al. 1998, Eason et al. 2010).
Time to death	In birds and mammals large doses result in rapid death, usually occurring within 1-41 minutes (Lazarus 1956, Bell 1972, Sterner 1979, Ballantyne 1984, Wiemeyer et al. 1986, Gregory et al. 1998, Eason et al. 2010). Animals receiving smaller doses may take up to 1-3 hours to die (Gettler and Baine 1938).
Detoxification and excretion of sub-lethal doses	Sublethal doses of cyanide can be detoxified by several pathways (Towill et al. 1978, Egekeze and Oehme 1980). The primary pathway in higher animals is through the liver where cyanide reacts with thiosulphate in the presence of rhodanese to produce the comparatively nontoxic thiocyanate, which is mostly excreted in the urine (Pettigrew and Fell 1972). Small amounts can be eliminated unchanged through the lungs (Friedberg and Schwarzkopf 1969).
Accumulation of sub-lethal doses	Not accumulative in animal tissues (Eisler 1991).
Long term effects of sub-lethal doses	In laboratory tests a brushtail possum (*Trichosurus vulpecula*) which survived cyanide dosing recovered and subsequently appeared normal (Gregory et al. 1998). Sub-lethally dosed mice (*Mus* sp.) showed signs of impaired locomotor activity and neuronal damage (Kanthasamy et al. 1994). Many human survivors of mild intoxication appear to recover with no adverse affects, however where recovery has occurred after long-term, high sub-lethal doses there have been reports of thyroid enlargement and neurological consequences including dystonia, extrapyramidal syndromes, personality changes and memory defects (Solomonson 1981, Grandas et al. 1989, Valenzuela et al. 1992, Yen et al. 1995). Many studies have indicated that exposure to low concentrations of cyanide causes reproductive abnormalities in fish (Lind et al. 1977, Kimball et al. 1978, Lesniak and Ruby 1982).
Tolerance	No evidence of cyanide tolerance has been reported.
Resistance	No evidence of resistance to cyanide has been reported.
Aversion	Brushtail possums (*Trichosurus vulpecula*) have developed bait shyness when feed sub-lethal baits containing KCN paste and this was proportional to

	the doses received. This bait shyness persisted for at least 24 months (Warburton and Drew 1994, O'Connor and Matthews 1997, Gregory et al. 1998, Morgan et al. 2002).
Antidote	There are a variety of compounds used as cyanide antidotes and their use is determined by the nature of exposure and the severity of the poisoning (Rose et al. 1947, Bain and Knowles 1967, Hillman et al. 1974, Egekeze and Oehme 1980, Way 1981, Meredith et al. 1993): Thiosulphate (given as sodium thiosulphate) is a substrate for the enzyme rhodanese which converts cyanide to the less toxic thiocyanate. Nitrites (e.g. sodium or amyl nitrite) and various amino- compounds such as 4-dimethylaminophenol, and para-aminopropiophenone, convert haemoglobin to methaemoglobin which has a high affinity for cyanide. Methaemoglobin generation should be monitored so that oxygen transport to cells is not impaired, and can be corrected with methylene or toluidine blue. Cobalt compounds in the form hydroxycobalamin or as cobalt edetate react with cyanide to form non-toxic compounds. Oxygen is an important first-aid measure but it has been shown to offer some protection against cytochrome oxidase inhibition.
Treatment	Treatment must be commenced without delay. If the victim is conscious and the cyanide has been swallowed vomiting should be induced. If no breathing or pulse is detected cardio pulmonary resuscitation should be commenced immediately. The appropriate antidote should be administered and appropriate supportive care given (Meredith et al. 1993, Marks and Gigliotti 1996).
User safety	Cyanide is easily transformed into the gaseous HCN so inhalation poses a great risk to operators. Users should wear a respirator, latex or PVC gloves, protective clothing and footwear. They should carry a cyanide first aid kit and oxygen resuscitation kit (Marks and Gigliotti 1996).

Environmental fate:

Decay time in soils	Cyanide is not strongly adsorbed or retained within soils and leaching into the surrounding ground water will probably occur. Under aerobic conditions in soils, cyanide salts are microbially degraded to nitrites or form complexes with trace metals. Under anaerobic conditions, cyanides denitrify to gaseous nitrogen compounds that enter the atmosphere (Marrs and Ballantyne 1987).
Aquatic systems	Cyanide has low persistence in surface waters under normal conditions but may persist in ground water. Loss of cyanide is primarily through volatilization, sedimentation and microbial degradation. Some of the more complex cyanide compounds require sunlight to degrade (Marrs and Ballantyne 1987).
Atmosphere	Under normal conditions cyanide has relatively low persistence in air, usually between 30-365 days (Wade 1924) although some atmospheric HCN may persist for up to 11 years (Marrs and Ballantyne 1987).
Effects on plants	Although some plant species produce cyanide (present as cyanogenic glycosides), cyanide is toxic to other species, inhibiting respiration, germination and growth (Solomonson 1981).
Effects on microorganisms	There are many species of bacteria, fungi and algae that are able to metabolise and detoxify this toxin. Other species can be adversely affected (Castric 1981).

Acute toxicity to vertebrate species:

Cyanide is very toxic to all vertebrate species (Tables 6 and 7). This toxicity is affected by the method of administration and hence the absorption rate (Ballantyne 1984). This is illustrated in Table 8 which compares the sensitivity of rabbits (*Oryctolagus cuniculus*) by various routes of exposure. In humans the oral lethal dose of hydrogen cyanide is between 0.7-3.5 mg/kg (Halstrøm and Møller 1945), however the LC_{50} by inhalation is 748 mg/L (exposure time five minutes) or 220 mg/L (exposure time 30 minutes) (Hilado and Cumming 1977).

There is a difference in toxicity among bird species with predator species seemingly more vulnerable; e.g. the sodium cyanide LD_{50} of the Amercian kestrel (*Falco sparverius*) is 4.0 mg/kg compared to the domestic chicken (*Gallus gallus domesticus*), which is - 21 mg/kg (Wiemeyer et al. 1986). Sensitivity in fish is affected by temperature and oxygen levels. For most fish species juveniles are the most sensitive life stage and eggs more resistant (Smith et al. 1978).

Table 6. The sensitivity to cyanide for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of cyanide is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	6.4[a]	0.02	0.13	(Thomas and Ross 2007)
Rat - unspecified	10[b] 6.4[c]	0.32	3.2 2.1	(Gaines 1969) (Egekeze and Oehme 1980)
Brown rat, *Rattus norvegicus* (lab. strain)	7.5[b] 5.7[c] 4.2[d]	0.32	2.4 1.8 1.3	(Ballantyne 1984)
Rabbit, *Oryctolagus cuniculus*	5.8[b] 5.1[c] 2.5[d]	1.6	9.3 8.2 4	(Lazarus 1956, Ballantyne 1984)
Dog, *Canis lupus familiaris*	Min. LD 1.1[b]	16.0	17.6	(Gettler and Baine 1938)
Human, *Homo sapiens*	LD 0.7-3.5[d]	70	140	(Halstrøm and Møller 1945)
Native mammals				
Brushtail possum, *Trichosurus vulpecula*	8.7[c]	3.5	30.4	(Bell 1972)
Introduced birds				
Chicken, *Gallus gallus domesticus*	21[c]	2.8	58.8	(Wiemeyer et al. 1986)
Mallard duck, *Anas platyrhynchos*	2.2-3.3[c]	1.2	2.6-4.0	(Eisler 1991)
Starling, *Sturnus vulgaris*	17[c]	0.07	1.2	(Wiemeyer et al. 1986)

[a] unknown form of cyanide, [b] potassium cyanide, [c] sodium cyanide, [d] hydrogen cyanide

Table 7. The sensitivity to cyanide for a range of aquatic vertebrate species expressed as the median lethal concentration (LC_{50}) in micrograms of hydrogen cyanide per litre of water, where 50% mortality occurred within 96 hours.

Species	LC_{50} (µg/L)	Time (hours)	Water Temp. (°C)	Reference
Fish				
Bluegill sunfish, *Lepomis macrochirus*	75-125 180	96	8.4-25.1 18	(Smith et al. 1978) (Patrick et al. 1968)
Fathead minnow, *Pimephales promelas*	83-137	96	15-25.2	(Smith et al. 1978)
Rainbow trout,	57	96	10	(Smith et al. 1978)

Oncorhynchus mykiss				
Yellow perch, *Perca flavescens*	76-108	96	15-21.4	(Smith et al. 1978)

Table 8. The sensitivity to HCN, NaCN and KCN to rabbits (Oryctolagus cuniculus) by various routes of exposure (after Ballantyne 1984).

Route of administration	Form	LD_{50} (mg/kg)
Intravenous	HCN NaCN KCN	0.6 1.2 1.9
Intramuscular	HCN NaCN KCN	0.5 1.6-1.7 3.1-3.3
Intraperitoneal	HCN NaCN KCN	1.7-2.0 2.8-2.9 3.6-4.0
Oral	HCN NaCN KCN	2.5 5.1 5.8
Conjunctival instillation	HCN NaCN KCN	1.0 5.1 7.9
Percutaneous (intact skin)	HCN NaCN KCN	6.9 14.6 22.3
Percutaneous (abraded skin)	HCN NaCN KCN	2.3 11.3 14.3

Toxicity to invertebrate species:

Invertebrates can be poisoned by cyanide however knowledge of the toxicity levels is limited, especially for non-aquatic species. Many species can metabolise cyanide, and several species of centipedes, millipedes and insects produce this toxin (Duffey 1981).

Table 9. Sensitivity of cyanide to aquatic invertebrate species, expressed as the median lethal concentration (LC_{50}) in micrograms of hydrogen cyanide per litre of water where 50% mortality occurred within 96 hours.

Species	LC_{50} (µg/L)	Time (hours)	Water Temp. (°C)	Reference
Water flea, *Daphnia magna*	TLm 400[a]	96	-	(Dowden and Bennett 1965)
Mysid shrimp, *Mysidopsis bahia*	113	96	23	(Lussier et al. 1985)
Snail, *Physa heterostropha*	432	96	20	(Patrick et al. 1968)

[a] potassium cyanide

Non-target primary risk profile:

Cyanide is a non-selective toxin, and although application methods used in pest control are fairly selective, there are reports of non-target deaths. Burrowing owls (*Athene cunicularia*) were found dead after using calcium cyanide in prairie dog (*Cynomys* sp.) burrows (Wade 1924). Deaths of many species of birds including kiwis, magpies, crows, ravens, wild turkeys, hawks, vultures and condors have been reported, along with mammal species such as raccoons, wood rats, opossums, skunks, dogs, cattle, bears and potoroos (Robinson 1943, Orr 1952, Beason 1974, Matheny 1976, Krynitsky et al. 1986, Green 2004).

Non-target secondary poisoning risk profile:

There are no reports of secondary poisoning from cyanide, probably owing to its rapid detoxification (Eisler 1991).

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Fenthion

Chemical name: *O*,*O*-dimethyl *O*-4-methylthio-*m*-tolyl phosphorothioate

Synonyms: Phosphorothioicacid, Bayer 29493, DRC-632

Not to be confused with fenthion ethyl (the ethyl analogue of fenthion $C_{12}H_{19}O_3PS_2$) sold under the trade name of Luci-Jet.

Source: Can be synthesised by condensation of 4-methylmercapto-m-cresol and dimethylphosphorochloridothionate.

Physical chemistry:

Formula	$C_{10}H_{15}O_3PS_2$
Molecular wt	278.34
Physical form	Oily liquid
Colour	Colourless (tech. brown)
Odour	Tech. weak garlic / rotting cabbage odour
Melting point	7.5 ^{o}C
Solubility	Soluble in water, very soluble in hexane, dichloromethane, toluene, and isopropanol.
Stability	Unstable in the presence of sunlight and air, completely degrading within one to three days, with the oxidation products rapidly decomposing themselves to non-insecticidal compounds (Metcalf et al. 1963). Relatively stable in acidic conditions, and moderately stable in alkaline conditions.

Applications:

History	Developed by Schrader in 1960 (Francis and Barnes 1963).
Uses in Australia	Primarily used to control pest insects in agricultural, commercial and domestic situations however is registered for used to control non-native pest birds in and around buildings by authorised personnel only.
Poison Schedule	Australia: Schedule 6 poison Restricted chemical product
Formulation types	Viscous liquid mixed in a special grease or gel for surface application. Kills the bird on contact through its feet or body.

Toxicology:

Absorption	Readily absorbed through the gastro-intestinal tract, skin and respiratory tract (Debackere 1964, Martindale 1977).
Mode of action	Fenthion acts as a cholinesterase inhibitor and neurotoxin. It affects the central nervous, cardiovascular and respiratory systems. Death from acute poisoning primarily occurs from asphyxiation or cardiac arrest.
Latent period	Symptoms can begin within minutes of coming into contact with the toxin, or be delayed for up to a few hours, depending on the dose received.

Symptoms	Different species vary in their symptoms, which can include respiratory congestion, rapid breathing and / or shortness of breathe, foamy salivation, sweating, tearing of the eyes, cramps and diarrhoea, restlessness, dizziness, tremors, loss of muscular control, convulsions and eventually paralysis and coma (Jolly 1957, Tucker and Crabtree 1970, Martindale 1977).
Time to death	Death generally occurs within 1-12 hours, although 24-72 hours have been recorded in some species. Time to death is more dependent on the route of administration rather than the actual dose received (Jolly 1957, Francis and Barnes 1963).
Detoxification and excretion of sub-lethal doses	Fenthion is metabolised and excreted relatively quickly. Some of the oxidative metabolites are also toxic (Metcalf et al. 1963). Excretion occurs mainly in the urine, with only a small amount in the faeces (Brady and Arthur 1961, Debackere 1964, Knowles and Arthur 1966).
Accumulation of sub-lethal doses	Fenthion and its oxidative metabolites tend not to accumulate in the tissues. In rats residues are negligible after three days (Brady and Arthur 1961). However recovery of cholinesterase levels is slow, and repeated exposure can have an accumulative effect if the time between doses is less than the time for the affected acetylcholinesterase enzyme to be replaced and the cholinesterase levels to return to normal. Young animals are more susceptible as they already posses a low cholinesterase level (Jolly 1957).
Long term effects of sub-lethal doses	No permanent damage or side effects have been noted in mammals treated systemically with this insecticide. Recovery after toxic reaction is complete (Jolly 1957, Unwin 1965). Reduced fertility of eggs in mallard ducks (*Anas platyrhynchos*) has been reported (Tucker and Crabtree 1970).
Tolerance	No evidence of tolerance to fenthion has been found.
Resistance	The occurrence of resistance in vertebrates to fenthion has not been reported.
Aversion	No evidence of aversion to fenthion has been reported.
Antidote	Atropine is the accepted antidote, blocking the transmission of the nerve impulses and alleviating some of the symptoms. The oxim 2-pyridine-aldoxim-methyl-iodide (2-PAM) is used afterwards to help regenerate affected enzymes and thus speed recovery (Jolly 1957, Debackere 1964).
Treatment	Rapid treatment is essential. Ingested material can be removed by gastric lavage or activated charcoal, while animals that have been dipped or sprayed should be washed with soap and water. Atropine needs to be administered until symptoms have abated. Assisted respiration and oxygen may be needed. Convulsions treated with appropriate medication if required (Jolly 1957, Solly 1971, Martindale 1977).
User safety	Will irritate eyes and skin so user should wear protective clothing, especially rubber gloves. If contaminated wash thoroughly with water. Clothes and gloves should be washed after day's use.

Environmental fate:

Decay time in soils	In soil fenthion degradation ranges from 4-6 weeks, occurring through photodegradation as well as anaerobic or non-photolytic organisms. Soil particles adsorb fenthion reducing its leaching potential.

Aquatic systems — Fenthion is very toxic to aquatic organisms, particularly invertebrates, and dependent on concentration may cause long-term adverse effects in the aquatic environment. It is degraded primarily by light and microorganisms present in the water, and is affected by pH and temperature. In the atmosphere half-life is 5 hours, while the half-life in various water bodies ranges between 3-21days (Wang et al. 1989).

Effects on plants — Fenthion is metabolised rapidly by plants, primarily by oxidation. This process is faster in the presence of sunlight and air, and the metabolites are quickly degraded (Brady and Arthur 1961, Metcalf et al. 1963).

Acute toxicity to vertebrate species:

Fenthion is a broad spectrum organophosphorus insecticide which is moderately toxic to mammals and fish, and highly toxic to birds (Table10). Female rats (*Rattus* sp.) have been found to be more tolerant than males (Francis and Barnes 1963, DuBois and Kinoshita 1964, Clarke 1976). Fenthion at lower and higher dosages resulted in only slight or non mortality of mosquito fish (*Gambusia affinis*) after 48 hours so considered safe (Mulla 1961).

Table 10. The sensitivity to fenthion for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of fenthion is calculated using the average male body weights derived from McIlroy 1984, Strahan 1991.

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	150-190	0.02	3-3.8	(Francis and Barnes 1963)
Rat - unspecified	178-615	0.32	57-197	(Francis and Barnes 1963, Buck et al. 1976, Clarke 1976)
Brown rat, *Rattus norvegicus* (lab. strain)	190-310	0.32	61-99	(DuBois and Kinoshita 1964, Jones et al. 1968, Gaines 1969)
Rabbit, *Oryctolagus cuniculus*	150-175	1.6	240-280	(Francis and Barnes 1963)
Sheep, *Ovis aries*	25-50	50	1250-2500	(Buck et al. 1976)
Cattle, *Bos primigenius*	20-25	500	10000-12500	(Buck et al. 1976)
Horse, *Equus caballus*	>20	700	>14000	(Buck et al. 1976)
Birds				
English sparrow, *Passer domesticus*	5.6-22.7	0.03	0.16-0.66	(Tucker and Crabtree 1970, Schafer et al. 1973)
Chicken, *Gallus gallus domesticus*	15-40	2.8	42-112	(Francis and Barnes 1963, DuBois and Kinoshita 1964)
Domestic pigeon, *Columba livia*	1.8-4.6	0.27	0.49-1.24	(Tucker and Crabtree 1970)
Mallard duck, *Anas platyrhynchos*	5.9	1.2	7.1	(Tucker and Crabtree 1970)
Ring-necked pheasant, *Phasianus colchicus*	17.8	1.2	21.4	(Tucker and Crabtree 1970)
Starling, *Sturnus vulgaris*	5.3-17.8	0.07	0.37-1.2	(Schafer 1972)

Toxicity to invertebrate species:

Fenthion is toxic to most invertebrates and has been used widely for the control of many pest species and parasites such as flies, mosquitoes and ticks (Jolly 1957, Unwin 1965, Wang et al. 1989).

Table 11. Sensitivity of fenthion to invertebrate species, expressed as either the Median Lethal Dose (LD_{50}), the Median Lethal Concentration (LC_{50}) or the Median Effective Concentration (EC_{50}).

Species	Sensitivity	Reference
Honey bee, *Apis mellifera*	LD_{50}: 0.16 µg/bee	(Tomlin 2009)
Worm, *Eisenia foetida*	LC_{50} : 375 mg/kg dry soil	(Tomlin 2009)
Water flea, *Daphnia pulex*.	EC_{50} (3hr, 10°C): 2.7	(Hashimoto and Nishiuchi 1981)
	EC_{50} (3 hr, 25°C): 0.033	(Hashimoto and Nishiuchi 1981)
Algae, *Scenedesmus subspicatus*	EC_{50} :1.79	(Tomlin 2009)

Non-target primary risk profile:

The risk of non-target bird mortality is high. There are reports from overseas of non-target bird and small mammal fatalities when their habitats where sprayed for insect control (Seabloom et al. 1973, Zinkl et al. 1981, DeWeese et al. 1983) and pest bird control (Bruggers et al. 1989). There are no published reports of non-target deaths when this toxin has been applied on surfaces. McKenzie et al. (1996) suspect this toxin was used in several cases in Queensland to deliberately contaminate food and poison a range of native bird species.

Non-target secondary poisoning risk profile:

The risk of secondary poisoning of avian predators is high. There have been several overseas reports of birds being killed or seriously debilitated after feeding on carcasses, on scavengers of carcasses, or on skin debris and hair from fenthion-treated livestock (Henny et al. 1987, Bruggers et al. 1989, Bowes et al. 1992). American kestrels (*Falco sparverius*) died after eating live sparrows (*Passer domesticus*) exposed previously to perches treated with fenthion, and hence were contaminated mainly on their feet (Hunt et al. 1991, 1992).

The residues from the mass mortality of insects could pose a risk to insectivorous birds (Bruggers et al. 1989).

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Para-aminopropiophenone

Chemical name: 1-(4-aminophenyl)-1-propanone

Synonyms: 4'-aminopropiophenone, *p*-aminopropiophenone, PAPP

Physical chemistry:

Formula	$C_9H_{11}NO$
Molecular wt	149.19
Physical form	Crystalline needles
Colour	Yellow
Melting point	140 ^{o}C
Solubility	Low solubility in water and many organic solvents (Coleman et al. 1960).
Stability	PAPP is both a ketone and an amine. Reacts with acids to form salts and water.

Applications:

History	PAPP was originally studied as a treatment for cyanide poisoning (Rose et al. 1947), but due to its high toxicity to dogs (*Canis* sp.) it has been evaluated as a potential agent for use against coyotes (*Canis latrans*) in the USA (Savarie et al. 1983), and more recently against a variety of mammalian predators in NZ and Australia.
Uses in Australia	The registration documents have been submitted for the use of this toxin against fox (*Vulpes vulpes*) and free-ranging dogs (*Canis* sp.) in Australia, however at the time of writing this document it was not yet commercially available.
Poison Schedule	Australia: Classification not specified as yet
Formulation types	Commercial prepared baits

Toxicology:

Absorption	Absorption primarily through ingestion. Can be administered orally, intravenously or subcutaneously.
Mode of action	Induces the formation of methaemoglobin by oxidising haemoglobin in the blood. This reduces the oxygen carrying capacity of blood, leading to anaemia and hypoxia/anoxia due to the inhibition of cellular respiration leading to lethal deficit of oxygen in the heart and brain (Vandenbelt et al. 1944, Marrs et al. 1991, Coleman and Coleman 1996).
Latent period	First behavioural symptoms have been observed to occur within 2-5 minutes in rodents (Scawin et al. 1984), 16-204 minutes for cats (*Felis catus*), foxes (*Vulpes vulpes*) and stoats (*Mustela erminea*) (Marks et al. 2004, Fisher et al. 2005, Murphy et al. 2007), and 5-8 minutes for ferrets (*Mustela putorius furo*) (Fisher and O'Connor 2007).
Symptoms	First visible signs are the pale appearance of gums and tongue or cyanosis (bluish discolouration of skin and mucous membranes). Breathing difficulties, nausea, vomiting, headache and dizziness, occur at methaemoglobin levels

	of >30%, while lethargy, stupor and deteriorating consciousness occur as methaemoglobin levels approach 55%. Higher levels may cause cardiac arrhythmias, circulatory failure and neurological depression, while levels of 70% and above are usually fatal (Vandenbelt et al. 1944, Coleman and Coleman 1996, Marks et al. 2004, Fisher et al. 2005, Fisher and O'Connor 2007).
Time to death	Death is relatively quick; stoats (*Mustela erminea*) within the hour of dosing (Fisher et al. 2005), cats (*Felis catus*) within 37-246 minutes (Lapidge et al. 2007, Murphy et al. 2007), ferrets (*Mustela putorius furo*) between 103-131 minutes (Fisher and O'Connor 2007), foxes (*Vulpes vulpes*) between 43-60 minutes (Marks et al. 2004, Lapidge et al. 2007), and dogs (*Canis* sp.) averaged two hours (Lapidge et al. 2007).
Detoxification and excretion of sub-lethal doses	PAPP is rapidly metabolised and excreted however there are differences between species in the metabolic pathways for this process (Wood et al. 1991). Most species metabolise PAPP primarily to non-toxic compounds in the liver for excretion in the urine, however some more susceptible species such as canids, produce more of one of the products para-hydroxy-aminopropiophenone (PHAPP) than others, leading to higher concentrations of methaemoglobin (von Jagow et al. 1966). Also there is a difference between species in being able to reduce methaemoglobin back to normal haemoglobin using the enzyme methaemoglobin reductase.
Accumulation of sub-lethal doses	PAPP does not accumulate in animal tissues.
Long term effects of sub-lethal doses	No evidence of any abnormal effects or pathological changes in mammals after sub-lethal exposure to PAPP (Lapidge 2004) (NWR 2006- commercial in confidence). However ravens (*Corvus* sp.) did show potential for debilitating effects and death (NWR 2006- commercial in confidence).
Resistance	There is no evidence of resistance to PAPP.
Aversion	There are no reports of aversion to PAPP.
Antidote	The effect of PAPP can be overcome by any agent that reduces methaemoglobin back to haemoglobin. A common antidote is methylene blue, administered both orally and intravenously.
Treatment	Treatment is most effective when initiated within 30 minutes. Any external contamination should be washed with soap and water. Vomiting can be induced only if patient conscious and it has been less than 30 minutes since the toxin was ingested. Otherwise activated charcoal should be used. Excretion can be promoted using saline or sorbitol and respiratory support or oxygen given if required. The antidote should be administered and blood monitored. If the patient does not respond to the antidote an exchange blood transfusion may be required. Dapsone-mediated chronic methaemoglobin formation can be reduced by coadministration of cimetidine to aid patient tolerance (Coleman and Coleman 1996).
User safety	When preparing baits users are advised to wear PVC gloves and protective clothing which should be washed after use. If skin is exposed wash thoroughly with soap and water.

Environmental fate:

PAPP is readily broken down in the soil and water by microorganisms (Southwell et al. 2011).

Acute toxicity to vertebrate species:

Mammalian carnivores and monitors (*Varanus* sp.) are more susceptible to PAPP than other species (see Table 12) due to the unique way that they metabolise PAPP. Birds tend to be less susceptible, although some species such as mallard ducks (*Anas platyrhynchos*) are adversely affected (Savarie et al. 1983, Eason et al. 2010).

There has been a sex difference detected in the response to PAPP in dogs (*Canis lupus familiaris*) and rats (*Rattus* sp.), with females more susceptible (Scawin et al. 1984, Bright et al. 1987). Also a difference has been reported between strains of laboratory mice (*Mus musculus*) and rats (*R. norvegicus*) (Savarie et al. 1983).

Table 12. The sensitivity to PAPP for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of PAPP is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	168-233 >5000	0.02	3.4-4.7 100	(Pan et al. 1983, Savarie et al. 1983)
Brown rat, *Rattus norvegicus* (lab. strain)	144[a] 177-475	0.32	46.1 56.6-152	(Scawin et al. 1984)
Ferret, *Mustela putorius furo*	15.5	2.0	31	(NWR 2006)
Stoat, *Mustela erminea*	9.3 37-95	0.4	3.7 14.8-38	(Pan et al. 1983, Savarie et al. 1983, Scawin et al. 1984)
Cat, *Felis catus*	5.6 20-34	5.0	28 100-170	(Fisher and O'Connor 2007)
Fox, *Vulpes vulpes*	<25.2 15.4[a]	6.5	<164 100	(Fisher et al. 2005)
Dog, *Canis lupus familiaris*	26-43	16.0	416-688	(Murphy et al. 2007)
Native mammals				
Fat-tailed dunnart, *Smiththopsis crassicaudata*	105[a]	0.015	1.6	(NWR 2006)
Brown antechinus, *Antechinus stuartii*	>571[a]	0.035	>20.0	(NWR 2006)
Bush rat , *Rattus fuscipes*	697[a]	0.125	87.1	(NWR 2006)
Brushtail possum, *Trichorus vulpecula*	>500 615[a]	3.5	>1750 2153	(Fisher et al. 2008) (NWR 2006)
Brown bandicoot, *Isoodon obesulus*	6.4[a]	0.85	5.4	(NWR 2006)
Tammar wallaby, *Macropus eugenii*	89	5	445	(Fisher et al. 2008)
Tasmanian devil, *Sarcophilus harrisii*	120[a]	8	960	(NWR 2006)
Spotted-tail quoll, *Dasyurus maculatus*	24.8[a]	5.0	124	(NWR 2006)
Dingo, *Canis familiaris dingo* (hybrid)	8.5[a]	16.0	136	(NWR 2006)

Introduced birds				
Mallard ducks, *Anas platyrhynchos*	32-38	1.2	38.4-45.6	(Fisher et al. 2008, Eason et al. 2010)
Starling, *Sturnus vulgaris*	>316	0.07	22.1	(Savarie et al. 1983)
Native birds				
Australian magpie, *Gymnorhina tibicen*	1387	0.32	444	(Eason et al. 2010)
Little Australian raven, *Corvus coronoides*	130[a]	0.61	79.3	(NWR 2006)
Silver gull, *Larus novaehollandiae*	>1000[a]	0.29	>290	(NWR 2006)
Native repitiles				
Rosenberg's goanna, *Varanus rosenbergis*	12	1.1	13.2	(Frappell and Andrewartha 2006)
Lace monitor, *Varanus varius*	3	4.3	12.9	(Frappell 2007)

[a] Calculated 80% increase in methaemoglobin concentration which was found to strongly correlate with LD_{50} values (NWR 2006).

Toxicity to invertebrate species:

PAPP is not toxic to earthworms and other soil dwelling invertebrates.

Non-target primary risk profile:

Although most species of non-target animals and birds are less susceptible to PAPP than the targeted mammalian carnivore species, there is still a slight risk of poisoning. A small number of native animals have been found to be at least as sensitive as foxes (*Vulpes vulpes*) (NWR 2006), however as most of them are herbivores they are unlikely to eat the meat-based baits. Goannas (*Varanus sp.*) appear to be the most vulnerable to PAPP baiting programs. The risk to this species can be managed by altering the timing and presentation of baits (e.g. baiting at cooler times when goannas are less active) (Frappell and Andrewartha 2006, Frappell 2007)

Non-target secondary poisoning risk profile:

Residue analysis has indicated that there is low risk of secondary poisoning due to the rapid degradation of this toxin and the low concentrations of PAPP in tissues of poisoned animals (Wood et al. 1991, Eason et al. 2010).

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Phosphorus

Chemical name: Phosphorus

Synonyms: yellow phosphorus, white phosphorus, elemental phosphorus

Physical chemistry:

There are two forms of elemental phosphorus yellow or white and red. The former is highly toxic while the latter is relatively non-poisonous.

Formula	P_4
Molecular wt	123.88
Physical form	Wax-like
Colour	Colour-less / white, in sunlight turns yellow
Taste	Distinct taste
Odour	Garlic-like odour
Melting point	44.2^{o}C
Solubility	Not soluble in water. Soluble in fat and organic solvents.
Stability	Oxidises when exposed to air to red phosphorus. Ignites at 30^{o}C in air, vapour emits a blue 'phosphorescent' glow. In solid state should be stored under water.

Applications:

History	Yellow phosphorus has been extensively used as a rodenticide (Doty 1945). In Australia it has been used against rats (*Rattus* sp.) in cane fields (Redhead 1968) and pigs (*Sus scrofa*), although it is currently being phased out, and is not recommended for use.
Uses in Australia	Currently only registered in Queensland and Northern Territory for the control of feral pigs (*Sus scrofa*).
Poison Schedule	Australia: Schedule 7 poison
Formulation types	Liquid concentrate

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, respiratory system and skin.
Mode of action	Causes severe burns, gastrointestinal irritation and liver and renal damage (Clarke and Clarke 1975).
Latent period	Symptoms develop 1-2 hours after ingestion (Clarke and Clarke 1975).
Symptoms	Initial symptoms include acute abdominal pain, salivation, vomiting and bloody diarrhoea. Animals appear to recover for a few hours or a few days only to relapse. This secondary phase is the result of liver and renal damage with additional symptoms including skin eruptions, jaundice, convulsions, collapse, coma and death (Clarke and Clarke 1975, Gumbrell and Bentley 1995). In fish, many species turn a red colour and show signs of extensive rupturing

	of red blood cells (Fletcher et al. 1970, Fletcher and Hoyle 1972). Other fish species show erratic swimming speeds and fish swim in a spiral motion with their heads pointed upwards (Zitko et al. 1970, Maddock and Taylor 1976).
Time to death	Time to death has been reported between 2 hours - 4 days (Lazarus 1956, Clarke and Clarke 1975).
Detoxification and excretion of sub-lethal doses	Phosphorus circulates in the blood at first but is gradually oxidised to phosphate. Some phosphorus is eliminated by the lungs (Clarke and Clarke 1975).
Accumulation of sub-lethal doses	Sub-lethal doses are cumulative. Aquatic invertebrates can accumulate this toxin in their tissues, however it is cleared rapidly (within seven days) when placed in non-contaminated water (Fletcher 1971, Maddock and Taylor 1976). Liver half-life in cod (*Gadus morhua*) is five hours, salmon (*Salmo salar*) around one hour (Fletcher 1974). Also found to accumulate in avian predators but cleared relatively quickly if phosphorus removed from diet (Nam et al. 1994).
Long term effects of sub-lethal doses	The feeding of sub-lethal doses to rats (*Rattus* sp.) has resulted in retardation of growth and bone development (Fleming et al. 1942). The effects of chronic poisoning in humans are different from those of acute poisoning, and include anaemia, bronchitis, loss of appetite, digestive complaints, slight jaundice, bleeding of the mucous, and necrosis of the mandible ('phossy jaw') (Heimann 1946).
Tolerance	There are no reports of any tolerance to phosphorus.
Resistance	There is no evidence of resistance to phosphorus.
Aversion	In chronic experiments the decreased uptake over time was thought to be related to distaste of toxin in the food (Fleming et al. 1942).
Antidote	There is no specific antidote (Gratz 1973).
Treatment	Treatment should be given immediately, firstly directed at removing the toxin by either washing any external contamination or gastric lavage using copper sulphate or alternatively potassium permanganate to render any remaining orally dosed phosphorus inert. General supportive care to maintain vital functions and combat shock should be administered including the use of appropriate drugs for seizure control and heart stimulation as required (Clarke and Clarke 1975, Simon and Pickering 1976).
User safety	Phosphorus is dangerous to handle as its effects are cumulative and severe skin burns can result from spontaneous ignition in air above 30^{o}C (Freeman et al. 1954, Gratz 1973). It should only be used in well ventilated areas as the vapour is corrosive and should not be inhaled. Users should wear protective clothing, elbow-length PVC or nitrile gloves. If skin contact is made, immediately wash area with soap and water. Wash hands and face immediately after use, and wash contaminated clothing and gloves after each day's use.

Environmental fate:

Decay time in soils	Phosphorus does not break down readily in the environment.

Aquatic systems	Phosphorus oxidises in water with a half-life of 2-7.5 hours, dependent on the degree of dispersion. Adsorption onto bottom sediment decreases the rate of oxidation (Zitko et al. 1970).
Effects on micororganisms	Phosphorus does not limit the reproduction of phytoplankton (Finenko and Krupatkina-Akinina 1974).

Acute toxicity to vertebrate species:

Yellow phosphorus is highly toxic to animals and humans (Table 13), and extremely toxic to fish (Table 14) when present in sea water or freshwater (Fletcher et al. 1970, Zitko et al. 1970, Fletcher and Hoyle 1972, Burrows and Dacre 1973, Maddock and Taylor 1976).

No oral LD_{50} values have been recorded for phosphorus, so the lethal doses for a range of vertebrate species are given in Table 13. Toxic doses vary considerably according to the state of the phosphorus (Clarke and Clarke 1975).

Table 13. The sensitivity to phosphorus for a range of species expressed as the oral lethal dose. The amount of phosphorus is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	Lethal dose (LD)(mg/kg)	Av body weight (kg)	LD (mg) / animal	Reference (LD data)
Introduced mammals				
Mouse, *Mus musculus*	25	0.02	0.5	(Cameron and Patrick 1966)
Rat, unspecified	6-100	0.32	2-32	(Cameron and Patrick 1966, Gratz 1973)
Rabbit, *Oryctolagus cuniculus*	4.7-12.5	1.6	7.5-20	(Frank and Issac 1910, Hirz 1913, Lazarus 1956, Cameron and Patrick 1966)
Cattle, *Bos primigenius*	1-4	500	500-2000	(Clarke and Clarke 1975)
Pig, *Sus scrofa*	0.5-3	70	35-210	(Clarke and Clarke 1975)
Dog, *Canis lupus familiaris*	3-6	16.0	50-100	(Clarke and Clarke 1975)
Human, *Homo sapiens*	1	70	70	(Diaz-Rivera et al. 1950)
Introduced birds				
Chicken, *Gallus gallus domesticus*	10	2.0	20	(Clarke and Clarke 1975)
Mallard duck, *Anas platyrhynchos*	*ca* 3	1.2	3.6	(Coburn et al. 1950)

Table 14. The sensitivity to phosphorus for a range of aquatic vertebrate species expressed as the median lethal concentration (LC_{50}) in milligrams per litre of water, where 50% mortality occurred within 96 hours. Results are from both static and continuous tests in fresh and salt water (as indicated).

Species	LC_{50} (mg/L)	Time (hours)	Temp. (^{o}C)	Test	Reference
Bluegill, *Lipomis macrochicus*	39.5	96	26	Static Fresh	(Isom 1960)
Atlantic salmon, *Salmo salar*	2.3	96	10-13	Cont. salt	(Fletcher and Hoyle 1972)
Cod, *Gadus morhua*	2.5	96	9-10	Cont. salt	(Zitko et al. 1970, Fletcher and Hoyle 1972)
Herring, *Clupea harenqus*	3.7	96	7-9	Static Salt	(Zitko et al. 1970)

Toxicity to invertebrate species:

Yellow phosphorus is very toxic to aquatic invertebrates when present in sea water or freshwater, however some species (e.g. lobsters) are more tolerant than fish (Zitko et al. 1970, Fletcher 1971). The lethal level

for lobster (*Homarus americanus*) is 40 µg/L, and the beach flea (*Gammarus oceanicus*) 3-4mg/L (Zitko et al. 1970).

Non-target primary risk profile:

There have been large numbers of aquatic animals and waterfowl deaths from phosphorus contamination of waterways, however the source of contamination has rarely, if at all, resulted from pest control activities that used this toxin (Fletcher et al. 1970, Racine et al. 1992).

Domestic animals such as dogs (*Canis lupus familiaris*), cats (*Felis catus*) and poultry have been reported being poisoned by consumption of rodent baits (Orr 1952, Buck et al. 1976). Humans, particularly children, are vulnerable (Simon and Pickering 1976).

Non-target secondary poisoning risk profile:

Aquatic invertebrates and fish can accumulate this toxin in their tissues (Fletcher 1971, Dyer et al. 1972), and other fish species have died from phosphorus poisoning after eating contaminated tissues (Fletcher 1973). High residues can remain in fish muscle, even after commercial processing and pose a risk to humans (Dyer et al. 1972).

There are reports of cats (*Felis catus*) being poisoned after eating contaminated rats (*Rattus* sp.)(Hughes 1952). Dogs (*Canis lupus familiaris*) have died from eating phosphorus-poisoned brushtail possums (*Trichosurus vulpecula*) in NZ (Gumbrell and Bentley 1995). Also deaths have been reported in animals consuming the vomit from poisoned animals.

Avian predators have been found with residues after feeding on contaminated prey (Nam et al. 1994, Roebuck et al. 1994). American kestrels (*Falco spaverius*) have died after eating poisoned birds (Sparling and Federoff 1997).

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Rotenone

Chemical name: (2*R*,6a*S*,12a*S*)-1,2,6,6a,12,12a-hexahydro-2-isopropenyl-8,9-dimethoxychromeno[3,4-*b*]furo[2,3-*h*]chromen-6-one

Synonyms: derris, derrin, nicouline, tubatoxin

Source: Rotenone is a natural plant toxin originally extracted from the roots of *Derris elliptica*. Current commercial sources include rosewood *Tephrosia* spp., cube or barbasco *Lonchocarpus* spp. and Rabbit's pea *Dalbergia paniculata* (Ling 2003).

Physical chemistry: (Haag 1931, Jones 1931, Tomlin 2009)

Formula	$C_{23}H_{22}O_6$
Molecular wt	394.43
Physical form	Orthorhombic crystals
Colour	Colourless to brownish crystals, or white crystalline powder
Melting point	163 – 166 ^{o}C
Solubility	Limited solubility in water. Readily soluble in most organic solvents including acetone, benzene, carbon disulphide, ethyl acetate and chloroform. Less readily soluble in diethyl ether, alcohols, petroleum ether and carbon tetrachloride. Crystallises from some solvents with the formation of solvates.
Stability	Unstable compound, readily oxidised especially in the presence of light and air.

Applications:

History	The insecticide and piscicide properties of the Derris root were known to the indigenous people of Southeast Asia and South America well before it was isolated by French chemists in 1895. It has been used as a commercial insecticide for more than 150 years and used for fish management in North America since the 1930's (Leonard 1939, McClay 2000, Ling 2003).
Uses in Australia	Registered for general use as insecticidal and acaricidal, but currently can be used to control pest fish populations under the APVMA off licence Permit 13011 in all states and territories except Victoria. Also currently used to control the Smooth Newt (*Lissotriton vulgaris*) in Victoria only.
Poison Schedule	Australia – Schedule 5 or 6 poison
Formulation types	Powder / dust (0.5% formulation), may be synergised with piperonyl butoxide (insecticide) and liquid solution (5% concentrate).

Toxicology:

Absorption	Rotenone is more toxic when inhaled or injected than when ingested. It is not absorbed by the skin in mammals and birds, but can penetrate the skin of snakes (Haag 1931, Ambrose and Haag 1936, Lehman 1949, Brooks et al. 1998).
Mode of action	Rotenone is a highly specific metabolic poison that inhibits the respiration of cells by blocking the mitochondrial electron transport, and

	thus ultimately depriving cells of oxygen and reducing the production of cellular energy (Lindahl and Öberg 1961, Perry and Conway 1977, Beasley 1997).
Latent period	Signs of intoxication may appear within a few minutes to a few hours, depending on the route of administration and size of dose, with oral administration being the slowest (Haag 1931).
Symptoms	In mammals and birds, symptoms are dependent on the route of exposure, causing gastric, pulmonary or skin irritation. Other symptoms include vomiting, lethargy, tremors, loss of muscle control, excessive urination, stupor, convulsive seizures, and respiratory failure (Haag 1931, Tucker and Crabtree 1970, Beasley 1997). In reptiles symptoms include gaping mouth, lethargy and respiratory distress (Brooks et al. 1998, Savarie et al. 2010). Symptoms in fish include erratic swimming, slow opercular movements, listlessness and loss of equilibrium, eventually sinking to the bottom where they remain until death (Rach and Gingerich 1986, Fajt and Grizzle 1993).
Time to death	Time to death in mammals and birds is dependent on route of administration and dose received. It can occur within hours of ingestion or may be delayed for as long as 10 days, with the critical period falling between the first and second day (Haag 1931, Lehman 1949, Tucker and Crabtree 1970). High doses kill snakes in 37- 55 minutes (Brooks et al. 1998, Savarie et al. 2010). Time to death in fish is dependent on the route of administration, exposure times, temperature, acidity and hardness of the water, and the size and species of the fish (Leonard 1939, Gilderhus 1972, Meadows 1973, Marking and Bills 1976, Hall 1988). Death in carp (*Cyprinus carpio*) has been recorded as occurring as quickly as 40 minutes when rotenone is added to water (entry via the gills), up to 16 hours when administered orally (Fajt and Grizzle 1993, 1998).
Accumulation, detoxification and excretion of sub-lethal doses	Sub-lethal doses of rotenone do not accumulate in animals, and this toxin is readily metabolised and excreted. The liver plays an important part in the detoxification of rotenone (Fukami et al. 1969), with some species able to process the toxin faster than others (Haag 1931, Rach and Gingerich 1986). Large oral doses usually stimulate vomiting in birds and mammals. These species generally recover from sub-lethal doses, although may suffer from slight symptoms such as mild diarrhoea and salivation, lasting several days (Haag 1931).
Long term effects of sub-lethal doses	The long term effects of sub-lethal doses have been studied in rats (*Rattus* sp.), rabbits (*Oryctolagus cuniculus*), dogs (*Canis lupus familiarus*), and guinea pigs (*Cavia porcellus*). Various degrees of liver damage was found in adult animals and retarded growth reported in young animals. Large doses over several months caused weight loss and haematological effects in rats and dogs. When rotenone was fed to pregnant guinea pigs, the young were either born dead, died within five days of birth or suffered from slow rate of growth, although no effect was noted in rats (Haag 1931, Ambrose et al. 1942, Marking 1988).
Tolerance	An increased tolerance to rotenone has been reported in mosquito fish, *Gambusia affinis* (Fabacher and Chambers 1972).

Resistance	Resistance to rotenone has been reported in some invertebrate species (Brown 1968, Mangum and Madrigal 1999).
Aversion	No aversion to this pesticide has been reported.
Antidote	There is no specific antidote for rotenone for birds and mammals. In the early stages of poisoning fish can be revived by transferring to clean, aerated water (Willis and Ling 2000). The addition of methyl blue reduces the inhibition of oxygen uptake (Lindahl and Öberg 1961) and has been used successful to revive non-target fish collected from treated waters (Bouck and Ball 1965). Once fish lose equilibrium however, it is usually impossible to revive them by any method (Ling 2003). Rotenone in water can be rapidly detoxified by the addition of a strong oxidising agent such as potassium permanganate (Marking and Bills 1976).
Treatment	In birds and mammals treatment usually involves support and symptomatic care. Priority is to reduce absorption, so depending on route of exposure either bathe with detergent, or use emetic, enterogastric lavage, activated charcoal, and saline cathartic (Beasley 1997).
User safety	Rotenone is far more toxic to humans if inhaled rather than swallowed so users should take precautions to reduce the risk of inhaling dust or aerosols. Contact with concentrated powders and liquids may also cause eye and skin irritation. Users are advised to wear full body protection including respirator mask, eye protection, protective clothing and gloves.

Environmental fate:

Rotenone is non-persistent in the environment, being broken down by heat, light and oxygen. The photodecomposition of rotenone produces a range of non-toxic by-products, with the exception of one, 6aβ,12aβ-rotenolone (Cheng et al. 1972).

Decay time in soils	Rotenone is adsorbed strongly to organic matter in soil and is rapidly degraded (Dawson et al. 1991).
Aquatic systems	Rotenone is very toxic to most aquatic organisms and can have serious impact on aquatic ecosystems. Its application can disrupt the trophic structure of the system, not only eliminating fish but their food sources as well, (i.e. zooplankton), and limiting restocking success for six months or longer (Anderson 1970, Morrison 1977, Beal and Anderson 1993, Mangum and Madrigal 1999). Rotenone persistence in natural waters varies from a few days to several weeks, and is directly related to water temperature (Loeb and Engstrom-Heg 1970, Meadows 1973, Gilderhus et al. 1986, Dawson et al. 1991). The decay of rotenone is also influenced by light, the type of sediments present (water hardness) and acidity (Meadows 1973, Gilderhus 1982, Dawson et al. 1991). It is highly unlikely to contaminate ground water. A decrease in water turbidity after rotenone use has been associated with the elimination of bottom-scavenging fishes, and the reduction in phytoplankton and zooplankton (Bradbury 1986). This increased clarity allows greater light penetration and hence, greater plankton growth (Bonn and Holbert 1961). In some circumstances rotenone treatment can cause an increase in blue/green algae, due to the removal of invertebrate

predators (Hall 1988).

It is unlikely that poisoning would occur from drinking waters treated with normal use concentrations. There is a slight change in odour and taste of water treated with rotenone but this can be managed by using activated carbon in waters used for human consumption (Bonn and Holbert 1961).

Effects on plants — There are no known effects of rotenone on aquatic or land plants.

Acute toxicity to vertebrate species:

Rotenone is highly toxic to fish, amphibians and some reptiles but has moderate to low toxicity to birds and mammals, although there is a wide variation between species, with pigs (*Sus scrofa*) particularly sensitive (Oliver and Roe 1957). Cutkomp (1943) found that young birds were more susceptible than adults. The sensitivity to orally administered rotenone for a range of vertebrate species is given in Table 15. The toxicity of rotenone ingested orally depends upon the physical state of the toxin, with finely divided rotenone more toxic than coarse crystals (Lightbody and Mathews 1936). Rotenone is more toxic when inhaled or injected than when administered orally (Haag 1931, Ambrose and Haag 1936, Hashimoto and Nishiuchi 1981), so care must be taken when using these figures. For example, although the oral LD_{50} for rabbits (*Oryctolagus cuniculus*) is 1.5 grams, if injected intramuscular the LD_{50} drops to 5mg, and if given intravenously the LD_{50} is about 0.35mg (Haag 1931).

Most birds and mammals gain some protection from the vomiting reflex. Dogs (*Canis lupus familiaris*) fed large doses (up to 500 mg) of rotenone almost immediately vomited, and survived the treatment, however when the vomiting centre was depressed with morphine, the animals succumbed to doses around 150mg (Ambrose and Haag 1936). Reptiles seem to gain some protection from their relative slow digestion process. When rotenone was included inside mouse baits, brown tree snakes (*Boiga irregularis*) could survive doses 40-80 times higher than the straight oral gavage amounts due to the slow release of the toxin from the bait matrix allowing for detoxification before lethal amounts could accumulate (Savarie et al. 2010).

Poisoning of aquatic organisms such as fish is usually achieved by adding rotenone to the water (dispersed application), and thus the toxin gains access across the gills. Many species are more sensitive to rotenone when it is applied by this method, for example, carp (*Cyprinus carpio*) have an oral LD_{50} around 6.5 mg per kg bodyweight, but succumb in concentrations of 0.03 mg per litre (Hashimoto and Nishiuchi 1981). The sensitivity to rotenone expressed as median lethal concentrations for a range of aquatic vertebrates is given in Table 16. Both the length of exposure and concentration contribute to the lethal concentration for aquatic animals, with exposure time mainly influenced by water temperature and movement, although acidity and hardness of the water may also have some affect (Leonard 1939, Farringer 1972, Gilderhus 1972, Meadows 1973, Marking and Bills 1976, Hall 1988). The eggs of fish and amphibians, and adult amphibians such as frogs tend to be less susceptible because of their slower uptake rate compared to adult fish and amphibian larvae with gills (Hamilton 1941, Marking and Bills 1976, Fontenot et al. 1994). Little is known of the susceptibility of other aquatic species such as turtles and snakes (Fontenot et al. 1994).

Table 15. The sensitivity to rotenone for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of rotenone is calculated using the average male body weights derived from (Weaver 1942, McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Mammals				
Mouse, *Mus musculus*	350	0.02	7	(James and Kidd 1991)
Brown rat, *Rattus norvegicus* (lab. strain)	75-1500	0.32	32-160	(Ambrose and Haag 1936, Shimkin and Anderson 1936, James and Kidd 1991)
Rabbit, *Oryctolagus cuniculus*	600-1500	1.6	960-2400	(Haag 1931, Ambrose and Haag 1936)
Pig, *Sus scrofa*	3.7	100	370	(Oliver and Roe 1957)
Dog, *Canis lupus familiaris* –	~150	16	1200	(Ambrose and Haag 1936)

vomit reflex depressed				
Human, *Homo sapiens*	300-500	70	21000-35000	(Tomlin 2009)
Birds				
Chicken, *Gallus gallus domesticus* (5 days old)	1000	0.5	500	(Cutkomp 1943)
Chicken, *Gallus gallus domesticus* (4 weeks old)	3100	2.8	8680	(Cutkomp 1943)
Mallard duck, *Anas platyrhynchos*	>2000	1.2	>3120	(Tucker and Crabtree 1970, Hill et al. 1975)
Ring-necked pheasant, *Phasianus colchicus*	>1414	1.2	1930	(Tucker and Crabtree 1970, Hill et al. 1975)
Domestic pigeon, *Columba livia*	>500	0.27	135	(Haag 1931)
English sparrow, *Passer domesticus* (3-10days)	200	0.013	2.6	(Cutkomp 1943)
English sparrow, *Passer domesticus* (adult)	900	0.03	26	(Cutkomp 1943)
Reptiles				
Brown treesnake, *Boiga irregularis*	~1.75	0.05-0.1	0.09-0.18	(Brooks et al. 1998, Savarie et al. 2010)
Fish				
Common carp, *Cyprinus carpio*	6.5-8.1	0.15	0.98-1.2	(Hashimoto and Nishiuchi 1981, Fajt and Grizzle 1993)

Table 16. The sensitivity to rotenone for a range of aquatic vertebrate species expressed as the median lethal concentration (LC_{50}) in milligrams per litre of water, where 50% mortality occurred within the specified time frame. Results are from static water tests.

Species	LC_{50} (mg/L)	Time (hours)	Water Temp. (°C)	Reference
Fish				
Goldfish, *Carassius auratus*	0.033 0.497	48 96	- 12	(Hashimoto and Nishiuchi 1981) (Marking and Bills 1976)
Common carp, *Cyprinus carpio*	0.031 0.084 0.032	24 24 48	11 12 -	(Meadows 1973) (Marking and Bills 1976) (Hashimoto and Nishiuchi 1981)
Rainbow trout, *Oncorhynchus mykiss*	0.069 0.002 0.005	24 48 96	12 17 17	(Marking and Bills 1976) (Waller et al. 1993) (Holcombe et al. 1987)
Channel catfish, *Ictalurus punctatus*	0.400 0.007	24 48	12 17	(Marking and Bills 1976) (Waller et al. 1993)
Black bullhead, *Ictslurus melas*	0.665	24	12	(Marking and Bills 1976)
Yellow perch, *Perca flavescens*	0.092	24	12	(Marking and Bills 1976)
Mosquito fish, *Gambusia affins* – susceptible strain	0.017	24	-	(Fabacher and Chambers 1972)
Mosquito fish, *Gambusia affins* – resistant strain	0.031	24	-	(Fabacher and Chambers 1972)
Amphibians				
Northern leopard frog, *Rana pipiens* - adult	3.2-5.8	96	12	(Haag 1931, Farringer 1972)

Northern leopard frog, *Rana pipiens* - tadpole	0.1	-	-	(Hamilton 1941)
Southern leopard frog, *Rana sphenocephala* -tadpole	0.50	96	16	(Chandler and Marking 1982)

Toxicity to invertebrate species:

Rotenone is highly toxic to many insects and other invertebrates, although the sensitivity is variable (see Table 17). Many aquatic invertebrates are more resistant than fish, but may be still eliminated in field applications as excess toxin tends to be employed to ensure a complete fish kill (Ling 2003).

Table 17. Sensitivity of rotenone to aquatic invertebrate species, expressed as the median lethal concentration (LC_{50}) in milligrams per litre of water where 50% mortality occurred within the specified time frame.

Species	LC_{50} (mg/L)	Time (hours)	Water Temp. (^{o}C)	Reference
Flatworm, *Catenula* sp.	5.1 1.72	24 96	16	(Chandler and Marking 1982)
Water flea, *Daphnia pulex*	0.03	24	16	(Chandler and Marking 1982)
Ostracod, *Cypridopsis* sp.	0.49 0.34	24 96	16	(Chandler and Marking 1982)
Freshwater prawn, *Palaemonetes kadiakensis*	5.15 1.12	24 96	16	(Chandler and Marking 1982)
Dragonfly naiad, *Macromia* sp.	4.7 1.00	24 96	16	(Chandler and Marking 1982)
Giant stonefly naiad, *Pteronarcys californica*	2.9 0.38	24 96	15.5	(Sanders and Cope 1968)
Backswimmer, *Notonecta* sp.	3.42 1.58	24 96	16	(Chandler and Marking 1982)
Caddisfly larva, *Hydropsyche* sp.	0.61	96	16	(Chandler and Marking 1982)
Mosquito larvae, *Anopheles quadrimaculatus*	1.00	48	-	(Deonier et al. 1946)
Whirligig beetle, adult, *Gyrinus* sp.	3.55 0.7	24 96	16	(Chandler and Marking 1982)
Bladder snail, *Physa acuta*	6.8	48	-	(Hashimoto and Nishiuchi 1981)
Snail, *Helisoma* sp.	30.0 7.95	24 96	16	(Chandler and Marking 1982)
Zebra mussel, *Dreissena polymorpha*	0.22	48	17	(Waller et al. 1993)
Threehorn Wartyback, *Obliquaria reflexa*	>1.0	48	17	(Waller et al. 1993)
Asiatic clam, *Corbicula, manilensis*	7.5	96	16	(Chandler and Marking 1982)

Non-target primary risk profile:

Rotenone is relatively harmless to mammals at normal use pattern concentrations but very toxic to aquatic organisms. Since it decomposes relatively quickly in the presence of light, there is little risk to non-target animals consuming crops that have been treated with rotenone against insect pests (Haag 1931), however the risk is great if waterways are contaminated, eliminating not only fish (target and non-target species) but their food sources as well (Anderson 1970, Morrison 1977, Beal and Anderson 1993, Mangum and Madrigal 1999). There are a number of studies in Australia and overseas that document the deaths and recovery of aquatic animals in lakes and rivers treated with rotenone (Anderson 1970, Morrison 1977, Hall 1988, Beal and Anderson 1993, Mangum and Madrigal 1999). Nearly all non-target populations have been reported to recover although the timeframes vary according to several factors such

as species, season, and amount of toxin used. Naturally occurring substrates can give some form of protection to benthic species in treated waters (Chandler and Marking 1982).

Non-target secondary poisoning risk profile:

Rotenone has been used to harvest fish for human consumption for centuries (Leonard 1939) and has posed no known ill effects. Only about a quarter of the total body burden of rotenone in poisoned fish is found in the fillet, with most accumulating in the head, bones, skin and liver (Rach and Gingerich 1986). Ling (2003) calculated from the measured concentrations of rotenone in poisoned carp (*Cyprinus carpio*) that an adult human would have to consume approximately 10 tonnes of fish in one sitting to receive a fatal dose. Also given that heat decomposes rotenone rapidly, any residue is likely to be destroyed during cooking.

Deaths of fish-eating birds are not commonly reported and the risk is considered minimal (Ling 2003).

There is a very low risk of poisoning to birds and mammals consuming insects from vegetable crops which receive heavy applications of derris dust. Cutkomp (1943) reported that nestlings of the Eastern robin, *Turdus migratorius*, died when fed heavily dusted cabbage worm caterpillars, so nestlings of some species of songbirds might be endangered if dusted insects are fed to them by their parents.

Analysis of honey from beehives treated with rotenone (against *Varroa jacobsoni* mite) at recommended doses for one month found residues below 0.2mg/kg (Jiménez et al. 2000), and would thus pose no danger to humans.

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Sodium monofluoroacetate

Chemical name: Sodium monofluoroacetate

Synonyms: 1080, compound 1080, sodium fluoroacetate

The name 1080 was adopted by the manufacturer from the acquisition number assigned by the US Government laboratories when testing commenced in that country in 1944 (Atzert 1971).

Source: 1080 is created synthetically by treating either sodium or methyl chloroacetate with potassium or sodium fluoride, or by the reaction of hydrogen fluoride with carbon monoxide and formaldehyde at high pressure then neutralised with sodium hydroxide (Rammell and Fleming 1978, Aigueperse et al. 2005). It was first synthesized in Belgium by chemist F. Swarts in 1896 (Marais 1944).

1080 is the sodium salt of monofluoroacetic acid, a naturally occurring chemical biosynthesised in plants, although highly toxic concentrations are generally limited to five genera of plants, found across Africa and South America (Marais 1944, de Oliviera 1963, Vickery et al. 1973), with about 40 species found in Australia (Oelrichs and McEwan 1961, McEwan 1964, Twigg et al. 1996a, b, Twigg et al. 1999).

Physical Chemistry: (Tomlin 2009)

Formula	Empirical $C_2H_2FNaO_2$ Structural FCH_2COONa
Molecular wt	100.03
Chemical family	Fluoroacetic acid
Physical form	Fine, hygroscopic powder
Colour	Colourless to white
Taste	Tasteless
Odour	Pure – odourless, commercial – faint vinegary odour
Melting point	Unstable >110 ^{o}C and decomposes *c*.200^{o}C
Solubility	Very soluble in water (Kalmbach 1945, Meldrum et al. 1957, Tomlin 2009), Almost insoluble in ethanol, acetone and petroleum oils (Tomlin 2009, Pelfrene 2010).
Applications:	
History	Rodenticide properties first noted by Schrader in 1934 but not published until after the second world war (Kalmbach 1945, Atzert 1971). First used in Australia on rabbits (*Oryctolagus cuniculus*) (Meldrum et al. 1957).
Uses in Australia	1080 is registered in Australia for the control of rabbits (*Oryctolagus cuniculus*), free-ranging dogs (*Canis* sp.), foxes (*Vulpes vulpes*), feral cats (*Felis catus*) and pigs (*Sus scrofa*). It is permitted for use against rat (*Rattus* sp.) populations in Hoop Pine plantations in Queensland under a APVMA Minor (off label) Use permit.
Poison Schedule	Australia: Schedule 7 Poison Restricted chemical product
Formulation types	Manufactured baits and liquid concentrate (to be added to own bait substrate).

Toxicology:

Absorption	Readily absorbed by ingestion or inhalation. Can be absorbed through cuts and abrasions, but not readily absorbed through skin. Fatal dose levels are similar for administration orally, intravenously, or subcutaneously (Chenoweth and Gilman 1946, Saunders and Stacey 1948, Oliver et al. 1977).
Mode of action	The mode of action of 1080 is complex. Following absorption, cellular metabolism converts 1080 to fluorocitrate (Peters et al. 1953) which disrupts the tricarboxylic acid cycle (Krebs cycle) by inhibiting the action of aconitate hydratase, leading to an accumulation of citrate and lowering of adenosine triphosphate, the source of energy to cells. Mitochondrial functions within the cells are also inhibited (Twigg and King 1991), along with an increased production of ketone bodies, rapid hydrolysis of glycogen in liver, skeletal muscle and heart tissues and a parallel increase in blood glucose and lactate. The cause of death can be occur due to multiple actions and varies between species, as the resulting changes in ionic/osmotic modifications together with the decline in energy reserves can affect any organs with high metabolic rates (Chenoweth 1949, Peters et al. 1953, Morrison and Peters 1954, Buffa et al. 1973, Kirsten et al. 1978, Ataria et al. 2000).
Latent period	There is always an extended period between ingestion of 1080 and the first signs of poisoning. This is characteristic in all animals and is generally between 15 minutes-3 hours after dosing, however it can vary depending on the type of animal and the dosage received (with reports of up to 7 days). This latent period is presumably the time required for 1080 to be absorbed and converted so as to disrupt cellular processes and allow damage to accumulate and affect the sensitive organs (Chenoweth and Gilman 1946, Foss 1948, Meldrum et al. 1957, Rowley 1960, Robison 1970, McIlroy 1981b, 1982a, 1983a, 1984, McIlroy et al. 1985, McIlroy 1986, Sherley 2004, Twigg and Parker 2010).
Symptoms	Fluoroacetate poisoning can occur by a variety of pharmacological actions. Despite there being several symptoms common to most vertebrates, traditionally animals have been divided into symptomatic groups. Carnivores (e.g. canids) show a tendency to manifest central nervous system effects with death resulting from respiratory arrest following severe convulsions or depressions. Death in herbivorous animals tends to result from gradual cardiac failure or ventricular fibrillation. Omnivorous species could fall in either category, with death occurring due to progressive depression of the central nervous system with either respiratory or cardiac failure (Chenoweth and Gilman 1946, Chenoweth 1949, McIlroy 1982a, Sherley 2004). Severe necrosis of skeletal muscle occurs in birds (Ataria et al. 2000). Acute renal failure has also been recorded in humans (Chung 1984). Rabbit (*Oryctolagus cuniculus*) – motor disturbances are observed, including a sprawling position of forelimbs with the head placed flat on its side between them and sudden severe spasms in which the back arches and the head bends back and heels flex toward the back. Ventricular fibrillation occurs within 2-12 hours after receiving dose, immediately followed by anoxic convulsions and death (Chenoweth and Gilman 1946). Immediately prior to death a proportion of rabbits vocalise (Meldrum et al. 1957, McIlroy 1982a). Cat (*Felis catus*) –vomiting starts at approximately 1-2 hours, followed by salivation, pupil dilation, rapid breathing, hyperexcitablility, then inability to move limbs. Convulsions develop suddenly after approximately 2.5 hours, persisting for several hours. Death occurs from four hours due to either depression of the respiratory centre or resulting from ventricular fibrillation, but may take up to 24 hours depending on the dose received (Chenoweth and Gilman 1946, Foss 1948, Eason

	and Frampton 1991, Collicchio-Zuanaze et al. 2006). Pig (*Sus scrofa*) – Vomiting, occasional tremors, increased excitability and/or increasing lethargy, followed later by violent convulsions leading to either respiratory depression or ventricular fibrillation and death (Chenoweth and Gilman 1946, McIlroy 1983a). Canids (*Canis* sp.) – onset can start as soon as 30 minutes after lethal dose, with animal becoming hyperexcited, running about and barking, followed by salivation, defecation, panting and sudden convulsions (start off as sudden muscle contractions but develop into paddling movements of forelimbs with occasional jerking motions) interspersed by brief quiescent periods. Convulsions may persist for 1-2 hours ending in respiratory failure (Chenoweth and Gilman 1946, Foss 1948, McIlroy 1981b, Marks et al. 2000). Rat (*Rattus* sp.) – occasionally tremors and hyperexcitable, but mostly tend to remain quiet, huddle together with head curled under and refuse food or water. Convulsions may then occur with periods of shortness of breath and flaccidity. Death due to respiratory depression occurs within 4-6 hours. If animals survive longer they remain depressed and weak with irregular breathing and heartbeat (Chenoweth and Gilman 1946, Foss 1948).
Time to death	Death generally occurs within 5-48 hours after ingestion of a lethal dose, however it can vary within and between species. Factors such as physical condition and metabolism of the animal, environmental conditions and the size of the dose received all can have an effect. Deaths up to 10 days after dosing in some birds and 22 days in reptiles have been recorded (Lazarus 1956, McIlroy 1981b, 1982a, b, 1984, McIlroy et al. 1985, McIlroy 1986).
Detoxification and excretion of sub-lethal doses	The process of defluorination is the most widespread process for detoxification of 1080, and is known to occur in plants (Ward and Huskisson 1972, Hall 1974, Cooke 1976), fungi and bacteria (Kelly 1965, Kirk and Goldman 1970, Bong et al. 1979, Walker and Bong 1981, Wong et al. 1992), as well as a variety of animals (Foss 1948, Gal et al. 1961, Smith et al. 1977, Mead et al. 1979, Twigg et al. 1986, Hugghins et al. 1988, Twigg et al. 1988, Gregg et al. 1998). In mammals, reptiles and birds, defluorination occurs mainly in the liver. 1080 and its metabolites has been reported to be substantially eliminated through excretion after 1-2 days of sub-lethal dosing in many animal species. Some storage also occurs the skeletal system and incorporated in other fatty acids (Gal et al. 1961, Smith et al. 1977, Rammell 1993, Eason et al. 1994a, Ataria et al. 2000).
Accumulation of sub-lethal doses	There is evidence from a variety of species that multiple sub-lethal doses given over a relatively short time frame have a cumulative effect which can eventually lead to the death of the animal (Foss 1948, Annison et al. 1960, Rowley 1963, Smith et al. 1977, Hugghins et al. 1988). For example multiple sub-lethal doses accumulate in dogs (*Canis lupus familiaris*) becoming lethal if given within 24 hours of each other, however the animal could survive if doses are given at greater intervals (Foss 1948).
Long term effects of sub-lethal doses	The few studies on the long term sub-lethal effects of 1080 indicate that histopathological damage to key target organs may occur at extremely low dose levels. In rats (*Rattus* sp.), the chronic administration of low level doses of 1080 over 1-4 months causes an early but temporary retardation of growth and severe morphological damage in the testes (Miller and Phillips 1955, Smith et al. 1977, Sullivan et al. 1979). Cumulative damage to the heart and other organs has been reported in sheep

	(*Ovis aries*) (Annison et al. 1960, Whittem and Murray 1963, Schultz et al. 1982, O'Connor et al. 1999). Subacute dietary exposure to 1080 resulted in retardation of growth in mustelids, and severely impaired reproduction if given for two months prior to breeding (Hornshaw et al. 1986). Exposure to sub-lethal doses of 1080 indicated detrimental effects in muscle tissues of birds (Ataria et al. 2000). The defluorination process of 1080 by the liver leaves it vulnerable to chronic damage by constant sub-lethal doses of 1080 (Twigg et al. 1986).
Tolerance	Laboratory rats (*Rattus norvegicus*) acquired a short term tolerance by multiple feeding of sub-lethal doses over a period from 5-14 days. Once feeding ceased the rats lost their tolerance within seven days (Kalmbach 1945, Kandel and Chenoweth 1952, Miller and Phillips 1955). This effect could not be simulated in the rabbit (*Oryctolagus cuniculus*) (Chenoweth 1949), or dogs (*Canis lupus familiaris*) (Foss 1948). Diet protein appeared to protect sheep (*Ovis aries*) against sub-lethal 1080 doses (Jarrett and Packham 1956).
Resistance	Granivores and herbivores, and to a lesser extent omnivores and carnivores, which have had evolutionary exposure to naturally occurring fluoroacetate producing plants (or plant-eaters) in the northern and western areas of Australia are much less susceptible than unchallenged species (Oliver et al. 1977, King et al. 1978, Oliver et al. 1979, McIlroy 1982a, b, Mead et al. 1985, King et al. 1989, Twigg and King 1989, 1991). This increased tolerance seems to also appear in animals indigenous to the other continents where plants contain high amounts of fluoroacetate (Chenoweth and Gilman 1946, Atzert 1971, Twigg and King 1991). Laboratory studies have shown rats (*Rattus norvegicus*) are capable of developing genetic resistance to 1080 and some strains are quite resistant to 1080 (Kalmbach 1945, Chenoweth and Gilman 1946, Ward and Spencer 1947, Foss 1948, Howard et al. 1973). It is not known how much inherited resistance has been produced in wild populations. The development of resistance to 1080 has been demonstrated house flies (*Musca domestica*), and this was linked with high resistance to chlorinated hydrocarbons insecticides, and increased resistance to starvation and water deprivation (Tahori 1963). Reduced sensitivity has been reported for rabbits (*Oryctolagus cuniculus*) from Western Australia over a 25 year period, with those populations having the greatest exposure to 1080 baits, also having the greatest tolerance (Twigg et al. 2002).
Bait shyness	Laboratory rats (*Rattus norvegicus*) have developed slight aversion when offered as water-solution (Kalmbach 1945), but it is not long lasting. Bait shyness has been induced in captive brushtail possums (*Trichosurus vulpecula*) by feeding them sub-lethal doses of 1080, with the proportion of affected individuals related to the size of the dose given (Morgan et al. 1996, Morgan et al. 2002). Bait-shyness has been observed in wild possum population and is considered a threat to the control of this pest in New Zealand (Ogilvie et al. 2000).
Antidote	There has been no chemical substance found that can prevent or reverse the toxic effects of 1080, and hence no successful antidote has been developed. After initial positive reports (Chenoweth et al. 1951, Tourtellotte and Coon 1951), glycerol monoacetate and related compounds have been found to have

	limited prophylactic value (Annison et al. 1960). Administration of calcium gluconate and sodium succinate, has been shown to double the survival in cats (*Felis catus*) lethally dosed with 1080 (Collicchio-Zuanaze et al. 2006), but its action is therapeutic in nature, alleviating convulsions and combating possible hypocalcemia (Egekeze and Oehme 1979). Genetic manipulation of rumen bacteria from sheep (*Ovis aries*) and cattle (*Bos primigenius*) has produced a strain able to detoxify 1080. This modified bacterium is able to persist in the rumen of sheep for at least 5 months and has markedly reduced 1080 toxicological symptoms in this animal (Gregg et al. 1996, Gregg et al. 1998). Although a promising technique for reducing livestock loss in Australia, field testing has not been allowed owing to the contentious nature of releasing genetically modified organisms (Weinstein and Davison 2004).
Treatment	Treatment mainly consists of alleviating symptoms (emptying the stomach and administrating fluids, oxygen and anticonvulsants (Ward 1946, Tourtellotte and Coon 1951, Beasley 1997, Sharp and Saunders 2005). The intravenous application of calcium gluconate can also be beneficial (Egekeze and Oehme 1979).
User safety	When preparing baits users are advised to wear elbow-length PVC gloves and protective clothing which should be washed after use. If skin is exposed wash thoroughly with soap and water.

Environmental fate:

The process of defluorination is the most widespread process for detoxification of 1080 and commonly occurs in a variety of fungi, bacteria and plants in the environment. Evidence has shown that 1080 does not persist in the environment and any 1080 that may be leached from baits poses little risk.

Decay time in soils	1080 is defluorinated by common bacteria and fungi within the soil (Bong et al. 1979, Walker and Bong 1981, Wong et al. 1992) and within soils themselves (David and Gardiner 1966, Parfitt et al. 1995). The rate of breakdown is affected by temperature and moisture content (Parfitt et al. 1994).1080 takes 1-2 weeks under optimum conditions to break down in the soil (Livingstone 1994). Potentially traces of 1080 can be leached through soil, particularly after heavy rainfall (Parfitt et al. 1994).
Aquatic systems	There has been no significant contamination of surface and ground water detected after 1080 baiting programs, with 1080 rapidly degrading (Eason et al. 1992, Eason et al. 1993a, Hamilton and Eason 1994, Meenken and Eason 1995, Bowman 1999). The degradation rate is influenced by the water temperature and the microbial population present (Parfitt et al. 1994, Ogilvie et al. 1995, Ogilvie et al. 1996, Booth et al. 1999). 1080 has been shown to degrade in biologically active water in 2-6 days (Eason et al. 1993a, Parfitt et al. 1994). The degradation process can be achieved via several pathways, either converted to fluorocitrate in the same way as animals (Booth et al. 1999), or yielding glycollate and fluoride ions (Goldman 1965, Walker and Bong 1981, Wong et al. 1992, Walker 1994). The risk from these by-products is also considered minimal as fluorocitrate, like 1080 is rapidly degraded in water, and the concentration of fluoride falls well below that added to human drinking water (Eason et al. 1994b). Fish and some crustaceans (e.g. water fleas *Daphnia* sp.) are relatively tolerant to 1080, whereas some aquatic insects (e.g. mosquito larvae) are

	susceptible (Tables 18 and 19). Some aquatic plants, such as Duckweed (*Spirodela oligorrhiza*), have been found to be sensitive (Bong et al. 1979).
Effects on plants	Monofluoroacetate is a naturally occurring chemical, with a large number of plant species able to synthesise this toxin, with no ill effects to the plant itself. It has been proposed the presence of this toxin is a form of defence mechanism against grazing (Mead et al. 1985, Twigg and King 1991). The toxicity of those plants that are able to synthesise high levels of monofluoroacetate can be very variable and is dependent upon the locality and the season (Bell et al. 1955, Whittem and Murray 1963, Aplin 1968, Twigg et al. 1996a, b, Twigg et al. 1999). Although the process of fluoride uptake from surrounding soils and the synthesis of monofluoroacetate by these plants is not fully understood (Whittem and Murray 1963, Murray and Woolley 1968, Weinstein and Davison 2004), it has been shown that these plants do not contaminate surrounding soil and water sources (Twigg et al. 1996a). Although most plants never encounter monofluoroacetate in their environment, a variety of plants have also been shown to be able to defluorinate this compound with no adverse effects (Ward and Huskisson 1972, Hall 1974, Cooke 1976, Ogilvie et al. 2010). However it has also been shown that 1080, or its breakdown product fluoride, may be toxic for some plants. Growth inhibition and leaf necrosis has been reported in seedlings of sunflowers (*Helianthus annuus*), Perennial ryegrass (*Lolium perenne*) and Yarrow (*Achillea millefolium*) (Cooke 1976). Duckweed *Spirodela oligorrhiza* is sensitive, with growth inhibited in the presence of 0.5mg of 1080 (Bong et al. 1979).
Effects on microorganisms	Most studies involving microorganisms have concentrated on defluorination, rather than effects on growth and the environment but there are some reports of inhibition of bacteria (Liebecq and Osterrieth 1963) and yeasts (Aldous 1963, Stewart and Brunt 1968) grown in culture, as well as cyanobacteria (Bruemmer 1962). In contrast, common soil algae *Chlorella* sp. and *Chlamydomonas* sp. were found to be unaffected by the presence of 1080 (Bong et al. 1979).

Acute toxicity to vertebrate species:

Reptiles, amphibians and fish are generally insensitive to 1080 and primates and birds are generally the least susceptible, whereas carnivores and wild rodents appear to be the most sensitive, with eutherian carnivores more sensitive than there marsupial counterparts (Table 18) (Chenoweth 1949, Atzert 1971, McIlroy 1981b, 1982a, b, 1984, McIlroy et al. 1985, McIlroy 1986). Tolerance is due to result of variations in physiology or differing metabolic rates between phylogenetic groups (Mead et al. 1979, Twigg et al. 1986, Twigg and King 1991). There appears to be no general difference between the sexes (Kalmbach 1945, McIlroy 1981a), with the exception that pregnant females and very young mammals tend to be more sensitive (McIlroy 1981a, 1982a, O'Connor et al. 1999).

Table 18. The sensitivity to 1080 for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of 1080 is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991). Species from areas containing fluoroacetate-bearing plants are indicated with an "*".

Species	LD_{50} (mg/kg)	Av body weight (kg)	1080 Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	8.33	0.02	0.17	(McIlroy 1982b)
Brown rat, *Rattus norvegicus* (lab. strain)	1.71-2.5	0.32	0.55-0.8	(Kalmbach 1945, McIlroy 1982b)
Brown rat, *Rattus norvegicus* (wild strain)	0.22-5.0	0.32	0.07-1.6	(Kalmbach 1945, Dieke and Richter 1946)
Black rat, *Rattus rattus*	0.1-0.76	0.28	0.03-0.22	(Kalmbach 1945, McIlroy

				1982b)
Rabbit, *Oryctolagus cuniculus*	0.34-0.50	1.6	0.54-0.80	(Lazarus 1956, McIlroy 1982a)
*Rabbit, *Oryctolagus cuniculus*	0.49-1.02	1.6	0.78-1.6	(Wheeler and Hart 1979, Twigg et al. 2002)
Sheep, *Ovis aries*	0.25-0.52	50	12.5-26	(Meldrum et al. 1957, Annison et al. 1960, McIlroy 1982a)
Goat, *Capra hircus*	0.6-0.7 IM	58	34.8-40.6	(Chenoweth and Gilman 1946, Ward 1946)
Cattle, *Bos primigenius*	0.22-0.39	500	110-195	(Robison 1970)
Horse, *Equus ferus caballus*	0.35 - 1.0	700	245-700	(Ward 1946, Tucker and Crabtree 1970, Tomlinson and Gooding 1971)
Pig, *Sus scrofa*	1-1.04	70	70-72.8	(McIlroy 1983a)
Cat, *Felis catus*	0.07-0.49	5.0	0.35-2.4	(McIlroy 1981b, Eason and Frampton 1991)
Fox, *Vulpes vulpes*	*c.* 0.15	6.5	0.98	(McIlroy and King 1990)
Dog, *Canis lupus familiaris*	0.06-0.35	16.0	0.96-5.6	(Kalmbach 1945, Tourtellotte and Coon 1951, Tomlinson and Gooding 1971)
Human, *Homo sapiens*	2.0-5.0	70	140-350	(Ward 1946, Chenoweth 1949, Tomlinson and Gooding 1971)
Native mammals				
Fat-tailed dunnart, *Smiththopsis crassicaudata*	2.06	0.015	0.03	(McIlroy 1981b)
Brown antechinus, *Antechinus stuartii*	1.85	0.035	0.06	(McIlroy 1981b)
Bush rat , *Rattus fuscipes*	1.13	0.125	0.14	(McIlroy 1982b)
*Bush rat , *Rattus fuscipes*	36-40	0.125	4.5-5.0	(Oliver et al. 1977, King et al. 1978)
Brushtail possum, *Trichosurus vulpecula*	0.47-0.79	3.5	1.6-2.8	(Bell 1972, McIlroy 1982a)
*Brushtail possum, *Trichosurus vulpecula*	> 100	3.5	>350	(Oliver et al. 1977, King et al. 1978)
Brown bandicoot, *Isoodon obesulus*	*c.* 7	0.85	6.0	(McIlroy 1983b)
*Brown bandicoot, *Isoodon obesulus*	20	0.85	17	(Twigg and King 1991)
Long-nosed bandicoot, *Perameles nasuta*	7.70	0.98	7.5	(McIlroy 1981b, 1983b)
Common wombat, *Vombatus ursinus*	0.2	26	5.2	(McIlroy 1982a)
*Agile wallaby, *Macropus agilis*	0.2	19	3.8	(Oliver et al. 1977)
Eastern grey kangaroo, *Macropus giganteus*	0.1-0.35	40	4-14	(McIlroy 1982a)
Red kangaroo, *Macropus rufus*	2.0	37	74	(King et al. 1978)
Northern quoll, *Dasyurus hallucatus*	5.66	0.7	4.0	(McIlroy 1981b)
Spotted-tail quoll, *Dasyurus maculatus*	1.85	5.0	9.3	(McIlroy 1981b)
Dingo, *Canis familiaris dingo*	0.11	16.0	1.8	(McIlroy 1981b)

Introduced Birds				
Chicken, *Gallus gallus domesticus*	5.9-10	2.8	16.5-28	(Kalmbach 1945, Ward and Spencer 1947, Tomlinson and Gooding 1971)
Mallard duck, *Anas platyrhynchos*	9.11	1.2	10.9	(Tucker and Crabtree 1970, Tucker and Haegele 1971)
Ring-necked pheasant, *Phasianus colchicus*	6.46	1.2	7.8	(Tucker and Crabtree 1970, Tucker and Haegele 1971)
Domestic pigeon, *Columba livia*	2.5-9.0	0.27	0.68-2.4	(Ward and Spencer 1947, Tomlinson and Gooding 1971, Tucker and Haegele 1971)
English sparrow, *Passer domesticus*	3.00	0.03	0.09	(Tucker and Crabtree 1970, Tucker and Haegele 1971)
Native Birds				
Australian magpie-lark, *Grallina cyanoleuca*	8.83	0.95	8.4	(McIlroy 1984)
Australian magpie, *Gymnorhina tibicen*	9.93	0.32	3.2	(McIlroy 1984)
Pied currawong, *Strepera graculina*	13.09	0.31	4.1	(McIlroy 1984)
Pacific black duck, *Anas superciliosa*	18.91	0.98	18.5	(McIlroy 1984)
Wood duck, *Chenonetta jubata*	12.6	0.74	9.3	(McIlroy 1984)
Galah, *Cacatua roseicapilla*	5.53	0.33	1.8	(McIlroy 1984)
Kookaburra, *Dacelo novaeguineae*	*c.* 6.0	0.28	1.7	(McIlroy 1984)
Australian raven, *Corvus bennetti*	*c.* 5.1	0.61	3.1	(McIlroy 1984)
Little crow, *Corvus bennetti*	13.37	0.39	5.2	(McIlroy 1984)
Black kite, *Milvus migrans*	18.51	0.59	10.9	(McIlroy 1984)
Wedge-tailed eagle, *Aquila audax*	9.49	3.26	31	(McIlroy 1984)
Emu, *Dromaius novaehollandiae*	*c.* 278	26.5	7,367	(McIlroy 1984)
Amphibians and reptiles				
Spotted grass frog, *Limnodynastes tasmaniensis*	*c.* 60	0.01	0.6	(McIlroy et al. 1985)
Bearded dragon, *Pogona barbatus*	<110	475	<52250	(McIlroy et al. 1985)
Blotched blue tongue lizard, *Tiliqua nigrolutea*	336.4	0.75	252	(McIlroy et al. 1985)
Sand goanna, *Varanus gouldii*	43.6-50	5	218-250	(McIlroy et al. 1985)
Lace monitor, *Varanus varius*	100-119	4.3	430-512	(McIlroy et al. 1985)
Fish				
Rainbow trout, *Oncorhynchus mykiss*	50	-	-	(Bauermeister et al. 1977)

Fingerling bream and bass survive in concentrations of 1080 as great as 370 mg of 1080 per L for indefinite period and with no ill effects (King and Penfound 1946). Fingerling trout have been subjected to concentrations of 500 and 1000 mg/L without any visible effect (Rammell and Fleming 1978). Bluegill sunfish (*Lepomis macrochirus*) were subjected to concentrations of 960mg/L with no ill effects, however

rainbow trout, *Oncorhynchus mykiss*, were slightly susceptible with a 96 hour LC_{50} of 54mg/L (Fagerstone et al. 1994).

Toxicity to invertebrates:

1080 is lethal to many invertebrate species (Notman 1989). Fluoroacetic acid was first patented as a moth-proofing agent in 1930 (US EPA 1995), years before its potential as a vertebrate pesticide was recognised. 1080 is not registered for use against invertebrates in Australia, they are at risk of poisoning by directly eating the baits targeted for other animals, or indirectly (secondary) by eating carcasses, or coming into contact with the regurgitations or excretions of poisoned animals, or from material that has leached from baits or carcasses (Notman 1989).

Plants are capable of taking up 1080 from the soil, with only a small proportion translocating to the stems and leaves and the rest remaining in the roots (Hilton et al. 1969). This not only poses a threat to root eating and soil-dwelling invertebrates (Notman 1989), but studies have shown 1080 can act as an effective systemic poison (David and Gardiner 1951, 1953).

Table 19. Sensitivity of 1080 to invertebrate species, expressed as either the Median Lethal Dose (LD_{50}) in milligrams per kilo bodyweight or the Median Effective Concentration (EC_{50}) as the concentration in water (milligrams per litre) that immobilises 50% of individuals.

Species	LD_{50} (mg/kg)	Time frame (hours)	Mode of admin	Reference
adult NZ native ant, *Huberia striata*	72	24	oral	(Booth and Wickstrom 1999)
adult NZ native ant, *Huberia striata*	42	48	oral	(Booth and Wickstrom 1999)
adult honey bee, *Apis mellifera*	8[a]	acute	oral	(Palmer-Jones 1958)
larval wasp, *Perga dorsalis*	1.05	acute	Injection in haemocoel	(Twigg 1990)
larval autumn gum moth, *Mnesamplea privata*	3.88	acute	Injection in haemocoel	(Twigg 1990)
larval moth, *Spilosoma sp.*	42.73	acute	Injection in haemocoel	(Twigg 1990)
larval bag-shelter moth, *Ochrogaster lunifer*	c. 150	acute	Injection in haemocoel	(Twigg 1990)
housefly, *Musca domestica*	25-30[b]	acute	oral	(Zahavi et al. 1968)
Species	**EC_{50} (mg/L)**	**Time frame (hours)**	**Mode of admin**	**Reference**
Water flea, *Daphnia magna*	350	48	Added to water	(Fagerstone et al. 1994)
mosquito larvae, *Anopheles quadrimaculatus*	0.1-0.05	48	Added to water	(Deonier et al. 1946)

[a]assuming 1 bee = 100mg, [b]assuming 1 housefly= 10mg

Non-target primary risk profile:

Many cases of direct poisoning of non-target domestic and native wildlife have been reported following baiting programs (Table 20). Carnivores are at great risk because of their high susceptibility to 1080. Foxes (*Vulpes vulpes*) have been reported killed by consuming baits intended for pigs (*Sus scrofa*) (Twigg et al. 2007). Native carnivores in Australia tend to have a higher tolerance than dingoes (*Canis lupus dingo*), free-ranging and domestic dogs (*C.l. familiaris*) and foxes, however their smaller body size puts them at risk if they consume multiple baits (McIlroy 1981b). Quolls (*Dasyurus* sp.) in eastern Australia are known to consume baits targeted for foxes and free-ranging dogs and although occasional deaths have been attributed to 1080, the impact on the quoll population is argued to be minimal, especially if correct

baiting procedures are followed (Belcher 1998, Murray et al. 2000, Kortner et al. 2003, Kortner and Watson 2005, Claridge et al. 2006, Claridge and Mills 2007, Kortner 2007).

Many native species, as well as livestock, face risk from rabbit (*Oryctolagus cuniculus*) and pig baiting so bait placement and palatability and concentration of 1080 used are important in reducing non-target poisoning (Rowley 1960, McIlroy 1982a, b, 1983a, b). Rodents are also vulnerable, but to a lesser extent, to fox and dog baiting (McIlroy 1982b).

Birds in general eat a variety of foods, and could be at risk from various baiting campaigns in Australia aimed at rabbit, rodents, carnivores, and in particular pigs (Tomlinson and Gooding 1971, Bryant et al. 1984, McIlroy 1984, 1986, Twigg and King 1989). Bird deaths have been recorded following brushtail possum (*Trichosurus vulpecula*) baiting in New Zealand (Spurr and Powlesland 1997, Powlesland et al. 1999, Westbrooke and Powlesland 2005), and ground squirrel (*Spermophilus beecheyi*) baiting in the United States (Koenig and Reynolds 1987). Modification of baiting methods, such as leaving baits out only at night, burying baits, screening of carrot baits to remove small fragments, banning of lures that attract birds, using deterrents (e.g., cinnamon oil), masking appearance of baits using dyes, reducing bait application rates, or change of bait types have proved successful in reducing bird deaths in Australia and overseas (Bryant et al. 1984, McIlroy 1984, Ataria et al. 2000, Westbrooke and Powlesland 2005).

Since invertebrates are highly susceptible to 1080, they are at risk of poisoning by directly eating the baits targeted for other animals, although the species affected can be influenced by the type of bait used and its application (Notman 1989). The impact of baiting programs on invertebrate populations is considered by many to be minimal (McIntosh et al. 1964). However it may pose a dilemma in areas where economically beneficial insects, rare/endangered invertebrates or rare/endangered animals that rely on these invertebrates occur (Notman 1989).

Table 20. Reports of non-target primary poisoning after 1080 baiting programs.

Targeted Species	Bait presentation	Non-target Risk	Reference
Rabbit, (*Oryctolagus cuniculus*)	oats	Flocks of up to 20 wood ducks, *Chenonetta jubata*, found dead.	(Tomlinson and Gooding 1971)
Rabbit	pellet bait	All adult Silky mouse (*Pseudomys apodemoides*) residents in a marked population died	Cockburn pers. comm. in (McIlroy 1982b)
Rabbit	-	A small number of wombats (species not identified) found dead above ground, not sure if any died in burrows	(McIlroy 1982a)
Rabbit, free-ranging dogs (*Canis* sp.)	carrot baits & meat baits	Large proportion of native bush rat (*Rattus fuscipes*) population killed	(McIlroy 1982b)
Free-ranging dogs	dried meat baits	Evidence that Spotted-tail quolls (*Dasyurus maculatus*) consumed baits but only one death attributed to 1080	(Kortner and Watson 2005)
Free-ranging dogs	aerial – dried meat baits	2 collared cats (*Felis catus*) died of 1080	(Claridge and Mills 2007)
Fox (*Vulpes vulpes*)	buried fox baits	One Spotted-tail quoll death after 6 weeks – thought to be from a cached bait	(Kortner et al. 2003)
Feral pigs (*Sus scrofa*)	grain bait	Six foxes found dead	(Twigg et al. 2007)
Brushtail possum (*Trichosurus vulpecular*)	1080 jam bait	16 000 dead honey bees (*Apis mellifera*) observed after 21 hours with 57g removed from bait	(McIntosh et al. 1964)
Brushtail possum	Aerial baits	Inadvertent kills of native birds	(Spurr and Powlesland 1997, Powlesland et al. 1999)
Californian ground squirrel (*Spermophilus*	Grain	Hazard to 5 species of rodents and cottontail rabbits. Low risk to seed-eating birds.	(Hegdal et al. 1986)

beecheyi)			
Californian ground squirrel	Grain	Confirmed deaths due to 1080 of Yellow-billed magpies (*Pica nuttalli*).	(Koenig and Reynolds 1987)

Non-target secondary poisoning risk profile:

Secondary poisoning can occur when an animal eats another that has consumed toxic 1080 baits. Although most information in Australia is anecdotal or theoretical, some cases of secondary poisoning in other countries have been reported in the literature (see Table 21).

Carnivores are the most frequent victims, as many are scavengers and will tend to feed on carcasses of poisoned birds, rodents, possums or macropods. The extent to which these carrion-eating animals are affected depends on their feeding habits, particularly what parts and how much they eat, and the habits of the poisoned animals (i.e., dying in protected locations or underground), as well as factors that affect the rate of breakdown of 1080 in the carcasses. In their persistence study Meenken and Booth (1997) found that the poisoned carcasses of brushtail possum (*Trichosurus vulpecula*) still posed a risk to dogs (*Canis* sp.) 75 days after death. The risk can be minimised by using the minimum effective concentration of 1080 in the baits, the correct baiting protocol, and by removing dead animals from the treated area (McIlroy and Gifford 1992, Twigg et al. 2003). Domestic animals can be further protected by limiting their access to the baiting area and / or muzzling them (Ward 1946).

Raptors and scavenging birds can also be vulnerable after poisoning programs (Spurr 1979), however other reports have shown no ill effects on the populations of these birds (Burns et al. 1986, Hegdal et al. 1986, Miller and Anderson 1992, Spurr and Powlesland 1997, Twigg et al. 2005).

Insectivorous birds and mammals may also be at risk from eating invertebrates that have fed on bait (Spurr 1979, McIlroy 1984). Studies have shown that residues in exposed insects is generally low, and usually eliminated fairly quickly, so although there have been reports of individual deaths, there has been no evidence of detrimental effects on bird populations (Spurr 1979, Eason et al. 1993a, Eason et al. 1993b, Booth and Wickstrom 1999). (Lloyd and McQueen 2000) however, argued that some species of bats may be vulnerable due to their greater sensitivity to 1080.

Invertebrates themselves are also at risk from eating carcasses of poisoned animals, or coming into contact with the regurgitations or excretions of poisoned animals, or from material that has leached from baits or carcasses (Notman 1989).

The risk to humans is extremely remote. Researchers have found that the accidental consumption of poisoned sheep, rabbits, pigs or deer poses no risk to human health (McIntosh and Staples 1959, Eason et al. 1993a, Rammell 1993, Milne et al. 2001, Twigg et al. 2003, Twigg et al. 2005). Only traces of 1080 has been found in honey from hives that were intentionally fed large amounts of the poison, and it is considered highly improbable that commercial honey would ever present any risk to humans (McIntosh et al. 1964). Only trace amounts of 1080 was found in edible watercress crops, and an average human would need to consume 2.2 tonnes of the effected plant to receive a lethal dose (Ogilvie et al. 2010).

Table 21. Reports of non-target secondary poisoning after 1080 baiting programs.

Species – initially poisoned	Risk	Reference
Californian ground squirrel, *Spermophylus beecheyi*	1080 residues found in all main tissues of ground squirrel, highest in stomach and spleen. Coyote (*Canis latrans*) deaths after consuming one ‘high dose’ or five ‘low dose squirrels over five days.	(Casper et al. 1986)
Californian ground squirrel	Coyotes, bobcats (*Lynx rufus*), skunk (*Mephitis* sp.), domestic dog (*Canis lupus familiaris*) and cat (*Felis catus*) fatalities after consuming carcasses. Insectivorous birds may have died eating poisoned ants.	(Hegdal et al. 1986)
Rabbit, *Oryctolagus cuniculus*	7-15% of ferrets (*Mustela putorius furo*) died after aerially baiting for rabbits. Evidence that cats may also have been poisoned.	(Heyward and Norbury 1999)
Brushtail possum, *Trichosurus vulpecula*	All 13 radio-collared stoats (*Mustela erminea*) died and no signs of any were found after program.	(Murphy et al. 1999)

Brushtail possum & rodents (*Rattus rattus, R. norvegicus, Mus musculus*)	Six feral cats, single stoat and ferret being monitored all died after baiting	(Gillies and Pierce 1999)

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Sodium nitrite

Chemical name: Sodium nitrite

Synonyms: Nitrous acid sodium salt

Source: This salt is prepared by treating sodium hydroxide with mixtures of nitrogen dioxide and nitric oxide. Also it can be prepared by the reduction of sodium nitrate with various metals.

Physical chemistry: (Laue et al. 2002, CHEMSUPP 2005, OECD 2005)

Formula	$NaNO_2$
Molecular wt	69.00
Physical form	Crystalline powder
Colour	White to slight yellowish
Taste	Very salty
Odour	Odourless
Melting point	271 ^{o}C
Solubility	Very soluble in water and ammonia, soluble in methane and ethanol, slightly soluble in diethyl ether.
Stability	Sodium nitrite is a relatively unstable form of nitrogen. It is hygroscopic and very slowly oxidises to nitrate on exposure to air. It is decomposed even by weak acids with the evolution of brown fumes of dinitrogen trioxide. Non-corrosive and non-flammable but assists in the combustion of other substances.

Applications:

History	Sodium nitrite is used in the manufacture of a variety of organic compounds such as pharmaceuticals, dyes and pesticides, but best known as a food additive to prevent botulism (Laue et al. 2002). It is used in combination with sodium thiosulphate for treatment of cyanide poisoning (Meredith et al. 1993).
Uses in Australia	Currently being developed as a feral pig (*Sus scrofa*) toxin in Australia.
Poison Schedule	Australia: Schedule 2 or 7 poison depending on the preparation
Products	Commercially prepared baits

Toxicology:

Absorption	Absorption primarily through ingestion. Can be administered orally, intravenously, or subcutaneously.
Mode of action	Primarily induces the formation of methaemoglobin by oxidising haemoglobin in the blood. This reduces the oxygen carrying capacity of blood, leading to hypoxia, respiratory distress, unconsciousness and death (Humphreys 1978, Fahey and Isaacson 1990). Also may impair the release of oxygen from unaffected haemoglobin, increasing the hypoxia affect (Fahey and Isaacson 1990). Symptoms in pigs (*Sus scrofa*) appear when around 20% of the total

	haemoglobin is present as methaemoglobin, and signs become progressively severe as the methaemoglobin increases until death when the level reaches 75-87% (Curtin and London 1966, London et al. 1967, Institute of Medical and Veterinary Science 2010).
Latent period	Pigs (*Sus scrofa*) showed first clinical signs after 20-40 minutes (Cowled et al. 2008, Institute of Medical and Veterinary Science 2010). The mean time to first symptoms in tammar wallabies (*Macropus eugenii*) was 63 minutes (Shapiro and Eason 2009).
Symptoms	Symptoms include restlessness, infrequent vomiting, urination, lethargy, lack of coordination and shortness of breathe. Some pigs (*Sus scrofa*) had short convulsive seizures close to the time of death, and Tammar wallabies (*Macropus eugenii*) showed slight leg spasms and fell unconscious before death (Oltman and Crandall 1931, McIntosh et al. 1942, Wanntrop and Swahn 1953, Curtin and London 1966, London et al. 1967, Cowled et al. 2008, Shapiro and Eason 2009).
Time to death	Pigs (*Sus scrofa*) generally die within 1-3 hours (Curtin and London 1966, London et al. 1967, Counter et al. 1975, Cowled et al. 2008, Institute of Medical and Veterinary Science 2010). The mean time to death for tammar wallabies (*Macropus eugenii*) was 157 minutes (Shapiro and Eason 2009).
Detoxification and excretion of sub-lethal doses	After ingestion nitrite is reduced to ammonia by microorganisms in the rumen or lower intestine, with very little excretion (Lewis 1951, Burden 1961).
Accumulation of sub-lethal doses	Nitrite itself is not accumulative in animal tissues (Stormorken 1953), however multiple sub-lethal doses can be lethal if not enough time is allowed for the produced methaemoglobin to be reduced between doses (Burden 1961).
Long term effects of sub-lethal doses	Sub-lethal exposure of potassium nitrite produced no adverse effects in growing pigs (*Sus scrofa*) (London et al. 1967). Daily sub-lethal doses of nitrite given over 5-6 months did not affect the growth and development of rats (*Rattus* sp.) and cats (*Felis catus*), or the fecundity of rats (Tarr and Carter 1942), however problems associated with damage to their hemoglobin have been reported (Imaizumi et al. 1980).
Tolerance	Tolerance to sodium nitrite as an acute toxin has not been demonstrated.
Resistance	There is no evidence of resistance to sodium nitrite as an acute toxin.
Aversion	Sodium nitrite has a very salty taste that causes aversion and its breakdown products in baits can also cause aversion.
Antidote	The effect of sodium nitrite can be overcome by any agent that reduces methaemoglobin back to haemoglobin, such as methylene blue, thionine or ascorbic acid (Stormorken 1953, Clarke and Clarke 1975, Institute of Medical and Veterinary Science 2010).
Treatment	If the toxin has been ingested, and the patient is conscious, vomiting should be induced to remove any excess, otherwise use activated charcoal. Mineral oil can help speed elimination. The antidote should be administered and blood monitored. In severe cases the antidote may need to be re-administered and an exchange blood transfusion may be required (Clarke and Clarke 1975, Buck et al. 1976).

User safety	When preparing baits users are advised to wear elbow-length PVC gloves and protective clothing which should be washed after use. If skin is exposed wash thoroughly with soap and water.

Environmental fate:

Decay time in soils	Sodium nitrite is a naturally occurring chemical. Nitrite is the intermediate product in the nitrogen cycle and breaks down readily in the environment through nitrification (oxidation of ammonia to nitrate) and denitrification (breakdown of nitrate to nitrogen) by bacteria and other microorganisms, as well as assimilation by plants. Nitrites are water soluble so if added to the soil will leach readily and enter the water table (Konikoff 1975, Buck et al. 1976, Sofia et al. 2004).
Aquatic systems	Sodium nitrite dissociated immediately into sodium and nitrite ions in water (OECD 2005). Nitrites are present at varying levels in water. Decaying organic matter, fertilisers, animal metabolic wastes, and soil high in nitrogen-fixing bacteria may be sources of contamination in water (Winks et al. 1950, Counter et al. 1975, Konikoff 1975, Buck et al. 1976, McParland et al. 1980).
Effects on plants	Plants use nitrates to form plant protein. Nitrites are produced as an intermediate stage in the breakdown of plant vegetative tissue (such as in the anaerobic fermentation in stored forage in silos) (Riggs 1945, Buck et al. 1976).
Effects on micororganisms	Sodium nitrite inhibits the growth of some disease-causing microorganisms such as *Clostridium botulinum*, but not effective against others such as *Salmonella* and *Escherichia coli* (Sindelar and Milkowski 2011). Blue-green algae are sensitive to nitrites, while other algae species are more tolerant (Wodzinski et al. 1977, 1978).

Acute toxicity to vertebrate species:

Some mammals are very sensitive to sodium nitrite (Table 21). Fasting increases the susceptibility of livestock to nitrite poisoning, also the type of diet and delivery matrix (Gwatkin and Plummer 1946, Winks et al. 1950, Stormorken 1953, Sinclair and Jones 1967, Cowled et al. 2008). The mode of administration also affects toxicity. The minimum lethal dose of sodium nitrate administered in aqueous solution to cattle (*Bos primigenius*) is about 100mg/kg, however when administered in a dough it increases to 150-170 mg/kg, and when administered intravenously the dose is much lower at 30-35mg/kg (Stormorken 1953).

Nitrite is highly toxic to aquatic vertebrates, with sensitivity dependent on water chemistry (Russo et al. 1974, Russo et al. 1981, Lewis and Morris 1986), see Table 22. There was no acute lethal dose values found for birds, reptiles or amphibians.

Table 21. The sensitivity to sodium nitrite for a range of species expressed as the oral median lethal dose (LD_{50}) or lethal dose (LD). The amount of sodium nitrite is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	LD (mg/kg)	Av body weight (kg)	Amount for LD_{50} or LD (mg)	Reference (LD_{50} data)
Introduced mammals					
Mouse, *Mus musculus*	215		0.02	0.43	(Riemann 1950)
Brown rat, *Rattus norvegicus* (lab. strain)	85-150		0.32	27.2-48.0	(Wanntrop and Swahn 1953, Imaizumi et al. 1980, CHEMSUPP 2005)
Brown rat, *Rattus norvegicus* (lab. strain)		460-2000	0.32	147-640	(Tarr and Carter 1942)
Rabbit, *Oryctolagus cuniculus*	124		1.6	198	(Dollahite and Rowe 1974)

Rabbit, *Oryctolagus cuniculus*		80-90	1.6	128-144	(Oltman and Crandall 1931)
Pig, *Sus scrofa*	<90 <135[a] 270-540[b] 19-21[c]		70	<6300 <9450 18900-37800 1330-1470	(Wanntrop and Swahn 1953) (Cowled et al. 2008) (Cowled et al. 2008) (Curtin and London 1966)
Pig, *Sus scrofa*		70-90	70	4900-6300	(Winks et al. 1950, Stormorken 1953)
Sheep, *Ovis aries*		*ca* 167[d]	50	*ca* 8350	(Lewis 1951)
Cattle, *Bos primigenius*	20-50		500	10000-25000	Wright and Davison 1964
Cattle, *Bos primigenius*		100	500	50000	(Stormorken 1953)
Cat, *Felis catus*		73	5.0	365	(Tarr and Carter 1942)
Human, *Homo sapiens*	<250[e]		70	<17500	(Boink and Speijers 2001)
Human, *Homo sapiens*		32	70	2240	(Naidu and Venkatrao 1945)
Native mammals					
Brushtail possum, *Trichorus vulpecula*		393	3.5	1376	(Fisher et al. 2009)
Tammar wallaby, *Macropus eugenii*		245	6	1470	(Shapiro and Eason 2009)

[a] administered by gavage
[b] administered in bait matrix
[c] expressed as mg of nitrite / kg bodyweight (potassium nitrite used)
[d] administered by rumen fistula
[e] lowest observed effect level expressed as mg of nitrate ion/kg bodyweight

Table 22. The sensitivity to nitrite for a range of aquatic vertebrate species expressed as the median lethal concentration (LC_{50}) in milligrams of NO_2-N per litre of water, where 50% mortality occurred within the specified time frame.

Species	LC_{50} (mg/L)	Time (hours)	Water Temp. (^oC)	Reference
Fish				
Channel catfish, *Ictalurus punctatus*	44	96	30	(Colt and Tchobanoglous 1976)
Rainbow trout, *Oncorhynchus mykiss*	0.27	96	-	(Russo et al. 1974)
Sunshine bass, *Morone sp.* –freshwater	12.8	96	25	(Weirich et al. 1993)
Sunshine bass, *Morone sp.* -acclimatised to salinity	35	96	25	(Weirich et al. 1993)
Amphibians				
Smallmouth salamander, *Ambystoma texanum* larvae	1.09	96	25	(Huey and Beitinger 1980)

Toxicity to invertebrate species:

Nitrite is toxic to many species of aquatic invertebrates, although and oysters and clams are more tolerant (Table 23). Adults tend to be more tolerant than larvae (Epifanio and Srna 1975, Armstrong et al. 1976, Ary and Poirrier 1989).

Table 23. Sensitivity of nitrite to invertebrate species, expressed as the Median Lethal Concentration (LC_{50}) as the concentration in water (milligrams per litre) that immobilises 50% of individuals.

Species	LC_{50} (mg/L)	Time (hours)	Reference
Water flea, *Daphnia magna*	12.5-100	48	(CHEMSUPP 2005)
Australian redclaw crayfish, *Cherax*	25.9	96	(Meade and Watts 1995)

quadricarinatus juveniles			
Blue crab, *Callinectes sapidus*	71.3	96	(Ary and Poirrier 1989)
Giant Malaysian prawn, *Macrobrachium rosenbergii* larvae	8.6	96	(Armstrong et al. 1976)

Non-target primary risk profile:

Although most other mammalian and bird species are less sensitive than pigs (*Sus scrofa*) there is still a slight risk of poisoning (Institute of Medical and Veterinary Science 2010, Lapidge and Eason 2010).

Non-target secondary risk profile:

Sodium nitrite has a low probability of bioaccumulation (CHEMSUPP 2005), hence secondary poisoning risk would be low.

Sodium nitrite is part of humans' diet and is found in many vegetables as well as being used for food preservation (Correia et al. 2010). Data on the nitrite residues left in pig (*Sus scrofa*) meat after using the new pig baits is currently unavailable, however the risk of secondary poisoned is considered low. Humans can metabolise nitrogen oxides efficiently, and although there have been controversies over the years, most scientific evidence points to it being safe for humans (Sindelar and Milkowski 2011, 2012).

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Strychnine

Chemical name: strychnidin-10-one

Synonyms:

Source: Strychnine is an alkaloid extracted from the seeds and bark of many members of the *Strychnos* genus (family Loganiaceae), native to tropical Asia. It was first isolated in pure form from the St. Ignatius beans (*Strychnos ignatii*) in 1818. The main commercial common source is the Strychnine tree *Strychnos nux-vomica*.

Physical chemistry: (Brooks and Jackson 1973, Tomlin 2009)

Formula	$C_{21}H_{22}N_2O_2$
Molecular wt	334.41
Physical form	Crystals or crystalline powder
Colour	Translucent or white
Taste	Metallic bitter
Odour	Odourless
Melting point	268-290^{o}C (depending on speed of heating)
Solubility	Only slightly soluble in water, benzene and chloroform, sparingly soluble in ether and petroleum spirits, and insoluble in ethanol and diethyl ether. Forms water-soluble salts with acids (eg sulphate and hydrochloride). These salts however insoluble in most organic solvents.
Stability	Stable to light, and at pH 5-9. Emits toxic vapours when heated.

Applications:

History	The toxic effects of strychnine were well known by ancient Chinese and Indian cultures. Its first recorded use in Europe was as a mammal poison in the seventeenth century (Freeman et al. 1954, Buckingham 2008). This toxin and its salts have been extensively used in many countries, particularly against small mammals, canids and birds. It was banned from general use in the UK in 1935 (Freeman et al. 1954), and its usage has been restricted in most countries. In Australia strychnine has been progressively restricted since the 1980's and banned for use as broad-scale rodenticide in Australia in 1995 (Caughley et al. 1998).
Uses in Australia	Currently registered in Western Australia for use on cloths attached to dog (*Canis* sp.) traps and emu (*Dromaius* novaehollandiae) control, and in South Australia for mouse (*Mus* sp.) control. Off licence permits in Queensland for use on cloths attached to dog and fox (*Vulpes vulpes*) traps, as well as in baits (although not preferred). Also registered in NSW for use on cloths attached to dog traps only.
Poison Schedule	Australia: Schedule 7 poison
Formulation types	Bait concentrate, ready to use bait

Toxicology:

Absorption	Readily absorbed when ingested, inhaled, or injected. Can be absorbed through the mucous membranes of eyes or mouth, but not through intact skin. More toxic when administered through intravenous or subcutaneous route.
Mode of action	Strychnine acts as an antagonist of the neurotransmitters glycine and acetycholine, principally affecting the motor nerves in the spinal cord which control muscle contractions. Is used under medical supervision as a stimulant for the treatment of cardiac disorders.
Latent period	Latent period tends to be short as strychnine is rapidly absorbed. Symptoms can appear minutes after ingestion (but usually 10-30 minutes).
Symptoms	Symptoms are similar in all species and include restlessness, neck stiffness, nausea, muscular twitching in all muscular groups developing into violent spasms and convulsions, immense reflex sensitivity, and loss of consciousness. Arching of the body backwards, extended stiff legs, contracted facial muscles (‘*risus sardonicus*’) and dilated pupils are characteristic of strychnine toxicoses. Death results from asphyxia due to paralysis of the respiratory muscles (Freeman et al. 1954, Crabtree 1962).
Time to death	Death generally occurs within half an hour of dosage, although it may be as rapid as several minutes, depending on the dose received (Ward and Crabtree 1942, Freeman et al. 1954, Lazarus 1956, Schafer and Eschen 1986).
Detoxification and excretion of sub-lethal doses	Strychnine is readily detoxified by the liver, and has a biological half life of 10-16 hours. This toxin is detected unchanged in the urine within minutes of ingestion. Approximately 10 to 20% of a sub-lethal dose is excreted in the urine in the first 24 hours with excretion complete usually after 48-72 hours, although in humans it can be as long as five days. (Hale 1909, Weiss and Hatcher 1922, Crabtree 1962, Palatnick et al. 1997).
Accumulation of sub-lethal doses	Strychnine does not accumulate in the body tissues but is mostly detoxified and excreted from the body in a relatively short period of time (Hatcher and Eggleston 1917, Schwartze 1922, Crabtree 1962, Kamel and Afifi 1969, Lee et al. 1990).
Long term effects of sub-lethal doses	There was no organ and tissue damage or functional disorders in rats (*Rattus* sp.) after four weeks of oral administration of sub-lethal doses of strychnine hydrochloride (Seidl and Zbinden 1982). Long term effects of sub-lethal doses in birds included decreased body weight, liver, intestinal and testes damage, and decreased egg production. Hatchlings had lower body weights and decreased survivability. These effects were more pronounced in those species of birds that have a higher acute sensitive to this toxin (Sterner et al. 1998, Pedersen et al. 2000).
Aversion	Rats (*Rattus* sp.) find strychnine highly unpalatable, and acquire a marked aversion to this toxin (Howard et al. 1968). This aversion has also been noted in some squirrel species (Howard et al. 1990), but not in other rodents such as pocket gophers (*Thomomys* sp.) (Lee et al. 1990).
Tolerance	Acquired tolerance to strychnine has been reported in some species. Physiological tolerance whereby animals can tolerate increasingly higher doses of the toxin after ingesting a series of sub-lethal doses has been shown to occur in some rodent species, pigs (*Sus scrofa*) and dogs (*Canis lupus familiaris*) (Hale 1909, Schwartze 1922), although some of the results

	reported not conclusive. Pocket gophers (*Thomomys bottae*) display a type of acquired tolerance through their feeding strategy of eating small amounts of food periodically over a 24 hour period. This enables them to consume the equivalent of a lethal dose of strychnine but in smaller sub-lethal amounts spaced out so the toxin can be detoxified and excreted before the next dose is consumed (Lee et al. 1990).
Resistance	No evidence of resistance has been recorded.
Antidote	There is no specific antidote for strychnine.
Treatment	Recovery from strychnine intoxication is possible with early treatment. The first step is to remove as much drug from body. Activated charcoal is recommended. Only when convulsions and hyperactivity are controlled should gastric lavage with tannic acid or potassium permanganate to oxidise strychnine be performed. Treatment then mainly involves supportive care using intravenous fluids, medications against convulsions and spasms, cooling measures for high temperature and assistance with breathing if required (Sangiah 1985, Palatnick et al. 1997).
User safety	When handling strychnine users are advised to wear gloves, mask and appropriate protective clothing. It is difficult to clean up after using this toxin so it is strongly recommended to dispose of all protective clothing by burying or incineration, then hands and any other potentially exposed areas should be thoroughly washed with soapy water (Lund and Twigg 2009).

Environmental fate:

Decay time in soils	Treated grains placed on soil surface release strychnine slowly, however if treated grains are buried, strychnine is rapidly absorbed (90% within 15 minutes) (Kookana et al. 1997). The binding mechanism of strychnine to soil is a combination of cation exchange and surface absorption to the organic and inorganic fractions of soil (Miller et al. 1983). Sorption affinity varies with soil type and pH (Miller et al. 1983, Kookana et al. 1997). Mobility in the soil is minimal hence this toxin is not expected to leach rapidly (Smith 1982, Miller et al. 1983). Aerobic microbial processes are responsible for the degradation of strychnine, with soil pH affecting the process (Rogers et al. 1998a, Rogers et al. 1998b). Greater than 90% is biodegraded in soil within approximately 40 days (Starr et al. 1995, Rogers et al. 1998b). Strychnine does not degrade abiotically (Kookana et al. 1997).
Aquatic systems	No data available to make an assessment of whether strychnine is likely to contaminate river systems or groundwater.
Effects on plants	In glasshouse trials Oliver (2000) showed there was the potential for uptake of strychnine in some plants, however when applied at recommended baiting rates (0.4-0.5% w/w strychnine baits at 2-4 baits m^{-2}) there was no detectable translocation of strychnine from the soil to harvestable crops such as grain, legume and fruit crops (Smith 1982, Miller et al. 1983, Oliver et al. 2000).
Effects on micororganisms	Strychnine does not affect the microbial, bacterial or fungal population within soil (Starr et al. 1995).

Acute toxicity to vertebrate species:

Strychnine and its salts are highly toxic to mammals but not so toxic to birds. Cats (*Felis catus*) and dogs (*Canis lupus familiaris*) are the most susceptible among domestic mammals. With birds there is much

variability within groups. Gallinaceous birds (ground-feeding domestic or game birds) are less sensitive than waterfowl species and passeriformes.

The sensitivity to orally administered strychnine for a range of vertebrate species is given in Table 24. The toxicity of this toxin varies depending on the form of the toxin and the mode of delivery. The alkaloid is generally more toxic than its salts, although the difference depends on the mode of administration and the dosage size (Miller 1950, Kamel and Afifi 1969, Lewis 1992). Ward and Crabtree (1942) observed that the oral lethal dose of strychnine alkaloid for female rats (*Rattus* sp.) was lower than that for the sulphate salt.

Strychnine is less toxic when administered orally than when injected; for example the oral LD_{50} for chickens (*Gallus gallus domesticus*) is between 18.5 – 30.0 mg per kg bodyweight, however if injected subcutaneously the LD_{50} drops to 1.5-2.0 mg per kg bodyweight (Heinekamp 1925). A similar scenario has been measured in mammals, for example white rats (*R. norvegicus*) have the oral LD_{50} between 2.35 – 6.50 mg per kg but an LD_{50} between 1.45-2.8 mg per kg bodyweight after intraperitoneal injection, 1.81-8.2 mg per kg bodyweight after subcutaneous injection and 0.57 mg per kg bodyweight after intravenous injection (Ward and Crabtree 1942, Kato et al. 1962).

A sex difference in the toxicity to adult rats has been observed in all cases of administration except intravenous injection, with females more susceptible than males. This sex difference was not observed in guinea pigs (*Cavia porcellus*) and mice (*Mus* sp.) (Poe et al. 1936, Ward and Crabtree 1942, Kato et al. 1962). The toxicity has also been found to be reduced by the presence of food in the crop or gut and the administration of glucose (Weiss and Hatcher 1922, Heinekamp 1925).

Table 24. The sensitivity to strychnine for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of strychnine is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	Oral LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	2.0 [a]	0.02	0.04	(Prasad et al. 1981)
Brown rat, *Rattus norvegicus* (lab. strain)	2.35-6.5 [b] 2.6-6.5 [c] 5 [c, d]	0.32	0.75-2.08 0.83-2.08 1.6	(Ward and Crabtree 1942, Schafer 1972) (Fitzwater and Prakash 1973)
Brown rat, *Rattus norvegicus* (wild strain)	4.8 [c]	0.32	1.54	(Dieke and Richter 1946)
Rabbit, *Oryctolagus cuniculus*	0.6 [b] LD 6.5	1.6	0.96 10.4	(Fitzwater and Prakash 1973) (Lazarus 1956)
Cattle, *Bos primigenius*	LD 1.5 [a]	500	750	(Clarke 1976)
Horse, *Equus caballus*	LD 1.0 [a]	700	700	(Clarke 1976)
Pig, *Sus scrofa*	0.5-1.0 [a] 150-300 [c, d]	70	35-70 10500-21000	(Buck 1978) (Fitzwater and Prakash 1973)
Cat, *Felis catus*	2.0 [a] 0.75 [b] 0.5 [c]	5.0	10.0 3.75 2.5	(Buck 1978) (Fitzwater and Prakash 1973) (Moraillon and Pinault 1978)
Dog, *Canis lupus familiaris*	0.75 [b] 0.5 [c] 75-300 [c, d]	16.0	12.0 8.0 1200-4800	(Buck 1978) (Moraillon and Pinault 1978) (Fitzwater and Prakash 1973)
Human, *Homo sapiens*	1-30 [a]	70	70-2100	(Gratz 1973) (Fitzwater and Prakash 1973)
Native mammals				
Brushtail possum, *Trichosurus vulpecula*	22.4 [a]	3.5	78.4	(Bell 1972)
Introduced birds				

Chicken, *Gallus gallus domesticus*	5.0 [a] 18.5-30.0 [c] 30-40 [a]	2.8	14 51.8-84 84-112	(Buck 1978) (Heinekamp 1925) (Fitzwater and Prakash 1973)
Mallard duck, *Anas platyrhynchos*	2.9 [b]	1.2	3.5	(Tucker and Haegele 1971)
Ring-necked pheasant, *Phasianus colchicus*	24.7 [b]	1.2	29.6	(Tucker and Haegele 1971)
Domestic pigeon, *Columba livia*	8-11 7.7-21.3 [b] 30 [c]	0.27	2.2-3.0 2.1-5.8 8.1	(Fitzwater and Prakash 1973) (Tucker and Haegele 1971, Schafer and Eschen 1986) (Heinekamp 1925)
English sparrow, *Passer domesticus*	4.2 [b] 7.4 [a]	0.03	0.12 0.22	(Tucker and Haegele 1971) (Bird 1995)
Starling, *Sturnus vulgaris*	<5.0 [c]	0.07	0.35	(Schafer 1972)

[a] form not stated, [b] alkaloid, [c] sulphate, [d] hydrochloride

Toxicity to invertebrate species:

There is no information of the toxicity of strychnine to invertebrates.

Non-target primary risk profile:

Strychnine is a non-selective toxin, and the risk to non-target species is great if baiting procedures are not controlled. Overseas there have been many reports of non-target deaths after strychnine baiting programs. In the United States this toxin is still used to control several pest species (Table 25), and although a small number of non-target deaths have been recorded, no long term impacts on the population of these species have been found (Fagerstone et al. 1980, Anthony et al. 1984, Apa et al. 1991).

In Australia granivorous birds are the major casualties following broad-scale mice (*Mus* sp.) control programs. Pigeon, parrot and quail species, apostle bird (*Struthidea cinerea*) and sparrow (*Passer* sp.) deaths have all been recorded, as well as a small number of omnivore deaths, including magpie-lark (*Grallina cyanoleuca*) and magpies (*Cracticus* sp.) (Bird 1995, Brown and Lundie-Jenkins 1999). Many of these bird deaths were attributed to instances where the bait was spilt or applied at heavier rates than those recommended. Where bait was laid at recommended rates few mortalities were noted as birds could not locate and eat sufficient grains for a lethal dose before the onset of symptoms intervened to prevent further intake (Bird 1995). No data has been published for non-target mammal deaths, however this may be due to the low prevalence and hence detection rates of these species in baited areas.

There is no non-target information recorded regarding this toxin's use in free-ranging dog (*Canis* sp.) and fox (*Vulpes vulpes*) trapping programs in Australia, although the risk is considered minimal as it is a behaviour trait of these introduced carnivores to bite at the traps (Onderka et al. 1990, Fleming et al. 1998), and hence come in contact with the toxin.

Table 25. Reports of non-target primary poisoning after strychnine baiting programs in the United States.

Targeted Species	Bait presentation	Non-target risk	Reference
Pocket gophers, *Thomomys* spp.	Underground application of oat baits	Death of small number of deer mice and chipmunk species but monitoring showed no difference in small mammal populations after baiting	(Fagerstone et al. 1980)
Feral pigeon, *Columba livia*	Ground application of corn baits	Non-target cowbirds *Molothrus ater* and Mallard ducks *Anas platyrhynchos* died after eating bait	(Redig et al. 1982)
Western pocket gophers, *Thomomys mazama*	Underground application of oat baits	An immediate reduction in numbers but no long-term impacts on golden-mantled ground squirrel (*Callospermophilus lateralis*) population.	(Anthony et al. 1984)

Black-tailed prairie dog, *Cynomys ludovicianus*	Ground application of oat baits	Immediate reduction in Horned Lark (*Eremphila alpestris*) densities, but no long term impacts	(Apa et al. 1991)
Rodent control	Ground application of wheat seeds	First report of death in species of shorebirds, dunlins, *Calidris alpine* and killdeer, *Charadrius vociferus*	(Warnock and Schwarzbach 1995)
Ground squirrels, *Spermophilus richardsonii*	Ground application of oat, canary seed and alfalfa pellets	Poisoned deer mice species and songbirds were found in baited areas	(Prouix et al. 2010)

Non-target secondary poisoning risk profile:

The risk of secondary poisoning from the use of strychnine is thought to be low due to the rapid action, metabolism and excretion of this toxin. The risk, however, is dependent on the strychnine residue in carcass which in turn is a factor of the bait concentration, feeding behaviour of the target animal, period between dosage and death and feeding behaviour of the scavenger. Schafer and Eschen (1986) showed that by reducing feral pigeon (*Columba livia*) baits from 0.6% to 0.4% strychnine alkaloid the potential of secondary poisoning could be halved. Middleton (1891) demonstrated that the muscle meat of sheep (*Ovis aries*) killed by subcutaneous injection of strychnine was not toxic to dogs (*Canis lupus familiaris*) however injections of liver extracts from these same sheep were lethal to both dogs and mice (*Mus* sp.).

Raptors seem to be the main group reported at risk from secondary poisoning in Australia and overseas, although some canids may also be potentially at risk (Hood 1972). Deaths of owls, gulls and harriers have been reported after programs in the United States (Redig et al. 1982, Prouix et al. 2010). Multiple deaths of carnivorous birds such as Nankeen kestrels (*Falco cenchroides*), letter-winged kites (*Elanus scriptus*) and black-shouldered kites (*E*. axillaris) died from eating poisoned mice after aerial application of strychnine wheat baits in Queensland (Brown and Lundie-Jenkins 1999), however only one raptor (letter-winged kite) death was confirmed after broad-scale wheat baiting of mice in South Australia. Despite large flocks of Australian ravens (*Corvus coronoides*) observed feeding on poisoned mice, only one death could be attributed to strychnine and it was possibly due to primary poisoning as wheat bait was also found in gut (Bird 1995).

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Zinc phosphide

Chemical name: zinc phosphide

Synonyms: trizinc diphosphide

Physical chemistry: (Doty 1945, Freeman et al. 1954, Anon. 1967, Tomlin 2009)

Formula	Zn_3P_2
Molecular wt	258.1
Physical form	Powder
Colour	Dull grey-black
Taste	'Sweetish' taste
Odour	The garlic-like odour of phosphine gas is often associated with zinc phosphide and its formulations.
Melting point	420^{o}C (when heated in absence of oxygen)
Solubility	Practically insoluble in water and alcohols, slightly soluble in alkalis and oils, soluble in acids.
Stability	Stable when dry, but decomposes slowly in moist air or in presence of acids. Can either directly oxidise to form various phosphorous oxyacids or hydrolyse to produce phosphine gas. The presence of impurities when phosphine gas produced can render the gas spontaneously flammable.
Applications:	
History	Thought to be first synthesised by Marggraf in 1740, but first documented use as a rodenticide in Italy in 1911. Gained popularity in the 1930's across Europe and introduced in the US in 1943 due to war shortages of other pesticides (Doty 1945, Freeman et al. 1954). Not registered for use in Australia until 1997 (Caughley et al. 1998).
Uses in Australia	Mainly for control of mice (*Mus* sp.) populations in broad acre crops, but can also be used for control of rat (*Rattus* sp.) populations in specified circumstances.
Poison Schedule	Australia: Schedule 7 poison
Formulation types	Ready to use wheat grain bait or extruded pellet formulation. Use only permitted in crops.
Toxicology:	
Absorption	Readily absorbed by ingestion or inhalation. Can be absorbed through cuts and abrasions, but not through unbroken skin. More toxic when ingested with food.
Mode of action	Reacts with stomach acids and hydrolyses to liberate poisonous phosphine gas which is readily absorbed causing central nervous system depression, irritation of the lungs and damage to the liver, kidney and heart. Phosphine is believed to cause majority of acute symptoms, while intact zinc phosphide may cause liver and renal damage. Death occurs as a result of heart failure and pulmonary oedema leading to respiratory failure (Johnson and Voss

	1952, Freeman et al. 1954).
Latent period	Symptoms occur from 15 minutes to hours after ingestion, but may be delayed for up to 18 hours. Time dependent on the size of the dose received (Freeman et al. 1954, Southern 1954, Murphy 2009).
Symptoms	Progress through anorexia, lethargy, dyspnea, vomiting, ataxia, muscle tremors and coma. Death occurs suddenly with minimal outward signs in most animals, and as a result of heart failure, pulmonary oedema and kidney failure. Dead rats (*Rattus* sp.) are frequently found on their belly, with legs and tail spread out (Freeman et al. 1954, Fitzpatrick et al. 1955, Murphy 2009). In humans symptoms include nausea, vomiting, abdominal pains, chest tightness, excitement, and a chilly feeling (Schoof 1970, Stephenson et al. 1999).
Time to death	Time to death is dependent on size of dose. Large dosages have caused deaths in rats (*Rattus* sp.)within 20 minutes, while low dosages may take up to several days (Freeman et al. 1954, Schoof 1970).
Detoxification and excretion of sub-lethal doses	Zinc phosphide decomposes in the stomach over time, releasing mainly phosphine gas and zinc. Most of the zinc is excreted, with only small amounts absorbed (Robertson et al. 1945).
Accumulation of sub-lethal doses	Not accumulative in animal tissues to any degree, however as not all of the zinc phosphide initially consumed is broken down immediately, repeated sub-lethal doses can be fatal. Robertson et al. (1945) observed a chicken (*Gallus gallus domesticus*) feed daily sub-lethal doses died on the third day, whilst another lasted seven days before succumbing, however two others survived the repeated dosing.
Long term effects of sub-lethal doses	Rats (*Rattus* sp.) which have taken a sub-lethal dose appear to recover quickly without any display of persistent symptoms (Freeman et al. 1954, Schoof 1970), however the full impact of multiple doses requires further investigation, with inference of damage to the liver, kidney and lungs (Johnson and Voss 1952, Hill and Carpenter 1982).
Tolerance	There are no reports in the literature on the development of any tolerance to zinc phosphide.
Resistance	There is no evidence of genetic resistance to zinc phosphide.
Aversion	Consumption of sub-lethal doses has been reported to lead to bait aversion in several species of mice (*Mus* sp.) and rats(*Rattus* sp.). This aversion has been reported lasting up to 58 days (Southern 1954, Mohana and Prakash 1980, Parshad and Kochar 1995). The development of aversion can be reduced by adequate pre-feeding regimes (Doty 1945, Sterner 1994).
Antidote	There is no specific antidote.
Treatment	Treatment of poisoning is symptomatic; by emptying of the stomach and intestinal tract by induced vomiting and gastric lavage, administration of oxygen, treatment with cardiac and circulatory stimulants, and neutralisation of gastrc acids with sodium bicarbonate (Schoof 1970). Diazepam or pentobarbital may be needed for excessive muscloskeletal activity or seizures. Intravenous fluid therapy and live-supportive agents may be beneficial (Murphy 2009).

User safety	The user must exercise caution when handling zinc phosphide to prevent inhalation of dust or evolved phosphine, which is both toxic (see under fumigants) and highly flammable. The handling and preparation of baits should be conducted in a well ventilated area, and protective clothing worn so that dust is not absorbed through skin abrasions (Freeman et al. 1954, Anon. 1967).

Environmental fate:

Zinc phosphide is chemically stable for long periods of time when kept dry but deterioration is rapid under acid or damp conditions (Elmore and Roth 1943, Doty 1945, Hayne 1951, Guerrant and Miles 1969, Janda and Bosseova 1970, Bell 1972, Hilton and Robison 1972). When applied in the field, zinc phosphide is converted rapidly to phosphate and zinc ions with variable, usually undetectable, amounts of phosphine gas released (Hilton and Robison 1972). Under average conditions, the toxic activity of baits persists for approximately two weeks in the field, with decomposition rates affected by soil moisture and pH, rainfall duration, bait type and application technique (Doty 1945, Hayne 1951, Anon. 1967, Janda and Bosseova 1970, Hilton and Robison 1972, Sterner and Ramey 1995, Twigg et al. 2001).

Decay time in soils	In soils zinc phosphide can be hydrolysed to phosphine gas or oxidised yielding zinc, phosphate ions and various harmless phosphorous oxyacids. The rate of decomposition increases with soil moisture. Soil types differ in their ability to oxidise zinc phosphide, with decomposition occurring faster in more acidic soils (Hilton and Mee 1972, Hilton and Robison 1972). The influence of microbial activity on zinc phosphide decomposition or phosphine oxidation is not fully understood (Hilton and Robison 1972).
Aquatic systems	Zinc phosphide is poorly soluble in water and does not readily decompose in pure water. In the field, the bottom or suspended sediments and impurities present are the catalysts for decomposition, with very little phosphine released (Hilton and Robison 1972). Phosphine when it is in solution can be acutely toxic to aquatic life (see Table 27), however these levels are well above those produced from the decomposition of zinc phosphide in water (Hilton and Robison 1972).
Effects on plants	Zinc is a trace element required by plants. Translocation in plants is minimal. Residues found in broad range of crops have been well below the permitted maximum residue level and pose little threat of contamination for animal or human consumption (Robison and Hilton 1971, Hilton and Mee 1972, Tietjen 1976, Tickes 1985, Goodall et al. 1998).

Acute toxicity to vertebrate species:

Zinc phosphide is a nonspecific poison, and the toxicity varies according to the species exposed and the pH of the bait material or the stomach contents. Based on LD_{50} levels birds, especially chickens (*Gallus gallus domesticus*) and pheasant species, are the most sensitive to zinc phosphide poisoning. Rodents are also highly susceptible as they lack the ability to vomit, a reflex which is thought to offer a degree of protection from acute poisoning by this toxin (Johnson and Voss 1952, Schoof 1970, Schitoskey 1975, Hill and Carpenter 1982). Also the increased susceptibility rats (*Rattus* sp.) may be influenced by their continuous secretion of gastric acid, while animals such as cats (*Felis catus*) and dogs (*Canis lupus familiaris*) do so only intermittently under the influence of food (Oehme 1970).

Table 26. The sensitivity to zinc phosphide for a range of species expressed as the acute oral median lethal dose (LD_{50}). The amount of zinc phosphide is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991, Witmer et al. 2010).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				

Mouse, *Mus musculus*	25.8-53.3	0.02	0.52-1.07	(Bell 1972, Jing-Hui and Marsh 1988)
Brown rat, *Rattus norvegicus*	27-48	0.32	8.6-15.4	(Dieke and Richter 1946, Schoof 1970, Hood 1972)
Black rat, *Rattus rattus*	21.3	0.28	0.64	(Hood 1972)
Rabbit, *Oryctolagus cuniculus*	ca. 75	1.6	120	(Lazarus 1956)
Sheep, *Ovis aries*	40-70	50	2000-3500	(Fitzpatrick et al. 1955)
Cattle, *Bos primigenius*	50	500	25000	(Anon. 1967)
Pig, *Sus scrofa*	~40-60	70	2800-4200	(Fitzpatrick et al. 1955, Kaukeinen 1979)
Cat, *Felis catus*	~40	5.0	200	(Hood 1972)
Kit fox, *Vulpes macrotis*	93	2.0	186	(Schitoskey 1975)
Dog, *Canis lupus familiaris*	~40	16.0	640	(Hood 1972)
Human, *Homo sapiens*	40	70	2800	(Dipalma 1981)
Introduced Birds				
Chicken, *Gallus gallus domesticus*	7-26	2.8	19.6-72.8	(Blaxland and Gordon 1945, Robertson et al. 1945, Shivanandappa et al. 1979)
Mallard duck, *Anas platyrhynchos*	35.7-67.4	1.2	42.8-80.9	(Hood 1972)
Ring-necked pheasant, *Phasianus colchicus*	8.8-26.7	1.2	10.6-32.0	(Hayne 1951, Janda and Bosseova 1970, Hood 1972)
English sparrow, *Passer domesticus*	~20-50	0.03	0.6-1.5	(Hood 1972)
Amphibians and reptiles				
American alligator, *Alligator mississippiensis*	28	28	784	(Witmer et al. 2010)

Table 27. The sensitivity to phosphine to a range of aquatic vertebrate species expressed as the acute median lethal concentration (LC_{50}) in milligrams per litre of water.

Species	LC_{50} (mg/L)	Reference
Fish		
Rainbow trout, *Oncorhynchus mykiss*	0.5	(Hood 1972)
Carp. *Cyprinus carpio*	0.3	(Hood 1972)
Bluegill sunfish, *Lepomis macrochirus*	0.8	(Hood 1972)

Toxicity to invertebrate species:

No information is available on the effects of zinc phosphide or phosphine on terrestrial invertebrates. The median effective concentration for *Daphnia* sp. exposed to phosphine in a 24 hour test was 0.2 mg/L (Tomlin 2009).

Non-target primary risk profile:

Cases of primary poisoning of livestock, pets, and birds have been reported overseas where zinc phosphide can been applied in a range of situations. Horses (*Equus ferus caballus*), cattle (*Bos primigenius*), pigs (*Sus scrofa*), poultry, game birds and non-target rodents have died eating bait residues (Blaxland and Gordon 1945, Doty 1945, Hare and Orr 1945, Ingram 1945, Hayne 1951, Freeman et al. 1954, Collins 1966, Janda and Bosseova 1970, Schoof 1970, Glahn and Lamper 1983, Ruder et al. 2011). Although deaths have been recorded, several studies have concluded that zinc phosphide baiting programs do not pose a major threat to populations of non-target wildlife, in particular local seed-eating birds (Tietjen 1976, Matschke et al. 1983, Fellows et al. 1988, Apa et al. 1991).

In Australia, this toxin can only be applied in-crop, so the risk for many non-targets is considerably reduced if correct procedures are followed. Cases of individual deaths in wild birds have been reported in Australia (Paroz et al. 1999, Brown et al. 2002), thus confirming the occurrence of non-target poisoning, but studies into the impact on these populations are still required.

Table 28. Reports of non-target primary poisoning after zinc phosphide baiting programs.

Targeted Species	Bait presentation	Non-target Risk	Reference
Mice, *Mus musculus*	Grain – aerial application	Four birds poisoned	(Brown et al. 2002)
Gray-tailed voles, *Microtus canicaudus*	Steam rolled oat – ground application	18 of the 26 ring necked pheasants (*Phasianus colchicus*) in the trial enclosures died, while none of the Californian quail (*Callipepla californica*) succumbed	(Ramey and Sterner 1995)
Black tailed praire dogs, *Cynomys ludovicianus*	grain	45 dead wild turkeys, *Meleagris gallopavo*, recovered from multiple locations around an area baited with zinc phosphide	(Ruder et al. 2011)

Non-target secondary poisoning risk profile:

The toxic action of zinc phosphide on the target animal depends on the breakdown of the compound to phosphine gas, which does not accumulate in muscle tissue and causes no secondary problems to scavengers. However, not all of the zinc phosphide consumed by the target animal is initially broken down, so scavengers can still be poisoned by amounts of the toxin if they consume the victim's stomach and intestines (Freeman et al. 1954). Compared with many other toxins, the secondary risk from zinc phosphide is considered to be low (Doty 1945, Johnson and Fagerstone 1994, Sterner 1996, Sterner et al. 1998, Paroz et al. 1999), and is dependent on the baiting regime and the time elapsed, and hence the zinc phosphide residues in the target animals, along with the eating habits of the secondary species, and their susceptibility to the toxin (Hood 1972, Tkadlec and Rychnovsky 1990, Johnson and Fagerstone 1994, Sterner and Mauldin 1995, Sterner et al. 1998).

Overseas, deaths have been reported for poultry pecking at poisoned rats (*Rattus* sp.) (Christopher et al. 1982). Dogs (*Canis lupus familiaris*) have been reported dying after eating poisoned rats (Stowe and Fredrick 1978). Cats (*Felis catus*) have died eating rats and voles killed by 5% zinc phosphide (Freeman et al. 1954, Tkadlec and Rychnovsky 1990) but other researchers have reported that both cats and mongooses have showed no ill effects after eating rats killed by 1% phosphide (Doty 1945). Other studies have show that no fox (*Vulpes vulpes*), badger species, coyote (*Canis latrans*), mink species, ferret (*Mustela putorius furo*) or owl deaths occurred after consuming baited prairie voles (*Microtus ochrogaster*) (Bell 1972, Bell and Dimmick 1975), prairie dogs (*Cynomys* sp.) (Tietjen 1976, Matsche et al. 1992) or poisoned kangaroo rats (*Dipodomys* sp.) (Schitoskey 1975). The results of Witmer et al. (2010) suggest that nutria (*Myocastor coypus*) control in wetland areas poses only a very small risk to native alligators. Humans have had no ill effects after consuming the meat from poisoned geese (Freeman et al. 1954).

In Australia, the species thought to be at risk from secondary poisoning are mouse (*Mus* sp.) predators (especially raptors), and scavengers of dead mice such as crows (*Corvus* sp.) (Parker and Hannan-Jones 1996, Caughley et al. 1998). Paroz et al. (1999) investigated the residue levels in mice after a baiting program and calculated that an adult bird would need to consume at least nine mice to succumb.

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Anticoagulants - hydroxycouramins

Brodifacoum

Chemical name: 3-[3-(4'-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycouramin

Synonyms: Bromfenacoum, WBA 8119

Physical chemistry:

Formula	$C_{31}H_{23}BrO_3$
Molecular wt	523.42
Physical form	Powder
Colour	Off-white to buff or beige
Taste	Tasteless
Odour	Odourless
Melting point	228-232^{o}C
Solubility	Low solubility in water. Slightly soluble in alcohols and benzene. Soluble in acetone
Stability	Stable thermally up to 50 ^{o}C and for 30 days in direct sunlight. Degraded by UV light when in solution.

Applications:

History	Rodenticide properties reported in 1976 (Redfern et al. 1976). First marketed in 1978.
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.), especially warfarin-resistant strains. May only be used in and around buildings, not in open areas.
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Ready to use grain, and pellet baits, wax block, paste and bait concentrate.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001).
Latent period	As a second generation anticoagulant, brodifacoum usually requires only a single feed to deliver a lethal effect, but like all anticoagulants there is a considerable delay before the onset of symptoms which can be species specific. Clinical signs first appear in rats (*Rattus* sp.) after two days (Saxena and Sharma 1984). Symptoms where not observed in brushtail possums

	(*Trichosurus vulpecula*) for two weeks (Littin et al. 2000).
Symptoms	Characteristic clinical signs include pulmonary distress, lethargy, anorexia, pale extremities and external bleeding from mouth, nose and anal region noticed. Animals gradually become more inactive with some individuals became paralysed (Saxena and Sharma 1984) (Godfrey et al. 1981b, DuVall et al. 1989).
Time to death	Time to death in rabbits (*Oryctolagus cuniculus*) 4-18 days (Godfrey et al. 1981b, Williams et al. 1986), rats (*Rattus* sp.) 3-14 days (Lund 1981, Saxena and Sharma 1984, Littin et al. 2000), mice (*Mus* sp.) 3-18 days (Rowe and Bradfield 1976, Lund 1981, Newton et al. 1990), and the brushtail possum (*Trichosurus vulpecula*) 15-45 days (Littin et al. 2000).
Detoxification and excretion of sub-lethal doses	Brodifacoum undergoes little metabolism and is excreted mainly in the faeces (Laas et al. 1985, Parmar et al. 1987). Half-life in rat (*Rattus* sp.) liver 114-130 days (Parmar et al. 1987, Fisher et al. 2003), and mouse (*Mus* sp.) liver 307 days (Vandenbroucke et al. 2008).
Accumulation of sub-lethal doses	A highly cumulative poison due to its high lipophilicity and extremely slow elimination. It has the longest duration of action of all available anticoagulants, with sub-lethal residues persisting in rats (*Rattus* sp.) after three months (Murphy et al. 1998), sheep (*Ovis aries*) four months (Laas et al. 1985), brushtail possum (*Trichosurus vulpecula*) eight months (Eason et al. 1996a, Eason et al. 1996b), and in some cases more than a year after exposure (Spurr et al. 2005, Dowding et al. 2006).
Long term effects of sub-lethal doses	Has caused death of neo-natal puppies (*Canis lupus familiaris*) (Munday and Thompson 2003) and abortions and reduced lambing rates in sheep (*Ovis aries*) (Godfrey 1985), although no effects noted for pregnant rats (*Rattus* sp.) or rabbits (*Oryctolagus cuniculus*) (Gee 2005). No indicators of sub-lethal effects found in wild birds (Murray 2011), particularly bone density (Knopper et al. 2007). Although no studies have been conducted, sub-lethal haemorrhaging thought to interfere with locomotion and hence may predispose victims to predation, starvation and trauma (Stone et al. 2003) and impact on breeding success (Stephenson et al. 1999).
Aversion	Bait shyness has not been observed in rats (*Rattus* sp.) or mice (*Mus* sp.), however baits can be unpalatable at higher concentrations (Redfern et al. 1976, Dubock and Kaukeinen 1978, Saxena and Sharma 1984). Brushtail possums (*Trichosurus vulpecula*) also did not develop bait shyness after eating sub-lethal bait (Morgan et al. 2002).
Tolerance	No evidence of tolerance has been reported.
Resistance	There is little evidence of resistance to this anticoagulant (MacNicoll et al. 1996).
Antidote	Effective antidote is Vitamin K_1. As this toxin can affect the body for many months, the antidote must be administered regularly for an extended period.
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation.

Phenobarbital may accelerate the metabolism of some anticoagulants (Kohn et al. 2003, Cope 2004).

User safety — Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

No residues were found in soil or water after aerially baiting with cereal pellets or using wax-coated cereal blocks placed at bait stations (Morgan et al. 1996, Ogilvie et al. 1997).

Decay time in soils — Couramin anticoagulants are tightly bound to soil and tend not to leach from soils containing clay or organic materials. Degraded in soils (pH 5.5-8) under aerobic and flooded conditions (Tomlin 2009).

Aquatic systems — Very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment (Tomlin 2009).

Acute toxicity to vertebrate species:

Brodifacoum is extremely toxic to many mammals and birds. There is no published data for reptiles or amphibians. The acute (single dose) toxicity of brodifacoum for a range of species is compared in Table 29. Only a single dose is usually required, however it is equally effective in multiple doses (Dubock and Kaukeinen 1978, Godfrey et al. 1981b).

Table 29. The sensitivity to brodifacoum for a range of species expressed as the single oral median lethal dose (LD_{50}). The amount of brodifacoum is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	0.4	0.02	0.008	(Redfern et al. 1976)
Brown rat, *Rattus norvegicus*	0.26	0.32	0.083	(Redfern et al. 1976)
Rabbit, *Oryctolagus cuniculus*	0.2-0.3	1.6	0.32-0.48	(Dubock and Kaukeinen 1978, Kaukeinen 1979, Godfrey et al. 1981b)
Sheep, *Ovis aries*	c. 10	50	c. 500	(Godfrey 1985)
Pig, *Sus scrofa*	0.1-2.0	70	7-140	(Dubock and Kaukeinen 1978, Kaukeinen 1979)
Cat, *Felis catus*	25	5.0	125	(Dubock and Kaukeinen 1978, Kaukeinen 1979)
Dog, *Canis lupus familiaris*	0.25-3.5	16.0	4-56	(Dubock and Kaukeinen 1978, Kaukeinen 1979, Godfrey et al. 1981a)
Native mammals				
Brushtail possum, *Trichosurus vulpecula*	0.17	3.5	0.6	
Red-necked wallaby, *Macropus rufogriseus*	1.3	19	24.7	(Godfrey 1984)
Introduced birds				
English sparrow, *Passer domesticus*	>6	0.029	0.17	(Godfrey 1985, 1986)

Chicken, *Gallus gallus domesticus*	10-100	2.8	28-280	(Dubock and Kaukeinen 1978, Kaukeinen 1979)
Mallard duck, *Anas platyrhynchos*	4.6	1.2	5.52	(Godfrey 1985, 1986)
Ring-necked Pheasant, *Phasianus colchicus*	10	1.2	12	(Godfrey 1985, 1986)

Toxicity to invertebrate species:

A wide range of invertebrate species have been reported feeding on brodifacoum baits but there have been few reports of adverse effects. One exception is the death of an unspecified snail species by Gerlach and Florens (2000). The majority of terrestrial invertebrates sampled contained no detectable residues of this toxin, with low concentrations found in slugs and cave weta, suggesting that invertebrates are not likely to accumulate this toxin, metabolising and/or excreting it within a few days (Morgan et al. 1996, Ogilvie et al. 1997, Pain et al. 2000, Booth et al. 2003, Brooke et al. 2011). Brodifacoum was found to persist longer in marine invertebrates such as shellfish, mussels and paua, for up to 31 months after exposure (Primus et al. 2005).

Brodifacoum was found to be toxic to earthworms at 500mg/kg of soil, a concentration unlikely to be attained after field application of baits (Booth et al. 2003).

Table 30. The sensitivity to brodifacoum for a range of invertebrate species expressed as the oral median lethal concentration (LC_{50}) or the Median Effective Concentration (EC_{50}) as the concentration in water (milligrams per litre) that immobilises 50% of individuals.

Species	Toxicity	Time frame (hours)	Reference
Water flea, *Daphnia* sp.	LC_{50} >0.04 mg/L	48	(Tomlin 2009)
Algae, *Selenastrum capricornutum*	E_rC_{50} >0.04 mg/L	72	(Tomlin 2009)

Non-target primary risk profile:

Because of its toxicity and persistence brodifacoum poses a major threat to non-target species (Eason and Spurr 1995, Bowie and Ross 2006). In the USA over 80% of anticoagulant deaths recorded in a ten year period involved this toxin, with non-target species including squirrels, chipmunks, racoons, deer, and opossums (Stone et al. 1999). Overseas it is linked to both mortality and sub-lethal contamination in many different species of birds (Rammell et al. 1984, Williams et al. 1986, Robertson et al. 1993, Taylor and Thomas 1993, Eason and Spurr 1995, Alterio 1996, Morgan et al. 1996, Ogilvie et al. 1997, Dowding et al. 1999, Robertson et al. 1999, Stephenson et al. 1999, Dowding et al. 2006, Hoare and Hare 2006). Deaths of non-target rodents, hares (*Lepus* sp.), sheep (*Ovis aries*), brushtail possums (*Trichosurus vulpecula*) and hedgehog species have been reported after rabbit (*Oryctolagus cuniculus*) poisoning (Rammell et al. 1984, Williams et al. 1986, Alterio 1996). A study on reef fish found no evidence of deaths after aerial baiting (Empson and Miskelly 1999).

Although the non-target effects after the broadcast use of this toxin are often severe with the death of large number of individuals there has been no reports of major impacts on non-target populations. Despite a number of robin (*Petroica australis*) deaths after rodent poisoning, no impact was noted on their island population (Taylor and Thomas 1993). A number of skinks were found dead after eating rabbit and rat baits but their populations were found to actually increase in the long term (Merton 1987, Towns 1991).

In Australia this toxin is not permitted to be used in the field, and there is no information on the effects, if any on native wildlife. Reports of non-target deaths are limited to domestic animals such as cats (*Felis catus*) and dogs (*Canis lupus familiaris*) consuming baits meant for rodents (Cope 2004, Haines 2008).

Non-target secondary poisoning risk profile:

Due to its extreme persistence within both target and non-target animals, brodifacoum presents a high secondary poisoning risk (Eason et al. 1996b, Meenken et al. 1999, Fisher et al. 2004, Hoare and Hare 2006). Although poisoned rodents and other small mammal species are the main source of secondary intake, deaths from eating contaminated invertebrates such as arthropods and gastropods have also been reported. The importance of reptiles as source of secondary intake is unknown (Hoare and Hare 2006).

Overseas reports of secondary poisoning of avian predators and scavengers in the laboratory and field include owls, hawks, eagles, gulls, ravens and crows (Mendenhall and Pank 1980, Rammell et al. 1984, Williams et al. 1986, Hegdal and Colvin 1988, Newton et al. 1990, Howald et al. 1999, Stephenson et al. 1999, Stone et al. 1999, Carter and Burn 2000, Stone et al. 2003, Albert et al. 2010, Murray 2011, Thomas et al. 2011). Baby turkey vultures (*Cathartes aura*) died after being fed brodifacoum poisoned mice (*Mus* sp.) by their parents in a zoo, as well as other species dying after eating poisoned mice or cockroaches (Borst and Counotte 2002). Dottrels, stilts and plovers died after consuming contaminated sandhoppers (Dowding et al. 2006). Contaminated weta pose a low risk (Bowie and Ross 2006).

There are also overseas reports of mammalian predators such as mustelids, foxes (*Vulpes vulpes*), cats (*Felis catus*) and dogs (*Canis lupus familiaris*) dying from secondary brodifacoum poisoning (Godfrey et al. 1981a, Rammell et al. 1984, Williams et al. 1986, Alterio et al. 1997, Brown et al. 1998, Dowding et al. 1999, Stone et al. 1999, 2003). Carnivorous/scavenger snails may also be at risk from eating other contaminated snail species (Gerlach and Florens 2000).

Although there has been a large number of individual deaths reported overseas, several authors have reported there have been no long-term population impacts (Rammell et al. 1984, Williams et al. 1986, Newton et al. 1990, Ogilvie et al. 1997), as most are resilient enough to withstand this additional mortality (Hegdal and Colvin 1988). However the results from modelling indicate that 11% of the sampled great horned owl (*Bubo virginianus*) population in Canada may be at risk from second generation anticoagulants such as brodifacoum (Thomas et al. 2011).

Humans may be potentially at risk from consuming contaminated meat from deer, goats (*Capra* sp.), pigs (*Sus scrofa*) and land crabs, however as only low residues have been detected the risk is considered minimal (Eason et al. 1999, Pain et al. 2000, Eason et al. 2001, Morriss et al. 2005).

In Australia this toxin is currently restricted to indoor use and reports of secondary poisoning are limited to domestic animals such as dogs and cats (Cope 2004, Haines 2008). This restriction has not always been in place and in a long-term 21 year study Young and de Lai (1997) detected a major decline in populations of several species of raptors in Queensland coinciding with the introduction of brodifacoum baiting in cane-fields. Although secondary poisoning was not proven to be direct cause, the patterns of decline were more consistent with the sudden introduction of this additional mortality factor than the alternative proposals of prey species decline or habitat change.

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Bromadiolone

Chemical name: 3-[3-(4'-bromobiphenyl-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxycoumarin

Synonyms: broprodifacoum, LM-637

Source: Mixture of two diastereoisomers

Physical chemistry:

Formula	$C_{30}H_{23}BrO_4$
Molecular wt	527.4
Physical form	Powder
Colour	Yellowish
Melting point	172-203 ^{o}C
Solubility (at 20^{o}C)	Only slightly soluble in water. Soluble in acetone, slightly soluble in chloroform, practically insoluble in diethyl ether and hexane.
Stability	Thermally stable below 150 ^{o}C. Flash point 218^{o}C. Rapidly degraded by photolysis.

Applications:

History	First reported in 1976 (Grand 1976).
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.), especially warfarin-resistant strains. May only be used in and around buildings, not in open areas (Meehan 1978).
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Bait concentrate, contact powder, wax block, ready to use grain, and pellet bait.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001).
Latent period	Requires only a single feed to deliver a lethal effect, but like all anticoagulants there is a considerable delay before the onset of symptoms.
Symptoms	Characteristic anticoagulant clinical signs included lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (DuVall et al. 1989).
Time to death	Time to death in rats (*Rattus* sp.) 2-16 days, and mice (*Mus* sp.) 3-19 days.

	Not significantly influenced by amount of poison eaten (Meehan 1978, Redfern and Gill 1980, Rowe et al. 1981).
Detoxification and excretion of sub-lethal doses	Bromadiolone undergoes little metabolism and is excreted mainly in faeces. There is an initial rapid elimination phase lasting up to 4-8 days in rats (*Rattus* sp.) and mice (*Mus* sp.), followed by a slower phase. The half-life in mice liver is 28 days and rat liver is 170 days (Kamil 1987, Parmar et al. 1987, Poche 1988, Vandenbroucke et al. 2008). The half-life in humans is 28 days (Lo et al. 2006). Bromadiolone is not degraded in the rumen of sheep (*Ovis aries*) (Berny et al. 2006).
Accumulation of sub-lethal doses	Bromadiolone is a highly cumulative poison and elimination tends to be very slow. It has a relative long duration of action, with sub-lethal residues still persisting up to 135 days in voles (Sage et al. 2008).
Long term effects of sub-lethal doses	Sub-lethal doses cause severe liver damage in rats (*Rattus* sp.) (Kumar and Saxena 1993), but has no effect on the breeding performance of mice (*Mus* sp.) (Twigg and Kay 1995). No long-term effect found on the bone density in range of wild predatory birds (Knopper et al. 2007). Found to adversely affects body condition and fitness in mustelids (Elmeros et al. 2011). Thought that sub-lethal haemorrhaging may interfere with locomotion hence predisposing victims to predation, starvation and trauma (Stone et al. 2003).
Aversion	No reports of bait shyness. Highly palatable to rats (Marsh 1977).
Tolerance	No evidence of tolerance to this anticoagulant reported.
Resistance	In rats (*Rattus* sp.) there is evidence of cross resistance with warfarin (Rowe et al. 1981) and also difenacoum (MacNicoll et al. 1996), although not resistant in large numbers (Endepols et al. 2007). Resistance reported in water voles (*Arvicola* sp.) in France (Vein et al. 2011).
Antidote	Antidote is Vitamin K_1 which needs to be administered regularly over a prolonged period to be fully effective.
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Kohn et al. 2003, Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Field tests with grain and pellet baits over 21 days demonstrated that the active ingredient degraded by 78 and 45%, respectively (Poche 1988).

Decay time in soils	Half-life in soil ranging from 1.8 - 23 days depending on conditions. In presence of light may be lower than 0.1 day. Not readily leached in soils containing

organic matter so not expected to contaminate water supplies and aquifers. Low solubility in water and adsorption to soil particles appears to cause retention in upper soil strata (Askham 1986).

Effects on plants — The uptake and transport of this chemical by plants, even under ideal conditions, is expected to be very low at the recommended field-use concentrations (Askham 1986).

Acute toxicity to vertebrate species::

Bromadiolone is very toxic to many mammals. There is no published data for reptiles or amphibians. The acute (single dose) toxicity of brodifacoum for a range of species is compared in Table 31.

Table 31. The sensitivity to bromadiolone for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of bromadiolone is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	0.86-1.75	0.02	0.02-0.04	(Meehan 1978)
Brown rat, *Rattus norvegicus* (lab. strain)	0.57-0.75	0.32	0.18-0.24	(Meehan 1978)
Brown rat, *Rattus norvegicus* (wild strain)	1.1-1.8	0.32	0.35-0.58	(Meehan 1978)
Rabbit, *Oryctolagus cuniculus*	0.3-1.0	1.6	0.96-1.6	(Grand 1976)
Pig, *Sus scrofa*	0.5-3.0	70	50-300	(Grand 1976)
Cat, *Felis catus*	>25.0	5.0	125	(Grand 1976)
Dog, *Canis lupus familiaris*	6-11	16.0	96-176	(Poche 1988)

Toxicity to invertebrate species:

The toxicity to bromadiolone for a range of invertebrate species is shown in Table 32. Krizkova et al. (2007) reported no mortality of earthworms.

Table 32. The sensitivity to bromadiolone for a range of invertebrate species expressed as the oral median lethal concentration (LC_{50}) or the Median Effective Concentration (EC50) as the concentration in water (milligrams per litre) that immobilises 50% of individuals.

Species	Toxicity	Time frame (hours)	Reference
Worms	LC_{50} >1054mg/kg dry weight	-	(Tomlin 2009)
Water flea, *Daphnia* sp.	EC_{50} 5.79mg/L	48	(Tomlin 2009)
Algae	E_rC_{50} 1.14mg/L	72	(Tomlin 2009)

Non-target primary risk profile:

Overseas bromadiolone is responsible for a number of non-target deaths including lagomorphs, opossums and skunks (Stone et al. 1999, Berny 2007). When trialled for mouse (*Mus* sp.) control in a small crop area in Australia, no deaths in non-targets were recorded (Twigg et al. 1991).

Non-target secondary poisoning risk profile:

Due to its persistence bromadiolone may poses a secondary poisoning risk, particular after large field-baiting programs (Berny et al. 1997, Giraudoux et al. 2006, Sage et al. 2008). In laboratory research owls have died after eating poisoned rats (*Rattus* sp.) (Mendenhall and Pank 1980), although only a small number of stoats (*Mustela erminea*) and no buzzards (*Buteo* sp.) died when fed poisoned voles. Many stoats only became sick and recovered fully after one month (Grolleau et al. 1989). There have been secondary deaths recorded in the field including owls, buzzards, foxes (*Vulpes* sp.) and stoats (Berny et

al. 1997, Stone et al. 1999, Carter and Burn 2000, Stone et al. 2003, Kupper et al. 2006, Thomas et al. 2011).

One study revealed that even though there were no mustelid deaths, high residues adversely effected their body condition (Elmeros et al. 2011). Many wild owl species have been found with high bromadiolone residues (Albert et al. 2010), but the impact of chronic levels on fitness needs further investigation (Stone et al. 2003). Also requiring further research is the impact of secondary poisoning on the populations of these predators and scavengers. The modelling by Thomas et al. (2011) indicates that 11% of the sampled great horned owl (*Bubo virginianus*) population in Canada may be at risk from second generation anticoagulants such as bromadiolone.

The risk to animals eating contaminated invertebrates seems lower. Residues have been detected in species of hedgehogs but no deaths have been recorded (Dowding et al. 2010). Similarly no death were recorded in common voles (*Microtus arvalis*) fed contaminated earthworms (*Eisenia fetida*) (Krizkova et al. 2007).

In Australia this toxin is currently restricted to indoor use and reports of secondary poisoning are limited to domestic animals such as cats (*Felis catus*) and dogs (*Canis lupus familiaris*) (Cope 2004, Haines 2008).

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Coumatetralyl

Chemical name: 4-hydroxyl-3-(1,2,3,4-tetrahydro-1-naphthyl)coumarin

Synonyms: B-25634

Source: Condensation of 4-hydroxycouramin and 1,2,3,4-tetra-1-naphthol

Physical chemistry:

Formula	$C_{19}H_{16}0_3$
Molecular wt	292.3
Physical form	Crystalline powder
Colour	Yellowish - white
Taste	Tasteless
Odour	Slight characteristic odour
Melting point	169 ^{o}C
Solubility	Slightly soluble in water. Slightly soluble in benzene, toluene and diethyl ether. Soluble in alcohols and acetone. Readily soluble in alkalis, with the formation of salts.
Stability	Thermally stable up to at least 150 ^{o}C. Not hydrolysed by water over 5 days (25 ^{o}C). Rapidly decomposed in aqueous solutions exposed to sunlight or UV light.

Applications:

History	Known since 1957 and commercialised in 1962 (Pospischil and Schnorbach 1994).
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.) although unlikely to control warfarin-resistant mice effectively (Rowe and Redfern 1968). Only be used in and around buildings for mice, however can be used against rats in certain crops.
Poison Schedule	Australia: Schedule 5 or 6 (depending on formulation type)
Formulation types	Wax block bait, ready to use grain or pellet bait, liquid or oil concentrate, tracking powder.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Blocks the vitamin K cycle by inhibiting vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic doses can cause damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over several days and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001).

Latent period	Coumatetralyl requires multiple feeds over several days to elicit lethal effects. As with all anticoagulants displays a considerable delay before the onset of symptoms.
Symptoms	Characteristic anticoagulant clinical signs included lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Savarie 1981).
Time to death	Time to death in sparrows (*Passer* sp.) is 3-11 days (Heyl 1986)
Detoxification and excretion of sub-lethal doses	There is minimal metabolism of this toxin and it is excreted mainly unchanged in the faeces and urine. Elimination is faster than the second generation anticoagulants. In rats (*Rattus* sp.) it has a liver half life 55 days (Parmar et al. 1987) and in mice (*Mus* sp.) 16 days (Vandenbroucke et al. 2008).
Accumulation of sub-lethal doses	Is cumulative in nature and consumption is required over a number of days for mortality.
Long term effects of sub-lethal doses	No obvious long-term effects have been reported.
Aversion	No evidence of aversion has been reported.
Tolerance	No evidence of tolerance has been reported.
Resistance	Some degree of resistance was first noted in 1969 in warfarin-resistant rats and is present at a low-level in populations throughout Europe, however it does not appear to have a significant impact on control efforts using this toxin (Greaves and Ayres 1969, Lund 1972, Endepols et al. 2007).
Antidote	Effective antidote is Vitamin K_1.
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Decay time in soils	Couramin anticoagulants are tightly bound to soil and tend not to leach from soils containing clay or organic materials. Half life ranges from 1.8 - 7.4 days.
Aquatic systems	Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment

Acute toxicity to vertebrate species:

Coumatetralyl is more toxic to rats (*Rattus* sp.) than mice (*Mus* sp.) (Table 33). For pigs (*Sus scrofa*) a dose of 1-2mg/kg over a period of 7-12 days is fatal (Dobson 1973), and piglets are especially sensitive. This anticoagulant has a relatively low toxicity to birds (Heyl 1986, Burn et al. 2002).

Table 33. The sensitivity to coumatetralyl for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of coumatetralyl is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	>1000	0.02	20	(Vandenbroucke et al. 2008)
Brown rat, *Rattus norvegicus*	16.5	0.32	5.3	(Tomlin 2009)
Rabbit, *Oryctolagus cuniculus*	>500	1.6	>800	(Tomlin 2009)

Toxicity to invertebrate species:

The 48 hour LC_{50} for *Daphnia* sp. is reported as >14 mg/L (Tomlin 2009).

Non-target primary risk profile:

In UK non-target rodent species most at risk with some local populations declining after baiting but recovered after three months (Brakes and Smith 2005). In the USA deer deaths have been reported (Stone et al. 1999).

Non-target secondary poisoning risk profile:

Direct risk to predatory and scavenging birds and mammals considered only low (Burn et al. 2002, O'Connor et al. 2003), however indirectly may limit food supply for some specialist predators (Brakes and Smith 2005).

Mammal deaths have been reported under laboratory conditions, but not birds. Ferrets (*Mustela putorius furo*) died after eating poisoned rats (*Rattus* sp.), but no weka (*Gallirallus australis*) succumbed (O'Connor et al. 2003). Cats (*Felis catus*) and rats died after being fed poisoned sparrows (*Passer* sp.) but all predatory birds survived (Heyl 1986).

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Difenacoum

Chemical name: 3-(3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthyl)-4-hydroxycouramin, 3-[3-(1,1'-biphenyl)-4-yl-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2*H*-1-benzopyran-2-one

Synonyms: diphenacoum

Source: Synthesized by the condensation of 4-hydroxycomarin and 3-biphenyl-4-yl-1,2,3,4-tetrahydro-1-naphthol.

Physical chemistry: (Anon. 2009)

Formula	$C_{31}H_{24}O_3$
Molecular wt	444.5
Physical form	Powder
Colour	White to off-white
Odour	Odourless
Melting point	215-217^{o}C
Solubility	Low soluble in water and alcohols. Soluble in organic solvents such as acetone, chloroform and benzene.
Stability	Thermally stable up to 250 ^{o}C, does not show oxidising or explosive properties. Degrades in presence of water and light.

Applications:

History	Rodenticide properties first reported in 1975 (Hadler et al. 1975, Hadler and Shadbolt 1975) and marketed in 1976.
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.). Effective against rats resistant to other anticoagulants, but not totally effective against resistant mice (Hadler et al. 1975, Rennison and Hadler 1975). May only be used in and around buildings, not in open areas.
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Ready to use grain, and pellet baits, wax block, gel, paste and liquid concentrate.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001).
Latent period	As a second generation anticoagulant, difenacoum usually requires only a single feed to deliver a lethal effect, but like all anticoagulants there is a delay before the onset of symptoms with clinical signs occurring within 18 hours of

	ingestion of a toxic dose.
Symptoms	Clinical signs are progressive and include lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Savarie 1981).
Time to death	Time to death in rats (*Rattus* sp.) 4-13 days, and mice (*Mus* sp.) 4-22 days (Hadler et al. 1975, Rowe and Bradfield 1976, Lund 1981, Rowe et al. 1981).
Detoxification and excretion of sub-lethal doses	Difenacoum is largely metabolised and the major route of elimination of these metabolites is via faeces with urine being only a minor route. Bile is also an important route of excretion. Elimination from the body is relatively slow. In rats (*Rattus* sp.) the liver half life is 120 days, in mice (*Mus* sp.) 62 days (Parmar et al. 1987, Vandenbroucke et al. 2008, Anon. 2009).
Accumulation of sub-lethal doses	Although only requires single dose for fatality, sub-lethal doses can accumulate and become lethal. The chronic cumulative doses for rats (*Rattus* sp.) and mice (*Mus* sp.) are about half of acute dose.
Long term effects of sub-lethal doses	Considered developmentally toxic to humans as per warfarin (Anon. 2009), but no developmental effects have been recorded in rats (*Rattus* sp.) and rabbits (*Oryctolagus cuniculus*) (Bull 1976). No long-term effects have been found on bone density in range of wild predatory birds (Knopper et al. 2007).
Aversion	Some evidence of unpalatability in rats (*Rattus* sp.) (Hadler et al. 1975), but no reports of bait shyness.
Tolerance	No evidence of tolerance to this anticoagulant reported.
Resistance	Resistance was discovered in wild brown rats (*Rattus norvegicus*) in parts of Europe within a few years of commercial use (Redfern and Gill 1978). Resistance occurs only in warfarin-resistant rats indicating a form of cross resistance and is more prevalent in females than males (Greaves et al. 1982). Cross-resistance also occurs with bromadiolone (Cowan et al. 1995, MacNicoll et al. 1996). The prevalence and degree of resistance has not had a long-term impact to effectiveness (Cowan et al. 1995). There are no reports of resistance in mice (*Mus* sp.) and black rats (*R. rattus*), but a lack of information does not necessarily mean lack of resistance (Anon. 2009).
Antidote	Effective antidote is Vitamin K_1, with prolonged administration over several weeks required (Bull 1976).
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing

should also be washed.

Environmental fate:

Decay time in soils	Difenacoum is not readily biodegradable. Half-life in marine sediment >180 days, freshwater sediment >120 days. Degrades slowly in soils and is not mobile so unlikely to leach and contaminate groundwater (Anon. 2009).
Effects on plants	No tests have been conducted on soil micro-organisms or plants as difenacoum not expected to be particularly toxic to them on the basis of its mode of action (Anon. 2009).

Acute toxicity to vertebrate species:

The acute (single dose) toxicity of difenacoum for a range of species is compared in Table 34. There is a difference in sensitivity between male and female rats (*Rattus* sp.) (Winn et al. 1987).

Difenacoum is very toxic to fish. The 96 hour LC_{50} for rainbow trout, *Oncorhynchus mykiss*, is reported as 0.10 mg/L (Tomlin 2009).

Table 34. The sensitivity to difenacoum for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of difenacoum is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	0.8	0.02	0.016	(Bull 1976, Kaukeinen 1979)
Brown rat, *Rattus norvegicus* (lab. strain)	1.8-2.5	0.32	0.58-0.8	(Bull 1976)
Brown rat, *Rattus norvegicus* (wild strain)	2.5-3.5	0.32	0.8-1.12	(Bull 1976)
Rabbit, *Oryctolagus cuniculus*	2.0	1.6	3.2	(Bull 1976, Kaukeinen 1979)
Pig, *Sus scrofa*	c. 80-100	100	8000-10000	(Bull 1976, Kaukeinen 1979)
Cat, *Felis catus*	>100	5.0	>500	(Bull 1976, Kaukeinen 1979)
Dog, *Canis lupus familiaris*	50	16.0	800	(Bull 1976, Kaukeinen 1979)
Introduced birds				
Chicken, *Gallus gallus domesticus*	>50	2.8	140	(Bull 1976, Kaukeinen 1979)

Toxicity to invertebrate species:

Difenacoum is toxic to aquatic invertebrates and algae, but not earthworms (Anon. 2009). The 48 hour LC_{50} for *Daphnia* sp. is reported as 0.52 mg/L (Tomlin 2009).

Non-target primary risk profile:

Although there are no reports in the literature, difenacoum would have similar potential to kill non-targets species as other anticoagulants if used inappropriately.

Non-target secondary poisoning risk profile:

Sub-lethal haemorrhaging was found in owls after feeding on poisoned rats (*Rattus* sp.) in laboratory trials (Mendenhall and Pank 1980). Several species of birds have died in zoos after consuming poisoned mice (*Mus* sp.) or cockroaches (Borst and Counotte 2002). There are reports of residues in wild avian raptors (Newton et al. 1990, Shore et al. 1999), and this toxin has been implicated in a small number of raptor deaths in the field (Carter and Burn 2000). Residues have also been found in mammal predators (Shore et al. 1999, Elmeros et al. 2011) as well as insectivores such as hedgehogs (*Erinaceus* sp.) (Dowding et al.

2010). Although no deaths have been recorded Elmeros et al. (2011) found a correlation between the fitness of some species of mustelids and the concentration of the anticoagulant residue.

Despite a number of individual deaths recorded, the risk of secondary poisoning in the field has been suggested as minimal (Bull 1976, Atterby et al. 2005), with no evidence that secondary poisoning has any impact on wild populations (Shore et al. 1999).

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Flocoumafen

Chemical name: 4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-(4-trifluoromethylbenzyloxy)phenyl]-1-naphthyl]coumarin

Synonyms: flocoumafène, WL 108366

Physical chemistry:

Formula	$C_{33}H_{25}F_3O_4$
Molecular wt	542.6
Physical form	Solid
Colour	Off-white powder
Melting point	166-168 ^{o}C
Solubility	Only slightly soluble in water. Soluble in acetone, alcohols, chloroform and dichloromethane (Bowler et al. 1984).
Stability	Thermally stable up to 250^{o}C. Stable to hydrolysis under normal conditions (Bowler et al. 1984).

Applications:

History	Flocoumafen was first synthesised in 1984 (Bowler et al. 1984).
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.), especially warfarin-resistant strains. May only be used in and around buildings, not in open areas.
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Ready to use grain and pellet baits, wax block and bait concentrate.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death from internal haemorrhages (Bowler et al. 1984, Petterino and Paolo 2001).
Latent period	Requires only a single feed to deliver a lethal effect, but like all anticoagulants there is a considerable delay before the onset of symptoms.
Symptoms	Characteristic anticoagulant clinical signs included lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Savarie 1981).
Time to death	Time to death in mice (*Mus* sp.) is between 3-11 days (Rowe et al. 1985, Lund 1988), and rats (*Rattus* sp.) 4-19 days (Bowler et al. 1984, Parshad and

	Chopra 1986, Lund 1988).
Detoxification and excretion of sub-lethal doses	Flocoumafen undergoes little metabolism and is excreted mainly in the faeces in rats (*Rattus* sp.) (Huckle et al. 1988, Huckle et al. 1989a), however there is extensive metabolism in quails (*Coturnix* sp.) and chickens (*Gallus* sp.), with elimination in excreta mostly within 24 hours (Huckle et al. 1989b, Eadsforth et al. 1993). Has a long half-life in liver of rats (220 days), shorter in quails (100 days) and mice (*Mus* sp.) (94 days) (Huckle et al. 1988, Huckle et al. 1989a, Huckle et al. 1989b, Vandenbroucke et al. 2008). Half-life in humans is seven days (Boettcher et al. 2011).
Accumulation of sub-lethal doses	Accumulative in nature (Bowler et al. 1984). Sub-lethal doses can accumulate and persist in rats (*Rattus* sp.) for 14 weeks (Huckle et al. 1988, Huckle et al. 1989a, Huckle et al. 1989b). Low residues in breast and leg muscle in hens (*Gallus* sp.), but higher in abdominal fat and skin fat. Residues also found in eggs, primarily the yolk (Eadsforth et al. 1993).
Long term effects of sub-lethal doses	No known long term effects have been reported.
Aversion	There is no evidence of aversion to this anticoagulant.
Tolerance	No evidence of tolerance to this anticoagulant have been reported
Resistance	Little evidence of resistance in rats *Rattus* sp.) (Bowler et al. 1984, Rowe et al. 1985, MacNicoll et al. 1996).
Antidote	Effective antidote is Vitamin K_1 (Bowler et al. 1984).
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Veenstra et al. 1991, Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Decay time in soils	Couramin anticoagulants are tightly bound to soil and tend not to leach from soils containing clay or organic materials (WHO 1995).
Aquatic systems	Very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. Ready-to-use formulations (50 mg/kg) are non-toxic to aquatic species.

Acute toxicity to vertebrate species:

The acute toxicity of flocoumafen for a range of species is compared in Table 35. Flocoumafen has a high order of acute toxicity to most mammalian species compared to bird species. This appears to mainly arise due to differences in metabolism (Huckle et al. 1989b).

Flocoumafen is very toxic to fish. The 96 hour LC_{50} for rainbow trout, *Oncorhynchus mykiss*, is reported as 0.067 mg/L (Tomlin 2009).

Table 35. The sensitivity to flocoumafen for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of flocoumafen is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	0.79-2.4	0.02	0.02-0.05	(Bowler et al. 1984), (Shell 1987 in Lund 1988)
Brown rat, *Rattus norvegicus*	0.25-0.56	0.32	0.08-0.18	(Bowler et al. 1984), (Shell 1987 in Lund 1988)
Black rat, *Rattus rattus*	1.0-1.8	0.28	0.28-0.50	(Shell 1987 in Lund 1988)
Rabbit, *Oryctolagus cuniculus*	0.2 - 0.7	1.6	0.32-1.12	(Bowler et al. 1984)
Pig, *Sus scrofa*	c. 60	100	c. 6000	(Roberts et al. 1985)
Cat, *Felis catus*	>10	5.0	>50	(Cope 2004)
Dog, *Canis lupus familiaris*	0.075-0.25	16.0	1.2-4	(Chesterman et al. 1984)
Introduced birds				
Chicken, *Gallus gallus domesticus*	>100	2.8	>280	(Bowler et al. 1984)
Mallard duck, *Anas platyrhynchos*	100 - 286	1.2	120-343	(Bowler et al. 1984)

Toxicity to invertebrates:

No toxicity to invertebrates detected (Bowler et al. 1984).

Table 36. The sensitivity to flocoumafen for a range of invertebrate species expressed as the median Effective Concentration (EC_{50}) as the concentration in water (milligrams per litre) that immobilises 50% of individuals.

Species	Toxicity	Time frame (hours)	Reference
Water flea, *Daphnia* sp.	EC_{50} = 0.17 mg/L	48	(Tomlin 2009)
Algae, *Selenastrum capricornutum*	E_rC_{50} >18.2 mg/L	72	(Tomlin 2009)

Non-target primary risk profile:

Non-target mammal species are more at risk than birds from baiting programs, however could still be problematic to birds if bait is a major food source over several days (Bowler et al. 1984). Shrews (*Suncus* sp.) have been reported dying after field baiting of rats (*Rattus* sp.) but no observable effect was measured on any of the non-target wildlife populations monitored (Hoque and Olvida 1988).

Non-target secondary poisoning risk profile:

Flocoumafen is less toxic to barn owls than brodifacoum, and only a single death occurred after owls were fed dosed mice (*Mus* sp.) in the laboratory (Newton et al. 1994). Only low residues have been detected in wild populations of mustelids (Elmeros et al. 2011) and none in barn owls in UK (Newton et al. 1990).

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Warfarin

Chemical name: 4-hydroxy-3-(3-oxo-1-phenylbutyl) coumarin

Synonyms: Compound-42, WARF-42, coumaphene, zoocoumarin, warfarine, Coumadin (sodium salt)

Source: Condensation of 4-hydroxylcoumarin and benzylacetone in the presence of piperidine

Physical chemistry:

Formula	$C_{19}H_{16}O_4$
Molecular wt	308.32
Physical form	Crystals
Colour	Colourless, white or light tan
Taste	Tasteless
Odour	Odourless
Melting point	162-164 ^{o}C
Solubility	Practically insoluble in water and benzene, moderately soluble in alcohols, and readily soluble in acetone and dioxane. Sodium salt is fully soluble in water.
Stability	Very stable, even to strong acids

Applications:

History	In 1939 biochemists first isolated dicoumarin in spoiled sweet clover that caused haemorrhaging and death in cattle (*Bos primigenius*). This discovery lead to the synthesis of a number of anticoagulant drugs including warfarin, which was named after the patent holder - Wisconsin Alumni Research Foundation (Link 1959).
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.).
Poison Schedule	Australia: Schedule 5 or 6 (depending on formulation type)
Formulation types	Bait concentrate, ready to use pellet baits, gel and tracking powder.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Blocks the vitamin K cycle by inhibiting vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic doses can cause damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over several days and lead to shock, loss of consciousness and eventually death (Coon and Willis 1972, Petterino and Paolo 2001).
Latent period	Warfarin and other first generation hydroxycoumarins require multiple feeds over several days to elicit lethal effects. All these anticoagulants display a considerable delay before the onset of symptoms, which is not dependent on the size of the dose or means of administration (Saunders et al. 1955, Coon and Willis 1972). In rats (*Rattus* sp.) this period is usually 2-3 days, but in

	chickens (*Gallus gallus domesticus*) it may be as short as 1-2 hours (Bai and Krishnakumari 1986).
Symptoms	Clinical signs included lameness, lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Humphreys 1978, Savarie 1981, Hone and Kleba 1984). Poisoned chickens (*Gallus gallus domesticus*) also displayed wing flapping and paralysis (Bai and Krishnakumari 1986).
Time to death	Time to death is dependent on the dose rate and frequency of feeding. In rats (*Rattus* sp.) death occurs 3-17 days after feeding, in mice (*Mus* sp.) 6-8 days (Hagan and Radomski 1953, Bentley and Larthe 1959, Lund 1981).
Detoxification and excretion of sub-lethal doses	Warfarin accumulates mainly in plasma and liver and is metabolised and eliminated comparatively rapidly compared to other anticoagulants. The metabolites do not possess any anticoagulant activities. In rats (*Rattus* sp.) the liver half-life is 10-26 days, and 90% is excreted in the urine and faeces within 14 days (Link et al. 1965, Barker et al. 1970, Coon and Willis 1972, Thijssen 1995, Fisher et al. 2003). In mice (*Mus* sp.) the liver half-life is 67 days (Vandenbroucke et al. 2008). There are large inter-species differences of warfarin metabolism in birds. Chickens (*Gallus gallus domesticus*) and ostriches (*Struthio camelus*) show higher metabolic activity than rats, while mallards (*Anas platyrhynchos*) and owls showed only a slight ability to metabolise this toxin (Watanabe et al. 2010). It is not degraded in the rumen of sheep (*Ovis aries*) (Berny et al. 2006).
Accumulation of sub-lethal doses	This toxin is cumulative by nature. Consumption is required over a number of days to maintain concentrations necessary for mortality to occur.
Long term effects of sub-lethal doses	Warfarin can cross the placenta and is known to cause abortions and interfere with foetus development in several animal species (Pugh 1968, Coon and Willis 1972, Fitzek and Gembardt 1977, Hone and Kleba 1984) including humans (foetal warfarin syndrome) (Robinson et al. 1978). Reduced bone density in children has been linked to long-term warfarin intake (Barnes et al. 2005). No long-term effects on bone density or moulting have been found in a range of wild predatory birds (Townsend et al. 1981, Knopper et al. 2007). The effects of sub-lethal haemorrhaging has not been studied, but is thought it may interfere with locomotion and hence predisposal to trauma, starvation and predation (Stone et al. 2003).
Aversion	There have been no observations of aversion to this toxin e.g. (Hone and Kleba 1984).
Tolerance	No evidence of tolerance to warfarin has been observed however a diet high in selenium can protect against toxic effects of warfarin in pigs (*Sus scrofa*) (Davila et al. 1983).
Resistance	The first observation of resistance in *Rattus norvegicus* in Scotland in 1958 (Boyle 1960) and later across Europe in 1960's, and US in 1970's (Jackson and Kaukeinen 1972). Resistance also reported in other *Rattus* species, and mice (*Mus* sp.) as well as humans around the world (O'Reilly 1970, Wallace and MacSwiney 1976, Saunders 1978, Misenheimer et al. 1994). This resistance has become widespread, including Australia, and has a significant

impact on control efforts using this toxin.

Resistance is inheritable, with a variety of mechanisms in different species. Considerable amounts of research have been undertaken on the genetic and biochemical mechanisms, as well as the development of cross resistance to other anticoagulants (Wallace and MacSwiney 1976, Thijssen 1995, Pelz et al. 2005).

Antidote — Effective antidote is Vitamin K_1. In dogs (*Canis lupus familiaris*) this is given at doses of five mg/kg initially administered intramuscularly then orally (preferably with fat-containing food to enhance absorption) for four to five days (Heisey et al. 1956, Coon and Willis 1972, Miller 1984). In humans it is usually administered slowly by intravenous drip (Hayes 1982).

Treatment — Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Kohn et al. 2003, Cope 2004).

User safety — Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Decay time in soils — Couramin anticoagulants are tightly bound to soil and tend not to leach from soils containing clay or organic materials (WHO 1995).

Acute toxicity to vertebrate species:

Warfarin is more toxic when given in multiple doses rather than one large single dose, so research has mainly concentrated on its chronic rather than its acute toxicity to target species. There is a lack of consistency in the reporting of the acute toxicity, especially in rodents and this can be partly explained by the various ways that death can occur when large doses of this toxin are consumed (Bentley and Larthe 1959). The toxicity is similar for oral and intra-peritoneal injection route of administration (Saunders et al. 1955). The acute (single dose) and the chronic (multiple dose) toxicity of warfarin for a range of species is compared in Table 37. Many bird species are more resistant to warfarin than rats (*Rattus* sp.) and other mammal species, however some species including owls are more sensitive (Watanabe et al. 2010).

Table 37. The acute and chronic oral sensitivity to warfarin for a range of species expressed as the median lethal dose (LD_{50}).

Species	Acute LD_{50} (mg/kg)	Reference	Chronic LD_{50} (mg/kg/day)	Reference
Introduced mammals				
Mouse, *Mus musculus*	374	(Hagan and Radomski 1953)	-	-
Rat (unspecified)	58-323	(Hagan and Radomski 1953)	-	-
Brown rat, *Rattus norvegicus*	186	(Petterino and Paolo 2001)	1.0 for 5 days	(Petterino and Paolo 2001)
Rabbit, *Oryctolagus cuniculus*	800	(Hagan and Radomski 1953)	-	-

Cattle, *Bos primigenius*	-	-	200 for 5 days	(Petterino and Paolo 2001)
Pig, *Sus scrofa*	1-15	(McGirr and Papworth 1955, Papworth 1958, Buck 1978, Kaukeinen 1979)	0.05 for 7 days 1.0 for 5 days	(Buck 1978, Kaukeinen 1979)
Cat, *Felis catus*	6-40	(Kaukeinen 1979)	3.0 for 5 days	(Petterino and Paolo 2001)
Dog, *Canis lupus familiaris*	200-300	(Hagan and Radomski 1953)	3.0 for 5 days	(Petterino and Paolo 2001)
Introduced birds				
Chicken, *Gallus gallus domesticus*	942 - 1000	(Hagan and Radomski 1953, Bai and Krishnakumari 1986)	-	-
Mallard duck, *Anas platyrhynchos*	620	(Erickson and Urban 2004)	-	-
Reptiles				
Brown tree snake, *Boiga irregularis*	c. 40	(Brooks et al. 1998)	-	-

Toxicity to invertebrate species:

The toxicity to invertebrates has not been reported.

Non-target primary risk profile:

Warfarin is considered safe for non-target species as it is metabolised comparatively quickly and repeated doses over several days are required for mortality.

Non-target secondary poisoning risk profile:

The secondary risk particularly under field use is considered very slight especially when compared to other anticoagulants (Bentley and Larthe 1959, Prier et al. 1962). A variety of owl species have been found with warfarin residues but no deaths have been attributed to this toxin (Albert et al. 2010).

No deaths have been reported in a variety of predatory species such as canids, mustelids, owls and magpies when feed poisoned rats (*Rattus* sp.), mice (*Mus* sp.) or rabbits (*Oryctolagus cuniculus*) in laboratory trials (Townsend et al. 1981, Aulerich et al. 1987, Poche 1999). Mink (*Mustela* sp.) and dog (*Canis lupus familiaris*) deaths have been noted after being feed warfarin poisoned nutria (*Myocastor coypus*) (Evans and Ward 1967).

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Anticoagulants - indandiones

Diphacinone

Chemical name: 2-(diphenylacetyl) indan-1,3-dione

Synonyms: diphenadione, diphacin, dipazin, diphenacin, ratindan

Physical chemistry:

Member of the indandione chemical group of anticoagulant.

Formula	$C_{23}H_{16}O_3$
Molecular wt	340.40
Physical form	Crystals
Colour	Yellow
Odour	Odourless
Melting point	145-147^{o}C
Solubility	Slightly soluble in water, more soluble than the second generation coumarin derivatives. Slightly more soluble in acetone, ethanol, and soluble in ether, toluene, xylene and chloroform. Soluble in alkalis with the formation of salts.
Stability	Stable for 14 days (pH 6-9), but hydrolysed in < 24hours (pH 4). Rapidly decomposed in water by sunlight. Decomposes at 338 ^{o}C without boiling.

Applications:

History	Rodenticide activity reported in 1952 (Correll et al. 1952). Was developed as alternate compound which was more effective than warfarin and free of patent restrictions.
Uses in Australia	Registered in all states and territories for the control of mice (*Mus* sp.) only. May only be used in and around buildings, not in open areas.
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Bait concentrate and ready to use nugget bait (Ramik).

Toxicology:

Absorption	Easily absorbed through the gastrointestinal tract, skin and respiratory system (Spiller et al. 2003).
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001). The indandione group of anticoagulants can have additional toxic effects when ingested in large quantities. When mice were given a large dose they showed signs of nervousness and muscle twitching, progressing to spasms prior to death (Cahill and Crowder 1979). Other symptoms recorded in

	humans include breathing difficulties, muscular weakness, pulmonary congestion and hyperexcitability (Savarie 1981).
Latent period	Lethal effects can be obtained from a single dose but as for all anticoagulants, there is a delay before the onset of symptoms. This period is not dependent on the size of the dose or the means of administration (Saunders et al. 1955, Heisey et al. 1956, Coon and Willis 1972).
Symptoms	Characteristic anticoagulant clinical signs included stiffness of limbs, lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Elias et al. 1978, DuVall et al. 1989).
Time to death	Dependent on dose rate and frequency of feeding; rats (*Rattus* sp.) 3-14 days, mice (*Mus* sp.) 3-21 days. (Bentley and Larthe 1959). A single dose of 40mg/kg resulted in death of a rabbit (*Oryctolagus cuniculus*) within 72 hours (Heisey et al. 1956).
Detoxification and excretion of sub-lethal doses	Accumulates in the liver of rats (*Rattus* sp.) and mice (*Mus* sp.). Not extensively metabolised and is excreted mainly in faeces. The half-life in rat liver is three days (Fisher et al. 2003). The half-life in kestrel (*Falco sparverius*) liver is shorter than rats, approximately 22 hours (Rattner et al. 2011). Approx. 75% eliminated in 2-4 days in mice and rats after 8 days (Cahill and Crowder 1979, Yu et al. 1982). Detected in cattle (*Bos primigenius*) liver after 90 days, but not detectable in other tissues and organs after 30 days (Bullard et al. 1976).
Accumulation of sub-lethal doses	Is cumulative in nature and consumption of sub-lethal doses over a number of days causes mortality.
Long term effects of sub-lethal doses	There have been no adverse chronic effects reported for rats (*Rattus* sp.) other than characteristic haemorrhages (Elias and Johns 1981, Gee 1996). Concentrations of toxin were found in the fallopian tubes of mice (*Mus* sp.) (Cahill and Crowder 1979) but there are no report of effects on fecundity in the literature. No adverse effects reported in cattle (*Bos primigenius*) treated systemically with this anticoagulant to control vampire bats (*Desmodus rotundus*) that feed on the blood (Thompson et al. 1972, Bullard et al. 1976, Elias et al. 1978). Sub-lethal haemorrhaging is thought to interfere with locomotion hence predisposing victims to predation, starvation and trauma (Stone et al. 2003) however this has not been studied.
Aversion	There have been no reports of aversion to this anticoagulant.
Tolerance	Rats (*Rattus* sp.) fed trace amounts of this toxin over time did not develop a tolerance (Gates 1957).
Resistance	Cross-resistance was first detected in warfarin-resistant *Rattus norvegicus* in the late 1950's (Boyle 1960). A low level of resistance has been found in other rats (*Rattus* sp.) in many European countries (Lund 1972), however it has not had such a significant impact on the control efforts of this toxin as for warfarin.
Antidote	Effective antidote is Vitamin K_1 but as diphacinone binds to body proteins for an extended period an increased dose and duration of administration is required. For example in dogs (*Canis lupus familiaris*), after the initial intramuscular injection, oral therapy at the rate of 5 mg/kg should continue for at least 30 days (Correll et al. 1952, Heisey et al. 1956, Mount and Feldman

1983, Miller 1984).

Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Mount and Feldman 1983, Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Not detected in seawater, fish, invertebrates and soil samples after aerial broadcast in Hawaii (Dunlevy and Swift 2010).

Acute toxicity to vertebrate species:

The acute (single dose) of diphacinone for a range of species is compared in Table 38. Diphacinone is more toxic when given in multiple doses rather than one large single dose. For example the LD_{50} associated with 14 daily oral doses in rats (*Rattus* sp.) is only 0.1mg/kg, and rabbits (*Oryctolagus cuniculus*) 0.25mg/kg/day (Correll et al. 1952), much smaller doses than the acute values detailed for these species in Table 38.

Diphacinone is generally less toxic to birds than rodents and domesticated mammals, although raptors are more sensitive than other bird species (Rattner et al. 2010, Rattner et al. 2011). Rats are more sensitive than mice (*Mus* sp.) (Yu et al. 1982). In mice it was noted that when doses greater than 300mg/kg were given, death was not caused by typical anticoagulant effects. Instead victims showed signs of nervousness and muscle twitching, progressing to spasms prior to death (Cahill and Crowder 1979).

The higher sensitivity of vampire bats, *Desmodus rotundus*, to diphacinone (oral LD_{50} 0.91 mg/kg) than cattle (*Bos primigenius*) has allowed its use for reducing attacks in Mexico. Adult cattle and calves greater than four months of age are more tolerant and can be treated systemically with this anticoagulant at dose rates which has no effect on them, or cause residue problem in their milk or meat, but is fatal to any bat that feeds on the blood (Thompson et al. 1972, Bullard et al. 1976, Elias et al. 1978).

Diphacinone is toxic to fish. The 96 hour LC_{50} for rainbow trout, *Oncorhynchus mykiss*, is reported as 2.8 mg/L (Tomlin 2009).

Table 38. The sensitivity to diphacinone for a range of species expressed as the acute oral median lethal dose (LD_{50}). The amount of diphacinone is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	340	0.02	6.8	(Correll et al. 1952)
Brown rat, *Rattus norvegicus*	1.9-20	0.32	0.6-6.4	(Ward and Crabtree 1942) (Correll et al. 1952) (Bentley and Larthe 1959) (Saunders et al. 1955) (Gaines 1969)
Rabbit, *Oryctolagus cuniculus*	35	1.6	56	(Correll et al. 1952)
Cattle, *Bos primigenius*	>5	500	>2500	(Elias et al. 1978)

Pig, *Sus scrofa*	>150	100	>15000	(Gates 1957)
Cat, *Felis catus*	14.7	5.0	73.5	(Gates 1957)
Dog, *Canis lupus familiaris*	3-7.5	16.0	48-120	(Gates 1957, Mount and Feldman 1983)
Introduced birds				
Mallard duck, *Anas platyrhynchos*	3158	1.2	3790	US EPA 1998
Northern Bobwhite quail, *Colinus virginianus*	2014	0.17	342.4	(Rattner et al. 2010)
American kestrel, *Falco sparverius*	97	0.1	9.7	(Rattner et al. 2011)
Native reptiles				
Brown tree snake, *Boiga irregularis*	20-40	-	-	(Brooks et al. 1998)

Toxicity to invertebrates:

Snails and slugs were not killed after feeding on baits (Johnston et al. 2005, Primus et al. 2006). There were no mortalities of weta that ate bait despite there being detectable residues in their bodies (Fisher et al. 2007).

The 48 hour LC_{50} for *Daphnia* sp. is reported as 1.8 mg/L (Tomlin 2009).

Non-target primary risk profile:

There are no published reports of non-target deaths due to this toxin in Australia, although its use is restricted. In the USA and New Zealand diphacinone baits are used for broadcast field applications. Numerous non-target species, particular smaller rodents and lagomorphs, have been found dead after broadcast baiting programs against ground squirrels (*Spermophilus beecheyi*) (Baroch 1996, Salmon et al. 2007). Illegal or incorrect baiting procedures are thought to have caused the death of deer, squirrels, racoons and a mountain lion (*Puma* sp.) (Littrell 1988, Stone et al. 1999). In contrast no non-target mortalities were reported after aerial baiting for rodents in Hawaii (Dunlevy and Swift 2010), and the field use of diphacinone baits is thought to present a low risk of mortality to non-native species such as pigs (*Sus scrofa*), cats (*Felis catus*) and mongooses in New Zealand (Dunlevy and Campbell 2002, Pitt et al. 2011).

Non-target secondary poisoning risk profile:

The secondary risk is considered very slight especially when compared to other anticoagulants (Fisher et al. 2004), although it may be slightly more risky than warfarin, especially for cats (*Felis catus*) (Bentley and Larthe 1959).

Raptors are sensitive and are thought to be at some risk (Rattner et al. 2010, Rattner et al. 2011). Owls died of haemorrhaging after feeding on poisoned rats (*Rattus* sp.) in laboratory trials (Mendenhall and Pank 1980). and a small number of deaths have been reported in the field in the USA (Stone et al. 1999) (Stone et al. 2003). In Canada, a variety of owl species have been found with diphacinone residues but there have been no deaths recorded (Albert et al. 2010). Vultures (*Cathartes aura*) were observed eviscerating poisoned ground squirrel (*Spermophilus beecheyi*) carcasses but no deaths reported (Baroch 1996). Mink (*Mustela* sp.) and dog (*Canis lupus familiaris*) died after being feed diphacinone poisoned nutria (*Myocastor coypus*) (Evans and Ward 1967).

Diphacinone residues are excreted slowly from slugs and snails which feed on baits, posing a small risk to quails and ducks but an unknown risk to other species, in particular endangered native birds in New Zealand (Johnston et al. 2005, Primus et al. 2006). The risk to species that eat weta has not been investigated (Fisher et al. 2007).

Feral pigs (*Sus scrofa*) are known to feed on diphacinone baits used against rodents in New Zealand. Cooking had little effect on the concentration of toxin (Pitt et al. 2011), and Fisher (2006) has recommended a conservative withholding period of 160 days for the consumption of feral pigs from areas baited with diphacinone to minimise the risk to humans.

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Pindone

Chemical name: 2-pivaloylindan-1,3-dione

Synonyms: pivaldione, Pival® (calcium salt), Pivalyl® (sodium salt)

Source: Prepared by reaction of pinacolone with diethylphthalate (Kilgore et al. 1942).

Physical chemistry: (Nelson and Hickling 1994)

Formula	$C_{14}H_{14}O_3$
Molecular wt	230.28
Physical form	Crystalline solid
Colour	Yellow
Taste	Tasteless
Odour	Slight mouldy odour
Melting point	110^{o}C
Solubility	Only slightly soluble in water, soluble in most organic solvents. Calcium and sodium salts soluble in water

Applications:

History	Pindone was developed as a rodenticide in the US in 1940s (Kilgore et al. 1942) but initial high production costs did not see it commercialised until the 1950s (Crabtree and Robinson 1953). Developed as a rabbit (*Oryctolagus cuniculus*) control agent in Australia in the late 1970s (Oliver and Wheeler 1978).
Uses in Australia	Registered in all states and territories for the control of rabbits (*Oryctolagus cuniculus*). Not to be used in urban areas <1000m^2.
Poison Schedule	Australia: Schedule 6 poison Restricted chemical product
Formulation types	Bait concentrate and ready to use oat baits.

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Blocks the vitamin K cycle by inhibiting vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic doses can cause damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over several days and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001). The indandione group of anticoagulants can also have additional toxic effects when ingested in large quantities. Symptoms recorded in humans include breathing difficulties, muscular weakness, pulmonary congestion and hyperexcitability (Savarie 1981).

Latent period	More effective in small multiple feeds over several days than large single dose to elicit lethal effects. As with all anticoagulants, displays a considerable delay before the onset of symptoms, which is not dependent on the size of the dose or means of administration (Beauregard et al. 1955, Saunders et al. 1955, Heisey et al. 1956, Coon and Willis 1972).
Symptoms	Characteristic anticoagulant clinical signs included lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Savarie 1981).
Time to death	Time to death is 5-20 days in rabbits (*Oryctolagus cuniculus*) (Oliver and Wheeler 1978, Eason and Jolly 1993), and 1-2 weeks for brushtail possums (*Trichosurus vulpecula*) (Jolly et al. 1994).
Detoxification and excretion of sub-lethal doses	There is minimal metabolism of pindone and it is excreted mainly unchanged (Fitzek 1978). Elimination is faster than the second generation anticoagulants. In rats (*Rattus* sp.) the liver half life is two days (Fisher et al. 2003). The half-life in both dogs (*Canis lupus familiaris*) and sheep (*Ovis aries*) is 5 days (Fitzek 1978) (Robinson et al. 2005).
Accumulation of sub-lethal doses	Pindone is cumulative by nature, and mortality occurs after multiple feeds over a number of days. It has a relative short duration of action compared to other anticoagulants, persisting in sheep (*Ovis aries*) up to 14 days (Robinson et al. 2005).
Long term effects of sub-lethal doses	Sub-lethal doses of pindone suppresses food intake in sheep (*Ovis aries*) and affects their breeding performance, causing an increase in stillborn and non-viable lambs. The motility of sperm in treated rams is also affected (Oliver and Wheeler 1978, Robinson et al. 2005). Also can affect pregnancies in dogs (*Canis lupus familiaris*), causing puppies to be either stillborn or die within one hour postpartum (Fitzek and Gembardt 1977). Liver damage has been reported in brushtail possums (*Trichosurus vulpecula*) (Eason and Jolly 1993, Jolly et al. 1994).
Aversion	No aversion to this anticoagulant has been reported.
Tolerance	No evidence of tolerance to this anticoagulant has been reported.
Resistance	A low level of resistance to pindone has been detected in rats (*Rattus* sp.) (Lund 1972).
Antidote	Effective antidote is Vitamin K_1 (Beauregard et al. 1955, Heisey et al. 1956). It is critical to continue treatment until toxic amounts of pindone are no longer present (Martin et al. 1991).
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out

immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Decay time in soils	Pindone residues were found in the soil of an airstrip six months after it was used in an aerial baiting program, however there have been no studies on the residues left from just the baits themselves after distribution (Twigg et al. 1999).
Effects on plants	No data is available on the uptake and translocation by plants

Acute toxicity to vertebrate species:

Pindone is more toxic when given in multiple doses rather than one large single dose, for example acute single oral dose for dogs (*Canis lupus familiaris*) ranges between 75-100 mg/kg but the chronic dose is approx. 15-35 mg/kg when given in daily doses of 2.5 mg (Beauregard et al. 1955). As most research has concentrated on the chronic rather than acute toxicity to target species a comparison of the acute (single dose) and the chronic (multiple dose) toxicity for a range of species is shown in Table 39.

Cattle (*Bos primigenius*) and cats (*Felis catus*) are considered the most vulnerable domestic animals (Twigg et al. 1999). There is considerable variation in birds' response to pindone, with the wedge-tailed eagle (*Aquila audax*) more susceptible than other species tested (Martin et al. 1994). There is no information on the effects of this toxin on reptiles and amphibians.

Brushtail possum (*Trichosurus vulpecula*) are very tolerant to anticoagulant effects of pindone and death from high doses is the result of liver failure, not haemorrhaging (Jolly et al. 1994).

Table 39. The acute and chronic oral sensitivity to pindone for a range of species expressed as the median lethal dose (LD_{50}).

Species	Acute LD_{50} (mg/kg)	Reference	Chronic LD_{50} (mg/kg/day)	Reference
Introduced mammals				
Brown rat, *Rattus norvegicus*	>50	(Saunders et al. 1955)	-	-
Rabbit, *Oryctolagus cuniculus*	25	(Eason and Jolly 1993)	0.52 for 7 days	(Oliver and Wheeler 1978, Martin et al. 1994)
Sheep, *Ovis aries*	>74	(Twigg et al. 1999)	> 50 for 7 days	(Oliver and Wheeler 1978)
Cattle, *Bos primigenius*	-	-	2 for 3 days	(Twigg et al. 1999)
Pig, *Sus scrofa*	>10	(Twigg et al. 1999)	-	-
Cat, *Felis catus*			1.0-1.25 for 4 days	(Twigg et al. 1999)
Dog, *Canis lupus familiaris*	75-100	(Beauregard et al. 1955)	2.5 for 6-14 days	(Beauregard et al. 1955)
Native mammals				

Brushtail possum, *Trichosurus vulpecula*	>100	(Eason and Jolly 1993)	51 for 5 days	(Jolly et al. 1994)
Western grey kangaroo, *Macropus fuliginosus*	-	-	1-2 for 7-14 days	(Twigg et al. 1999)
Introduced birds				
Chicken, *Gallus gallus domesticus*	-	-	2.5 for 4 days	(Twigg et al. 1999)
Native Birds				
Australian magpie, *Gymnorhina tibicen*	-	-	4 for 5 days	(Martin et al. 1994)
Wedge-tailed eagle, *Aquila audax*	-	-	0.25 for 5 days	(Martin et al. 1994)

Toxicity to invertebrate species:

Pindone possesses both insecticidal and fungicidal properties (Crabtree and Robinson 1953) and is effective against houseflies (Kilgore et al. 1942), body lice (Eddy and Bushland 1948) and numerous species of beetles and moths (Beauregard et al. 1955).

Non-target primary risk profile:

In Australia some native bird and mammal species are at risk from primary poisoning and animals reported to have died during rabbit (*Oryctolagus cuniculus*) poisoning programs in Australia include grey kangaroos (*Macropus fuliginosus*), swamp wallabies (*Wallabia bicolor*), bandicoots, pigeons and parrots (Martin et al. 1994, Twigg et al. 1999). Calves (*Bos primigenius*) have also been killed (Twigg et al. 1999), although if baits are correctly deployed poisoning of domestic stock should be avoided (Martin et al. 1991).

Non-target secondary poisoning risk profile:

The suspected deaths of eagles and kites after rabbit (*Oryctolagus cuniculus*) poisoning programs in Australia have been reported, while other raptors such as owls are thought to be at risk (Martin et al. 1994, Twigg et al. 1999).

Overseas, minks (*Mustela* sp.) and dogs (*Canis lupus familiaris*) have died after being feed pindone poisoned nutria (*Myocastor coypus*) (Evans and Ward 1967), however no cats (*Felis catus*) died after eating poisoned mice (*Mus* sp.) (Beauregard et al. 1955).

Both Australia and New Zealand enforce a withholding period between 3-5 weeks for animals exposed to pindone so secondary poisoning of humans does not occur (Nelson and Hickling 1994, Twigg et al. 1999).

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Anticoagulants - Hydroxyl-4-benzothiopyranones

Difethialone

Chemical name: 3-[3-(4'-bromo[1,1'-bipheyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2*H*-1-benzothiopyran-2-one

Synonyms: LM-2219

Physical chemistry:

Formula	$C_{31}H_{23}BrO_2S$
Molecular wt	539.5
Physical form	Powder
Colour	White, slightly yellowish
Melting point	233-236^{o}C
Solubility	Practically insoluble in water, also ethanol, methanol and hexane. Soluble in chloroform.
Stability	Stable at temperatures up to 230^{o}C. Highly sensitive to photolysis in aqueous solutions.

Applications:

History	First reported in 1986 by Lechevin.
Uses in Australia	Registered in all states and territories for the control of introduced rats (*Rattus* sp.) and mice (*Mus* sp.), especially warfarin-resistant strains. May only be used in and around buildings, not in open areas.
Poison Schedule	Australia: Schedule 6 poison
Formulation types	Grain and block baits (ready to use)

Toxicology:

Absorption	Absorbed through the gastrointestinal tract, skin and respiratory system.
Mode of action	Classic anticoagulant action which inhibits the vitamin K reductase, depleting the level of blood coagulation factors such as prothrombin, and disrupting the blood's ability to clot. In addition toxic dose causes damage to the capillaries, increasing their permeability and causing internal bleeding. These effects are cumulative in nature, developing over a period of time and lead to shock, loss of consciousness and eventually death (Petterino and Paolo 2001).
Latent period	Usually requires only a single feed to deliver a lethal effect, but like all anticoagulants there is a delay before the onset of symptoms.
Symptoms	Characteristic anticoagulant clinical signs included lethargy, shortness of breath, anorexia and pale extremities. There may also be some external bleeding and dark brown vomitus and/or faeces. Internally haemorrhaging may be present in any part of body with remaining blood thin and unable to clot (Savarie 1981).

Time to death	Time to death in rats (*Rattus* sp.) 2-16 days, and mice (*Mus* sp.) 2-20 days (Lechevin and Poche 1988, Nahas et al. 1989, Saxena et al. 1992).
Detoxification and excretion of sub-lethal doses	Undergoes little metabolism and is excreted mainly in faeces. Half-life in rat (*Rattus* sp.) liver is 108 days and mouse (*Mus* sp.) liver 29 days (Lechevin and Poche 1988) (Vandenbroucke et al. 2008).
Accumulation of sub-lethal doses	Although only requires single dose for fatality, sub-lethal doses can accumulate and become lethal.
Long term effects of sub-lethal doses	No long term effects reported in rats (*Rattus* sp.) other than expected haemorrhages (Hayes 2010).
Aversion	There have been no observations of aversion. Very palatable to rats (*Rattus* sp.) and mice (*Mus* sp.) (Lechevin and Poche 1988, Nahas et al. 1989).
Tolerance	No evidence of tolerance has been reported.
Resistance	There are no reports of resistance to this anticoagulant.
Antidote	Effective antidote is Vitamin K_1 (Lechevin and Poche 1988).
Treatment	Treatment aims to stabilise (maintain airway, control shock), decontaminate (gastric lavage / emesis followed by administration of activated charcoal), reverse anticoagulant effect (Vitamin K_1 antidote), and if necessary compensate for blood loss by transfusion of blood or plasma. Appropriate supportive care may include intravenous fluids and oxygen supplementation. Phenobarbital may accelerate the metabolism of some anticoagulants (Cope 2004).
User safety	Users are advised to wear gloves and appropriate protective clothing to avoid direct contact with eyes and skin. Precautions should also be taken to prevent inhalation of dust if appropriate. Contaminated eyes should be washed out immediately with water. Any exposed skin should be thoroughly washed with soap and water. After each day's use, gloves and contaminated clothing should also be washed.

Environmental fate:

Decay time in soils	Binds strongly to soil and is classified as immobile.

Acute toxicity to vertebrate species:

Difethialone is toxic to most birds, fish and rodents however better tolerated by mammals such as dogs (*Canis lupus familiaris*) and pigs (*Sus scrofa*) (Lechevin and Poche 1988). The 96 hour LC_{50} for rainbow trout, *Oncorhynchus mykiss*, is reported as 51 µg/L and bluegill sunfish, *Lepomis macrochirus*, 75 µg/L (Lechevin and Poche 1988).

Table 40. The sensitivity to difethialone for a range of species expressed as the oral median lethal dose (LD_{50}). The amount of difethialone is calculated using the average male body weights derived from (McIlroy 1984, Strahan 1991).

Species	LD_{50} (mg/kg)	Av body weight (kg)	1080 Amount for LD_{50} (mg)	Reference (LD_{50} data)
Introduced mammals				
Mouse, *Mus musculus*	0.47-1.29	0.02	0.009-0.026	(Vandenbroucke et al. 2008) Lorgue et al.

Brown rat, *Rattus norvegicus*	0.29-0.51	0.32	0.09-0.16	(Ward and Crabtree 1942) Lorgue et al.
Black rat, *Rattus rattus*	0.38	0.28	0.11	Lorgue et al.
Pig, *Sus scrofa*	2-3	100	200-300	Lorgue et al.
Cat, *Felis catus*	>16	5.0	80	Lorgue et al.
Dog, *Canis lupus familiaris*	4	16.0	64	(Tomlin 2009)
Introduced birds				
Bobwhite quail, *Colinus virginianus*	0.26	0.17	0.04	(Lechevin and Poche 1988)

Toxicity to invertebrate species:

The 48 hour EC_{50} for *Daphnia magna* is reported as 4.4 µg/L (Lechevin and Poche 1988).

Non-target primary risk profile:

This toxin is relatively toxic to birds indicating a potential non-target hazard but there are no reports in the literature (Saxena et al. 1992, Moran 1993).

Non-target secondary poisoning risk profile:

From residue studies this toxin is thought to be a relatively low risk for secondary poisoning (Lechevin and Poche 1988). There are no reported deaths in the literature, although a variety of owl species have been found with difethialone residues (Albert et al. 2010).

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Fumigants

Carbon monoxide

Chemical name: carbon monoxide

Synonyms: carbonous oxide, carbonyl

Source: Carbon monoxide results from the incomplete combustion of hydrocarbon fuels. It can be formed naturally through photochemical reactions in the troposphere, and from natural combustion processes such as forest fires. Main man-made sources include exhaust fumes of internal combustion engines, iron smelting, and burning of coal for domestic and industry processes.

Physical chemistry:

Formula	CO
Molecular wt	28.01
Physical form	Gas
Colour	Colourless
Taste	Tasteless
Odour	Odourless
Melting point	-205 ^{o}C
Solubility	Soluble in water, chloroform, acetic acid, ethyl acetate, ethanol, ammonium hydroxide and benzene.
Stability	CO is relatively short-lived in the atmosphere.

Applications:

History	The toxicity of carbon monoxide and its use as a form of euthanasia has been practised since the early history of mankind (Drinker 1938). It has been used for the control of a number of mammal species that either live or breed in underground warrens or dens across the United States, Europe, China and Australia.
Uses in Australia	Carbon monoxide has been used as a rabbit (*Oryctolagus cuniculus*) fumigant but is only currently registered as a fox (*Vulpes vulpes*) fumigant.
Poison Schedule	Not allocated
Formulation types	Cartridge (containing charcoal activated and sodium nitrate)

Toxicology:

Absorption	Absorbed primarily by inhalation, with ingestion and skin absorption unlikely.
Mode of action	The precise mechanisms by which carbon monoxide affects the body are complex. One main mechanism is the binding of CO to haemoglobin in the blood forming carboxyhaemoglobin (COHb) which is incapable of combining with oxygen and leads to tissue anoxia (Humphreys 1978). Other mechanisms include CO binding to myoglobin, mitochondrial and cytochrome oxidase (Hardy and Thom 1994).
Latent period	Time to first symptoms is dependent on the CO concentration. High levels can

	cause unconsciousness in canaries (*Serinus canaria*) after two minutes and rodents after three minutes (Burrell et al. 1914, Deng and Zhao 1986).
Symptoms	Symptoms develop as the COHb levels increase. At 6-8% COHb there is decreased ability to maintain attention. As levels rise above 20% symptoms progress through lethargy, vertigo, muscular weakness (many species loose control of hind legs), difficult and rapid breathing, nausea, vomiting, cardiac abnormalities then collapse, coma and death due to asphyxiation (Burrell et al. 1914, Humphreys 1978, Weaver 2009). A level of 30% COHb is associated with recognisable clinical illness and death occurs when COHb levels reach 50-70% (Buck et al. 1976).
Time to death	Time to death is dependent on the CO concentration and the length of exposure, and the age and size of the animal (Burrell et al. 1914). In laboratory trials the time to death ranged between 4-37 minutes for rats (*Rattus* sp.), 17-48 minutes for adult coyotes (*Canis latrans*) and 4-15 minutes for coyote pups (Savarie et al. 1980).
Detoxification and excretion of sub-lethal doses	The absorption of CO into the blood occurs quickly forming COHb. This molecule is broken down in the presence of oxygen (and carbon dioxide), with the CO being excreted mainly through exhalation (Drinker 1938). The half-life of CO in the body is between 4-5 hours.
Accumulation of sub-lethal doses	CO does not accumulate in the body however the effects of sub-lethal doses can be cumulative (Drinker 1938).
Long term effects of sub-lethal doses	Chronic exposure to CO may cause persistent headaches, depression, confusion, memory loss, nausea and vomiting in humans (Ryan 1990). Long-term exposures present the greatest risk to people with cardiovascular diseases (Allred et al. 1989) and pregnant females (Farrow et al. 1990). CO directly affects the foetus as well as the metabolic function of the placenta. Foetal COHb levels of 20-60% have resulted in stillbirths in humans, and severe brain damage in liveborn offspring. Chronic exposure results in smaller litters in rats (*Rattus* sp.) (Buck et al. 1976). Brain lesions have been found in dogs (*Canis lupus familiaris*), guines pigs (*Cavia porcellus*) and rabbits (*Oryctolagus cuniculus*) after chronic exposure (Semerak and Bacon 1930). Long term sub-lethal doses of CO can cause a disturbance in gait and position reflexes and brain lesions in dogs (Buck et al. 1976).
Tolerance	A variety of animal species, including humans, have become tolerant to, and can survive in higher than normal concentrations of CO after slow habituation and continued exposure (Campbell 1935, Drinker 1938).
Resistance	No evidence of resistance to this fumigant has been reported.
Antidote	Pure oxygen with 5-7% CO_2 (carbogen mixture) is considered the most effective antidote (Buck et al. 1976).
Treatment	The patient should be removed from hazardous environment. The objective of treatment is to restore an adequate oxygen supply to the heart and brain, while minimising any damage. The carbogen mixture is more effective than oxygen alone. Further treatment for other complications such as seizure, hypotension, cardiac abnormalities, pulmonary oedema and acidosis may be required (Hardy and Thom 1994, Weaver 2009). Rosenthal et al. (1945) have shown that the use of deep amobarbital anaesthesia with poisoned dogs (*Canis lupus familiaris*) can improve their survival and recovery with minimal brain damage.

User safety	The ingredients of the CO cartridges (charcoal and sodium nitrate) are relative harmless until ignited (Savarie et al. 1980). Once ignited large amounts of CO are generated which is highly toxic to humans. Although these cartridges are to be placed underground when ignited, precautions must be taken to prevent unintentional ignition during storage, transport and use (Ross et al. 1998). Also ignited cartridges can cause severe burns to exposed skin and clothes if users do not handle them carefully.

Environmental fate:

Decay time in soils	Carbon monoxide is not readily adsorbed by the soil itself, but microorganisms within the soil, especially fungi, do absorb and metabolise CO as an energy source (Inman and Ingersoll 1971).
Effects on plants	Carbon monoxide has no known effect on plants. Although green plant species use CO_2, they are not able to remove and use CO from their surroundings (Inman and Ingersoll 1971). Some species of plants and algae do produce carbon monoxide (Loewus and Delwiche 1963).

Acute toxicity to vertebrate species:

Burrell et al. (1914) tested a range of birds and animals to CO. Canaries (*Serinus canaria*) were the most sensitive to CO, followed by mice (*Mus* sp.) with rabbits (*Oryctolagus cuniculus*) the most resistant. Rabbits showed no signs of distress after three hours at the CO concentration of 3.1 mg/L. Dogs (*Canis lupus familiaris*) are more sensitive than humans (Buck et al. 1976). The toxicity of CO is summarised in Table 41.

Table 41. The sensitivity to carbon monoxide by inhalation for a range of species. Note Burrell et al. (1914) only measured up to time of collapse of their experimental animals, not necessarily death.

Species	CO dose (mg/L)	Time to distress (minutes)	Time to collapse/death (minutes)	Reference
Introduced mammals				
Mouse, *Mus musculus*	1.25 2.5	30 6-12	- 24-40	(Burrell et al. 1914)
Dog, *Canis lupus familiaris*	3.1 4.2	10-15 -	20-25 60-120	(Burrell et al. 1914) (Buck et al. 1976)
Introduced birds				
Canary, *Serinus canaria*	1.25 2.5	12 2-6	- 4-13	(Burrell et al. 1914)
Chicken, *Gallus gallus domesticus*	0.7-1.9 2.2-4.1 7.1	10-45 5-30 2	- 30-120 5	(Buck et al. 1976) (Burrell et al. 1914)
Pigeon, *Columba livia*	1.25 3.8	95 10	- 40	(Burrell et al. 1914)
Sparrow, *Passer domesticus*	3.9	10	40	(Burrell et al. 1914)
Starling, *Sturnus vulgaris*	*ca* 2.8 (2213ppm)		LC_{50}	(Schafer et al. 1983)

Toxicity to invertebrate species:

A carbon monoxide is toxic to all aerobic animals, invertebrates would be affected by this toxin, however there is little data reported in the literature.

Non-target primary risk profile:

Carbon monoxide is not a selective toxin and all non-target animals are at risk if they are present in the warren system or underground den when fumigation is conducted. Users must make sure that only target species are present before control operations commence, and that fumigation conducted in a manner that

does not allow accumulation of fumes in hollows or valleys in the surrounding landscape (Savarie et al. 1980, Pelz and Gemmeke 1988, Ross et al. 1998).

Non-target secondary poisoning risk profile:

No signs of secondary poisoning was observed in bobcats, *Lynx rufus*, after eating rats (*Rattus* sp.) that had died from CO fumigation (Savarie et al. 1980).

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Chloropicrin

Chemical name: trichloronitromethane

Synonyms: chloropicrine

Source: manufactured by the reaction of nitromethane with sodium hypochlorite (Markofsky 2000).

Physical chemistry:

Formula	CCl_3NO_2
Molecular wt	164.40
Physical form	Oily liquid
Colour	Colourless to faint yellow
Odour	Irritating odour
Melting point	-69^{o}C
Solubility	Slightly soluble in water. Soluble with alcohol, acetone, benzene, ethanol, methanol, carbon disulfide, diethyl ether, chlorides and carbon tetrachloride.
Stability	Stable in acidic media, unstable in alkali. Non-flammable, but can decompose explosively when heated above 112 ^{o}C. Highly phytotoxic.

Applications:

History	First discovered in 1848 by John Stenhouse. Used as a chemical weapon in World War 1 and as an insecticide since 1908. Products containing this toxin have been registered in Australia since 1945.
Uses in Australia	Rabbit (*Oryctolagus cuniculus*) and rodent fumigant (in association with methyl bromide with main purpose as a warning gas), also used as a fumigant against insects in stored grain, and nematodes in soil.
Poison Schedule	Australia: Schedule 7 Dangerous Poison
Formulation types	Oil miscible liquid or compressed liquefied gas.

Toxicology:

Absorption	Can be absorbed through inhalation, ingestion and the skin. It is extremely irritating to skin, and mucous membranes of eyes, nose, mouth and lungs.
Mode of action	Chloropicrin causes severe irritation to the skin, eyes, respiratory tract (if inhaled), and gastrointestinal tract (if inhaled or ingested). Eye tearing (lacrimation) is prominent and causes severe vomiting.
Latent period	Time to first symptoms is dependent on the concentration and usually occurs rapidly.
Symptoms	Symptoms from mild exposure include burns in the mouth, oesophagus, and stomach, stomach pain, sore throat; nausea and vomiting difficulty breathing or shortness of breath, headache; dizziness, anxiety, lethargy, and fatigue. Skin irritation can result in blisters A bluish discoloration of the skin (cyanosis) is possible due to methemoglobinemia. Severe exposure causes major inflammation of the lower respiratory tract, with potentially fatal accumulation

	of fluid in the lungs (pulmonary oedema) (Anon. 1995).
Time to death	Time to death is dependent on the concentration and the length of exposure At high concentrations rabbits (*Oryctolagus cuniculus*) die within 5-30 minutes. At low concentrations death may be delayed for up to a week in rabbits that escape fumigated warrens (Gleeson and Maguire 1957).
Accumulation of sub-lethal doses	Chloropicrin is not expected to accumulate in mammal tissues (Sassaman 1986).
Long term effects of sub-lethal doses	This toxin is still very irritating even at very low doses making long-term chronic studies difficult to conduct (Croft 2007). It is not classifiable as a carcinogen and does not appear to cause developmental or reproductive toxicity in rats (*Rattus* sp.) (Anon. 1995).
Tolerance	No evidence of tolerance to this fumigant has been reported.
Resistance	No evidence of resistance to this fumigant has been reported.
Antidote	No known specific antidote.
Treatment	The victim should be removed from the source of the exposure. Initial treatment is primarily supportive. It can include symptomatic treatment of early adverse health effects and support of respiratory function with oxygen. To minimize the effects of accumulation of fluid in the lungs, the victim should be kept warm and quiet. Initial irritation typically resolves within 15-30 minutes following decontamination. Gastrointestinal symptoms following ingestion of chloropicrin may persist for weeks. Adverse neurological and musculoskeletal effects may persist from weeks to months.
User safety	This toxin should not be used in an enclosed space. It is very toxic if inhaled and will irritate the eyes, nose, throat and skin. Avoid direct contact as the liquid can cause burns. When using this toxin wear protective clothes buttoned to the neck and wrists, elbow length PVC gloves, goggles, impervious footwear and the specified respirator. If eyes become contaminated flush with running water. If skin contamination occurs wash immediately with soap and water. All protective gear should be washed and /or aired before reuse (Croft 2007).

Environmental fate:

Decay time in soils	Chloropicrin degrades relatively quickly in soils mainly due to microbial activity. The degradation is accelerated as soil temperature increases, but is relatively independent of changes in soil moisture (Gan et al. 2000). Under aerobic conditions the final product is carbon dioxide, in anaerobic conditions chloropicrin is converted to nitromethane (Anon. 1995).
Aquatic systems	This toxin will degrade in water if exposed to light, producing carbon dioxide, bicarbonate, chloride, nitrate and nitrite (Anon. 1995).
Atmosphere	In the atmosphere, chloropicrin is extensively degraded to phosgene (which if further hydrolysed to carbon dioxide and hydrogen chloride), nitric oxide, chloride, nitrogen dioxide and dinitrogen tetroxide by photolysis (Moilanen et al. 1978).
Effects on plants	Chloropicrin is not taken up by plants from treated soils. The carbon dioxide formed from its breakdown in the soil can be metabolised by plants with no effect (Anon. 1995, Wilhelm et al. 1996).

Acute toxicity to vertebrate species:

There is little information available about the toxicity of chloropicrin to most vertebrate species ande a summary of known values is given in Table 42. No adverse affects were reported for chickens (*Gallus gallus domesticus*) at approx. 0.7 mg/L (100 ppm) for 120 days (Sassaman 1986).

In humans doses as low as 0.008-0.016mg/L air can be clearly detected and cause coughing and lachrymation. Exposure to 0.12 mg/L air for 30-60 minutes can be fatal (Tomlin 2009).

Table 42. The sensitivity to chloropicrin by inhalation for a range of species expressed as the median lethal dose (LD_{50}) for a range of kill times.

Species	Time to death	LC_{50} (mg/L)	Reference (LD_{50} data)
Introduced mammals			
Brown rat, *Rattus norvegicus* (lab. strain)	4 hours	0.08	(Anon. 1995)
Rabbit, *Oryctolagus cuniculus*	5 minutes 15 minutes 45 minutes 135 minutes	5.0 0.48 0.11 0.094	(Gleeson and Maguire 1957)
Cat, *Felis catus*	20 minutes	0.8	(Tomlin 2009)
Fish			
Bluegill sunfish, *Lepomis macrochirus*	96 hours	0.105	(Sassaman 1986)
Rainbow trout, *Oncorhynchus mykiss*	96 hours	0.0165	(Sassaman 1986)

Toxicity to invertebrate species:

Chloropicrin is used as an invertebrate fumigant and is toxic to many species of insects, and mites (Anon. 1995).

Non-target primary risk profile:

Chloropicrin is very toxic to mammals and invertebrates, so non-target animals are at risk if present when fumigation is conducted (Anon. 1995). Users must make sure that only target species are present before control operations commence.

Non-target secondary poisoning risk profile:

Chloropicrin has a low probability of bioaccumulation (Sassaman 1986), hence secondary poisoning risk would be low. There are no reports of secondary poisoning from fumigated rabbits (*Oryctolagus cuniculus*).

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Methyl bromide

Chemical name: bromomethane

Synonyms: monobromomethane, bromure de méthyle

Source: Produced by the interaction of methanol and hydrogen bromide. It is made commercially but also produced naturally by marine algae and other plants, as well as being a by-product of the combustion of plant materials (Piccirillo and Piccirillo 2010).

Physical chemistry:

Formula	CH_3Br
Molecular wt	94.9
Physical form	Gas at room temperature
Colour	Colourless
Odour	Generally odourless, chloroform-like odour at high concentrations
Melting point	-93^{o}C
Vapour pressure	190 kPa (20 ^{o}C)
Solubility	Soluble in water, forms a crystalline hydrate with ice-water. Readily soluble in most organic solvents.
Stability	Hydrolysed very slowly in water and more rapidly in alkaline media. Non-flammable in air, and a potent ozone depleting substance.

Applications:

History	Insecticidal properties reported by Le Goupil in 1932.
Uses in Australia	Multi-purpose fumigant for soil and stored products against insects, ticks, mites, weeds, disease-causing organisms and rodents (usually in association with chloropicrin as a warning agent). Methyl bromide is a restricted pesticide in many states and its use is governed under the Health (or similar named) Act and their associated regulations within these jurisdictions. It is only to be used by licensed or authorised personnel.
Poison Schedule	Australia: Schedule 7 Poison
Formulation types	Compressed liquefied gas

Toxicology:

Absorption	Inhalation and ingestion, but not through skin.
Mode of action	Neurotoxicity is the primary effect, with high concentrations causing death through pulmonary injury and associated circulatory failure (Bond 1984). Also leads to the degeneration of specific cell types in the olfactory epithelium (Hurtt et al. 1988).
Latent period	Time to first symptoms is delayed and may vary between 0.5 – 48 hours, depending on the concentration of methyl bromide (von Oettingen 1955).

Symptoms	At concentrations not immediately fatal, this toxin produces symptoms such as nausea and vomiting, diarrhoea, loss of appetite, weight loss, dizziness, abdominal pain, fatigue, headache, decreased coordination of muscles, eye and nasal discharge, and irregular breathing leading to more severe neurological symptoms, tremors and convulsions (von Oettingen 1955, Alexeeff et al. 1985).
Time to death	Time to death is dependent on the concentration and the duration of exposure (Irish et al. 1940, Piccirillo and Piccirillo 2010).
Detoxification and excretion of sub-lethal doses	After inhalation methyl bromide is rapidly metabolised and eliminated with elimination half-lives ranging from 1.5 to 8 hours. The main metabolite is carbon dioxide and is excreted as expired air. Small quantities of other metabolites excreted in urine and faeces (Bond et al. 1985, Honma et al. 1985).
Accumulation of sub-lethal doses	Repeated chronic exposures can have an accumulative effect.
Long term effects of sub-lethal doses	Single, low chronic doses do not cause any permanent effects and are usually reversible within 24 hours of exposure (Honma et al. 1985). Chronic dietary and inhalation studies in mice (*Mus* sp.), rats (*Rattus* sp.), rabbits (*Oryctolagus cuniculus*), guinea pigs (*Cavia porcellus*) and dogs (*Canis lupus familiaris*) show some long-term effects of this toxin at high dose rates, including severe weakness, lung or nervous system-related problems and inflammation lesions in the stomach and kidney (Irish et al. 1940, Danse et al. 1984, Alexeeff et al. 1985, Kato et al. 1986, Piccirillo and Piccirillo 2010).
Tolerance	No known reports of tolerance to this fumigant.
Resistance	Some species of insects have developed resistance (Hole 1981).
Antidote	No known antidote (Bond 1984).
Treatment	Treatment for methyl bromide poisoning is usually symptomatic with no known specific procedures to bring about immediate recovery. The patient should be removed from further contact with toxin and symptoms treated as they appear, i.e. anti-emetic drugs for nausea and vomiting, oxygen for support of respiratory system, and appropriate drugs for circulatory failure, central nervous system effects and seizures There is some evidence that early haemodialysis may be helpful (Bond 1984).
User safety	This toxin should not be used in an enclosed space. It is very toxic if inhaled and will irritate the eyes, nose, throat and skin. The liquid can cause burns on direct contact (Watrous 1942). When using this toxin wear protective clothes buttoned to the neck and wrists, elbow length PVC gloves, goggles, impervious footwear and the specified respirator. If eyes become contaminated flush with running water. If skin contamination occurs wash immediately with soap and water. All protective gear should be washed and /or aired before reuse.

Environmental fate:

Decay time in soils	Under normal circumstances gaseous methyl bromide does not present a residue problem. However, there is usually a small, variable amount of permanent residue resulting from the chemical reaction between this fumigant and the soil or organic matter to form bromide ion (Bond 1984).

Aquatic systems	Very toxic to aquatic organisms.
Effects on plants	Methyl bromide is extremely toxic to many growing plants. It can be applied to soils before planting at low doses as well as dormant plants and seeds for quarantine purposes (Bond 1984).
Effects on micororganisms	Methyl bromide has been reported to induce mutagenic effects in some species of bacteria (Djalali-Behzad et al. 1981).

Acute toxicity to vertebrate species:

Only a few oral toxicity studies of methyl bromide have been reported in the literature mainly as this toxin is a gas at temperatures above 4°C. The acute oral LD_{50} of methyl bromide for rats (*Rattus* sp.) is reported to be 214 mg/kg bodyweight (Danse et al. 1984) and the minimum oral lethal dose for rabbits (*Oryctolagus cuniculus*) is between 60-65 mg/kg (Dudley and Neal 1942). Naas (1990) reported that dogs (*Canis lupus familiaris*) died within 24 hours of receiving 500mg/kg, but there were no deaths after a dose of 50mg/kg. These authors were not able to determine an oral LD_{50} for dogs due to the complications of vomiting shortly after dosing.

Since inhalation is viewed as the primary method of intoxication by methyl bromide, studies have instead focused on evaluating the acute inhalation toxicity (Table 43). The time to death by this method of administration is dependent on the concentration and the duration of exposure. For example rabbits are able to tolerate exposure to 0.85 mg/L air (220ppm) methyl bromide for 20 hours, however all died after 32 hour exposure at the same concentration (Irish et al. 1940). The threshold limit value for humans is around 0.019 mg/L.

Table 43. The sensitivity to methyl bromide by inhalation for a range of species expressed as either the median lethal concentration (LC_{50}) or the lethal dose (LD) for a range of exposure times.

Species	Time to death (hours)	Toxicity (mg/L)	Reference
Introduced mammals			
Mouse, *Mus musculus*	1	LC_{50} 4.68	(Alexeeff et al. 1985)
Brown rat, *Rattus norvegicus* (lab. strain)	1 4 8 0.1 22	7.3 LC_{50} *ca*.3.3[a] LC_{50} *ca*.1.3[a] LD 50 LD 1.0	(Zwart et al. 1992) (Kato et al. 1986) (Honma et al. 1985) (Irish et al. 1940) (Irish et al. 1940)
Rabbit, *Oryctolagus cuniculus*	0.5 24	LD 50 LD 1.0	(Irish et al. 1940) (Irish et al. 1940)
Fish			
Rainbow trout, *Oncorhynchus mykiss*	96	LC_{50} 3.9	(Tomlin 2009)

[a] Converted from ppm

Toxicity to invertebrate species:

Methyl bromide is used as an invertebrate fumigant and is toxic to many species of insects, and mites (Bond 1984).

Non-target primary risk profile:

Methyl bromide is not a selective toxin and all non-target animals are at risk if present when fumigation is conducted. Users must make sure that only target species are present before control operations commence.

Non-target secondary poisoning risk profile:

No evidence of secondary poisoning after using this fumigant has been published.

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Phosphine

Chemical name: phosphine

Synonyms: hydrogen phosphide, phosphorus trihydride, phosphane, phosphamine.

Source: Phosphine can be generated naturally from decaying organic matter (Devai et al. 1988, Glindemann et al. 1996).

As a fumigant in Australia, phosphine is produced from exposing aluminium phosphide 'tablets' to moisture and air.

Physical chemistry:

Formula	H_3P
Molecular wt	34.00
Physical form	Gas
Colour	Colourless
Odour	Technical product has a slight garlic or rotten fish odour, depending on the impurities present.
Melting point	-132.5^{o}C
Solubility	Moderately low solubility in water and soluble in most organic solvents.
Stability	Remains gaseous at normal temperatures and spreads quickly, being only 20% heavier than air. Oxidised to phosphoric acid by oxidising agents and atmospheric oxygen. Spontaneous flammable in air (due to the presence of traces of other hydrides of phosphorus).

Applications:

History	Was first described by Lavioser in 1789, and before this was thought to be the gaseous form of the element phosphorus.
Uses in Australia	Registered as a rabbit (*Oryctolagus cuniculus*) fumigant in all states and territories except Tasmania and the Northern Territory.
Poison Schedule	Australia: Schedule 7 Poison
Products	Aluminium phosphide tablets

Toxicology:

Absorption	Inhalation is the most common route of phosphine absorption however ingestion can also occur (particularly of the salt formulation). There is no absorption through the skin.
Mode of action	The exact mechanism of action of phosphine poisoning is not clear, however it is known that the toxin has several chemical and cumulative biologic oxidant effects within the body. In addition these effects are known to be moderated by the environment and conditions of exposure. Principally phosphine is a strong inhibitor of mitochondria respiration by inhibiting cytochrome oxidase (Chefurka et al. 1976), but it also denatures haemoglobin under specific oxygen conditions, can lead to an accumulation of cellular peroxides, and inhibits cholinesterase (Lam et al. 1991, Potter et al. 1991, Chin et al. 1992). Phosphine causes severe lung irritation leading to acute pulmonary oedema

	and respiratory collapse, cardiovascular dysfunction, depression of the central nervous system, coma and death. Also gastrointestinal disorders, renal damage and a decrease of white blood cells may occur (Burrows and Dacre 1973, World Health Organisation 1988).
Latent period	Dependent on the concentration of phosphine and length of exposure, symptoms may occur immediately or up to 24 hours after exposure (Bond 1984).
Symptoms	Milder symptoms include fatigue, nausea, ear ringing and uneasiness and coughing. As exposure increases, symptoms progress through vomiting, diarrhoea, disturbance of equilibrium, difficulty in breathing, weakness, difficulty in walking, tremors, disturbances of kidney and liver functions, cardiac arrhythmia and finally violent convulsions and death (Bond 1984).
Time to death	Time to death is dependent on phosphine concentration and time of exposure. It can be within a few hours or occur several days later (Bond 1984, Lyubimov and Garry 2010).
Detoxification and excretion of sub-lethal doses	In the rat (*Rattus* sp.) phosphine that is not excreted in the expired air is slowly oxidised and excreted in the urine chiefly as hypophosphate and phosphite (Robinson and Bond 1970, World Health Organisation 1988).
Accumulation of sub-lethal doses	Can be cumulative if not given enough time for sub-lethal doses to be eliminated.
Long term effects of sub-lethal doses	Long-term chronic studies in rats (*Rattus* sp.) and mice (*Mus* sp.) found a dose related decrease in body weight gain with female showing a greater result (Waritz and Brown 1975, Newton et al. 1993, Barbosa et al. 1994). In rats there were no reproduction or developmental effects and all observed effects were reversible (Hackenberg 1972, Newton et al. 1993). There is some suggestion that phosphine may be a genotoxin (Garry et al. 1989, Barbosa et al. 1994), although other studies have found no evidence (Barbosa and Bonin 1994).
Tolerance	No known reports of tolerance to this fumigant.
Resistance	Some species of insects and mites have developed resistance to phosphine (Sinha et al. 1967, Hole 1981, Chaudhry 1997).
Antidote	There is no specific antidote.
Treatment	Treatment for phosphine poisoning is usually symptomatic. If toxin is inhaled, the patient should be removed from further contact into fresh air, and if ingested, early gastric lavage may be appropriate. Symptoms should be treated appropriately as they appear; in general, support of vital functions such as respiration and circulation, and treatment for central nervous system effects, shock and seizures (Bond 1984, Singh et al. 1985).
User safety	Users should wear impervious gloves and protective clothes to avoid contact with eyes and skin. A respirator is required particularly if placing the tablets by hand into the burrows as the gas is generated rapidly once the tablet comes into contact with any moisture. If eyes become contaminated flush with running water. If skin contamination occurs wash immediately with soap and water. All protective gear should be washed and /or aired before reuse (Croft 2007).

Environmental fate:

Decay time in soils	Phosphine is rapidly degraded by microorganisms in wet soil (Hilton and Robison 1972), hence its performance as a rabbit (*Oryctolagus cuniculus*) fumigant is affected by soil moisture (Oliver and Blackshaw 1979).
Aquatic systems	Very toxic to all aquatic organisms
Effects on plants	No reported effects on plants.
Effects on microorganisms	Phosphine had shown no detectable effect on the microorganisms living in most stored grain products (Sinha et al. 1967), however it is reported to inhibit the respiration and growth of microorganisms on wheat with a moisture content up to 29% (World Health Organisation 1988).

Toxicity to vertebrate species:

Phosphine is very toxic to all vertebrates (Table 44, including fish (Table 45).

A LD_{50} has not been calculated for humans, however a concentration of approximately 0.14 mg/L is the maximum that can be inhaled for an hour without serious consequences, Inhalation of around 0.57 mg/L for 30-60 minutes with have dangerous consequences, and above 1.4 mg/L is fatal after 30 minutes (Henderson and Haggard 1943, Freeman et al. 1954).

Table 44. The sensitivity to phosphine by inhalation for some vertebrate species expressed as the median lethal dose (LD_{50}) over a range of exposure times.

Species	Exposure time (hours)	LD_{50} (mg/L)	Reference (LD_{50} data)
Introduced mammals			
Mouse, *Mus musculus*	336	*ca* 0.01 [a]	(Barbosa et al. 1994)
Brown rat, *Rattus norvegicus*	4 4 4 6hours/day over 4 days 6hours/day over 3 days	*ca* 0.02 [a] *ca* 0.04-0.05[a] 0.02-0.06 *ca* 0.01 [a] *ca* 0.02 [a]	(Waritz and Brown 1975) (Omae et al. 1996) (World Health Organisation 1988) (Newton et al. 1993) (Newton et al. 1993)
Rabbit, *Oryctolagus cuniculus*	4	LD 0.03	(World Health Organisation 1988)

[a] Converted from ppm

Table 45. The sensitivity to phosphine to a range of aquatic vertebrate species expressed as the acute median lethal concentration (LC_{50}) in milligrams per litre of water.

Species	LC_{50} (mg/L)	Reference
Fish		
Rainbow trout, *Oncorhynchus mykiss*	0.5	(Hood 1972)
Carp, *Cyprinus carpio*	0.3	(Hood 1972)
Bluegill sunfish, *Lepomis macrochirus*	0.8	(Hood 1972)

Toxicity to invertebrate species:

Phosphine is toxic to most species of insects (Lindgren and Vincent 1966, Bond et al. 1969), and other invertebrates (Sinha et al. 1967). Oxygen concentrations effect the toxicity of phosphine to many insects (Bond et al. 1969). The larvae and adult insect stages are more sensitive than the egg and pupal stages (Lindgren and Vincent 1966, Bell 1976, Hole et al. 1976).

Non-target primary risk profile:

Phosphine is not a selective toxin and all non-target animals are at risk if they are present when fumigation is conducted. Users must make sure that only target species are present before control operations commence.

Non-target secondary poisoning risk profile:

Unchanged phosphine does not remain in any appreciable amounts within fumigated materials (Bond 1984), hence the risk of secondary poisoning is considered negligible. Feeding trials with phosphine fumigated foodstuffs have shown no effects on rats (*Rattus* sp.) and mice (*Mus* sp.) (Robinson and Bond 1970, Hackenberg 1972, World Health Organisation 1988). There are no reports of feeding trials of fumigated rabbits (*Oryctolagus cuniculus*) to predators.

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Glossary

Description of toxicity

Acute exposure: a single exposure to a toxic substance which may result in severe biological harm or death; acute exposures are usually characterized as lasting no longer than a day; often reversible.

Chronic exposure: prolonged or repeated exposure to a toxin over an extended period of time, often measured in months or years; it can cause irreversible side effects.

LD (lethal dose): a dose recorded to cause death.

Min. LD (minimum lethal dose): the lowest dose of the pesticide over any given time frame reported to cause death.

LD_{50} (lethal dose, 50% or median lethal dose): dose required to kill half of the members of a tested population. Oral LD_{50} is measured in mg of toxin per kg of bodyweight of the animal.

LC_{50} (lethal concentration, 50% or median lethal concentration): concentration in water or air required to kill half of the members of a tested population over a specified time frame. LC_{50} is measured in mg of toxin per L of water or air.

EC_{50} (effective concentration, 50% or median effective concentration): concentration in water or air that causes 50% reduction relative to control over a specified time frame. EC_{50} is measured in mg of toxin per L of water or air.

TL_m (median tolerance limit): a statistical estimate of the concentration of toxic substance in water that kills 50% of the test species over a specified time interval. TL_m is measured in mg of toxin per L of water.

Units of measurement

% = percent (parts per hundred)

^oC = degrees centigrade

g = grams

kg = kilograms

mg = milligrams

µg = micrograms

L = litres

ppm = parts per million

cm^3 = cubic centimetres

m^3 = cubic metres

Notes:

1. Toxicity measurements are given in mg/L, which for gases is equivalent to g/m^3.
2. Measurements of gases given in ppm were converted to mg/L by dividing the ppm by 1000 to give the number of cm^3 of gas per L of air then multiplying by the molecular weight of the gas, and dividing by 22.4.
3. Measurements of gases given in % volume were converted to mg/L by multiplying the percentage by 10 to give the number of cm^3 of gas per L of air then multiplying by the molecular weight of the gas, and dividing by 22.4.

Appendix 1

Australian Poisons Schedules

In Australia poisons are classified to the Schedules in which they are included. The following is a general description of the Schedules. For legal definitions check with the appropriate state or territory authority.

Schedule 1.	This Schedule is intentionally blank
Schedule 2.	**Pharmacy Medicine** – Substances, the safe use of which may require advice from a pharmacist and which should be available from a pharmacy or, where a pharmacy service is not available, from a licensed person.
Schedule 3.	**Pharmacist Only Medicine** – Substances, the safe use of which requires professional advice but which should be available from a pharmacist without a prescription.
Schedule 4.	**Prescription Only Medicine**, or **Prescription Animal Remedy** – Substances, the use and supply of which should be by or on the order of persons permitted by the State or Territory legislation to prescribe and should be available from a pharmacist on prescription.
Schedule 5.	**Caution** – Substances with a low potential for causing harm, the extent of which can be reduced through the use of appropriate packaging with simple warnings and safety directions on the label.
Schedule 6.	**Poison** – Substances with a moderate potential for causing harm, the extent of which can be reduced through the use of distinctive packaging with strong warnings and safety directions on the label.
Schedule 7.	**Dangerous Poison** – Substances with a high potential for causing harm at low exposure and which require special precautions during manufacture, handling or use. These poisons should be available only to specialised or authorised users who have the skills necessary to handle them safely. Special regulations restricting their availability, possession, storage or use may apply.
Schedule 8.	**Controlled Drug** – Substances which should be available for use but require restriction of manufacture, supply, distribution, possession and use to reduce abuse, misuse and physical or psychological dependence.
Schedule 9.	**Prohibited Substance** – Substances which may be abused or misused, the manufacture, possession, sale or use of which should be prohibited by law except when required for medical or scientific research, or for analytical teaching or training purposes with approval of commonwealth and/or state or territory health authorities.

Pesticides used in the Management of Vertebrate Pests in Australia: A Review