The Old School, Brewhouse Hill, Wheathampstead,
Hertfordshire AL4 8AN, UK

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Is sodium fluoroacetate (1080) a humane poison? The influence of mode of action, physiological effects, and target specificity

LE Twigg*† and RW Parker‡

† Vertebrate Pest Research Section, Department of Agriculture and Food, Western Australia, Lot 100 Bougainvillea Avenue, Forrestfield, WA 6058, Australia
‡ Biosecurity Queensland, Department of Employment, Economic Development and Innovation, Alan Fletcher Research Station, PO Box 36, Sherwood, Qld 4075, Australia
* Contact for correspondence and requests for reprints: landlconsult@iprimus.com.au

Abstract

1080 (sodium fluoroacetate)-baiting programmes are an important and often the only option for reducing the impact of invasive vertebrate pests on biodiversity and agricultural production in Australia and New Zealand. These programmes are generally recognised as being target specific, and environmentally and user safe. Nevertheless, although 1080 has few recognised long-term side-effects, its potential to disrupt endocrine systems has been recently raised, and there is some conjecture regarding the humaneness of 1080 for certain target species. However, the assessment of the humaneness of any vertebrate pesticide must be commensurate with its mode of action, metabolism, target specificity, and operational use. This has not always occurred with 1080, particularly regarding these aspects, and its overall effects. The actual risk faced by non-target species during baiting operations is not accurately reflected simply by their sensitivity to 1080. 1080 is not endocrine-disrupting or carcinogenic, and because of the lag phase before signs of poisoning occur, the time from ingestion to death is not a reliable indicator of its humaneness. Moreover, functional receptors and neurological pathways are required to experience pain. However, as 1080 impairs neurological function, mainly through effects on acetylcholine and glutamate, and as this impairment includes some pain receptors, it is difficult to interpret the behaviour of affected animals, or to assess their ability to experience discomfort and pain. This has implications for assessing the merits of including ameliorative agents in 1080 baits aimed at further improving welfare outcomes. We also suggest that the assessment of the humaneness of any vertebrate pesticide should follow the ethical pest control approach, and on this basis, believe that the use of 1080 to reduce the detrimental impacts of invasive vertebrates is ethical, particularly with respect to the expectations of the wider community.

Keywords: *1080, animal welfare, ethical pest control, fluoroacetate, humaneness, vertebrate pest*

Introduction

Introduced vertebrates, particularly rabbits (*Oryctolagus cuniculus*), foxes (*Vulpes vulpes*), feral pigs (*Sus scrofa*), wild dogs (*Canis lupus familiaris*), feral goats (*Capra hircus*), and feral cats (*Felis catus*), have a significant and profound impact on agricultural production and/or biodiversity in Australia. Such impacts can include endemic and potential exotic animal diseases and human health (Saunders *et al* 1995; Williams *et al* 1995; Choquenot *et al* 1996; Fleming *et al* 2001; Cooper *et al* 2007). In 2004, the annual cost of these species to Australian agriculture alone was estimated at approximately AUD$330 million (McLeod 2004). Although the direct impact of these and other pest species on biodiversity is considerable, placing an accurate monetary value on these impacts is not possible. However, over AUD$22 million were spent on fox and feral cat control programmes in Australia in 2004 in attempts to reduce the detrimental impact of these species on biodiversity (McLeod 2004).

With the exception of feral goats, baiting programmes with sodium fluoroacetate (ie 1080) form an integral and, in some cases the only, means by which the impacts of these introduced invasive species can be managed on a large scale (Saunders *et al* 1995; Williams *et al* 1995; Choquenot *et al* 1996; Fleming *et al* 2001). 1080 products play a vital and important role in protecting biodiversity and agriculture in New Zealand mainly through the management of rabbits, and in management programmes for bovine tuberculosis (especially through the control of introduced brushtail possums [*Trichosurus vulpecula*]; Eason *et al* 1994a,b; Seawright & Eason 1994). In addition to these target species (ie rabbits, foxes, wild dogs, feral pigs, brushtail possums, and feral cats), there are indirect benefits of these control programmes through secondary poisoning of stoats (*Mustela erminea*), ferrets (*M. putorius*), foxes, and feral cats (Aulerich *et al* 1987; Gooneratne *et al* 1995; Algar & Kinnear 1996; Meenken & Booth 1997). The active ingre-

dient of 1080, fluoroacetate, is produced naturally in biologically significant amounts by several plant genera on three continents (Australia, Africa, South America) as a chemically mediated defence against herbivory (de Oliveira 1963; Aplin 1971; Vickery & Vickery 1975; Twigg & King 1991). However, 1080 is produced synthetically for use in baits.

The assessment of the need, and methods used, to reduce the impact of pest species can be difficult because of the wide range of emotions and ethical stances that can be evoked. Complete agreement is unlikely to ever be reached on what is, and is not, desirable, but an acceptable middle ground must be found if Australia's and New Zealand's agricultural production and biodiversity are to be maintained. One way to help achieve such an outcome is to ensure that relevant and accurate information is available so that people are better placed to develop informed, sound, scientifically based opinions on what is, and what is not acceptable, including animal welfare outcomes (ie 'humaneness').

Any assessment of the humaneness of vertebrate pesticides must be commensurate with their mode of action, metabolism, physiological effects, target specificity, and operational use-patterns. In addition, any assessment needs to consider the wider rationale and implications as to why such pests are being targeted, particularly where remedial action results in an overall gain in animal welfare outcomes (eg decreased lamb predation). These aspects have not been fully considered in the two recent reviews regarding the reported humaneness and/or appropriateness of using 1080 (see Weaver 2006 and Sherley 2007), resulting in several misleading conclusions. These include, inappropriately using time to death as an indicator of humaneness of 1080, potential endocrine disruption, and suggesting laboratory-derived toxicity data equate to actual risks to non-target species during baiting operations. In particular, these reviews did not fully address the mode of action of 1080 or the known low-level persistence of 1080 in the environment and the positive implications of these aspects for animal welfare, or consider how 1080 is actually used in the field. Our paper addresses these omissions by summarising the mode of action, metabolism, and the physiological effects of 1080, and showing how these will influence any assessment of its humaneness. A case is then mounted to suggest that the argument presented, stating that 1080 should not be considered to be humane (Sherley 2007), is not supported by the available scientific evidence.

Mode of action

The mode of action of fluoroacetate is complex and not yet fully understood. However, its toxicity arises from its conversion within the animal to fluorocitrate (Peters 1952; Peters & Wakelin 1953; Peters 1957; Buffa *et al* 1973). Synthesis of fluorocitrate ([-]-erythro-2-fluorocitrate — the only active isomer) occurs in the mitochondria and the fluorocitrate thus formed competitively inhibits the tricarboxylic acid cycle (TCA) enzyme, aconitase (EC 4.2.1.3 -aconitate hydratase) but does not appear to affect the cytoplasmic isozyme *in vivo* (Morrison & Peters 1954; Buffa *et al* 1973). This ultimately results in decreased production of ATP and, hence, energy. Additionally, aconitase is now thought to be essential for maintaining the integrity of mitochondrial DNA (Klausner & Rouault 1993; Chen *et al* 2005) which is required to maintain proper cellular respiratory function and energy production (Buffa *et al* 1973; Chen *et al* 2005). As little as 0.1 to 3% of ingested 1080 needs to be converted to fluorocitrate to exert its lethal effects (Gal *et al* 1961; Clarke 1991), and if vomiting occurs, this does not improve the survival of poisoned individuals as sufficient fluoroacetate has been absorbed before this happens (O'Brien 1988; O'Brien & Lukins 1988; Twigg *et al* 2005).

Fluorocitrate also inhibits citrate transport into and out of mitochondria (Kirsten *et al* 1978; Kun 1982), and this interferes with the metabolism of citrate, including in the brain (Fonnum *et al* 1997). Although there is still some debate over which metabolic effect is the more important, the effect on citrate transport occurs at much lower concentrations of fluorocitrate than do the effects on aconitase (Peters 1952, 1972; Buffa *et al* 1973; Kirsten *et al* 1978; Kun 1982; Clarke 1991). For example, the concentration of fluorocitrate (0.1 μM) in the mitochondria of lethally poisoned rats is less than the inhibition coefficient (K_i) for aconitase (26 μM), but this concentration is sufficient to inhibit citrate transport enzymes in the mitochondrial membrane (Kun *et al* 1977; Kirsten *et al* 1978; Twigg & King 1991; Goncharov *et al* 2006).

Fluorocitrate can also have an inhibitory effect on succinate dehydrogenase in intact mitochondria (rats: Fanshier *et al* 1964; fish: Zurita *et al* 2007). Although the effects may vary slightly between tissue types (Buffa *et al* 1973; Fonnum *et al* 1997), the resulting block in the TCA cycle, and the inhibition of citrate transport mechanisms, ultimately result in the accumulation of citrate in the tissues and plasma, energy deprivation, and death (Peters 1957; Buffa *et al* 1973). In addition, the high levels of citrate can inhibit the glycolytic enzyme, phosphofructokinase (Peters 1972). At high concentrations, citrate chelates with serum calcium, resulting in hypocalcaemia and ultimately heart failure (Roy *et al* 1980; Omara & Sisodia 1990; Parton 2001; Goh *et al* 2005). Citrate can chelate with magnesium, and this may also contribute to the toxic effects of fluoroacetate (Roy *et al* 1980).

The actual cause of death from fluoroacetate poisoning is not fully known, but it is a multifactorial event (Peters 1952, 1972; Buffa *et al* 1973; Omara & Sisodia 1990; Parton 2001; Goh *et al* 2005). Accumulation of citrate results in changes in cation concentration which can cause ion imbalance within cells (Buffa *et al* 1973). The resulting ionic and osmotic modifications, together with the associated decline in ATP and serum calcium concentrations, may be sufficient to induce death (Buffa *et al* 1973; Roy *et al* 1980). Energy, and ionic, dependent transport mechanisms can also be affected (Buffa *et al* 1973). Neurotoxic effects also occur, particularly in many highly sensitive species (Buffa *et al* 1973; Kirsten *et al* 1978; Kun 1982). These effects, together with the depletion of glutathione (protects aconitase and catalyses defluorination of fluoroacetate; Buffa *et al* 1973; Twigg *et al* 1986; Twigg & King 1991),

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are responsible for many of the clinical signs of fluoroacetate poisoning. The outward signs of poisoning are generally neurological in carnivores, cardiac/respiratory in herbivores, and a mixture of neurological and cardiac signs in omnivores (Chenoweth 1949; Sherley 2004). However, because of the varied responses to 1080 intoxication, the classification of individual species into these groupings can be problematical (see Sherley 2004). There is a latent period (ie the lag phase) between the time fluoroacetate is ingested and the appearance of the first signs of poisoning (at least 30 min to 3 h in endotherms: Chenoweth 1949; McIlroy 1981; Twigg *et al* 1986; Twigg & King 1991), which results from the time required for fluoroacetate to be absorbed, to penetrate cells, be converted into fluorocitrate, and then to disrupt cellular processes.

Fluoroacetate poisoning and neurotransmitters

The metabolic effects of fluoroacetate/fluorocitrate also occur in nerve tissue. For example, fluoroacetate intoxication can reduce the activity of the TCA cycle in nerve tissue (mainly the glial cells) by 35–55% (Patel & Koenig 1968), and this can cause neurological dysfunction (Fonnum *et al* 1997; Goncharov *et al* 2006; Sun *et al* 2009). Sequelae include incoordination, tremors, and seizures (Buffa *et al* 1973; Littin *et al* 2009). At least part of this neurological dysfunction results from the effect of fluoroacetate poisoning on two primary neurotransmitters, acetylcholine and glutamate (see below).

Although it is often unrecognised, the high citrate concentrations generated during fluoroacetate poisoning also result in major metabolic interference. Citrate is an inhibitor of the production of acetylcholine. This important neurotransmitter has a wide range of key roles in the nervous system. It is the main neurotransmitter involved in the communication between muscles and their associated nerve junctions (Strand 1978; Rang 2003; Goncharov *et al* 2006), and is an important neurotransmitter in the brain (including in memory function), for interneural communication, and in the autonomic nervous system (Strand 1978; Hogg *et al* 2003; Rang 2003; Watanabe *et al* 2009). The active role of acetylcholine in memory formation may partially explain why human patients often have no recollection of the adverse effects which can occur during 1080 intoxication (Chi *et al* 1996). Acetylcholine also has neurohumoral roles, such as the control of insulin secretion through the activation of the phospholipase carbon and calcium signalling pathway (Goncharov *et al* 2006). Although it has been proposed that the neurotoxic effects of fluorocitrate may result from the inhibition of cholinergic (acetylcholine) receptors (Kun 1982), such effects are more likely to result from the inhibition of acetylcholine synthesis in nerve cells.

The inhibition of acetylcholine synthesis by citrate seems to occur via two main mechanisms. Firstly, hydroxycitrate, which can be formed in the presence of fluorocitrate, aconitase, cysteine, and Fe^{2+} (Kirsten *et al* 1978), is a specific inhibitor of ATP-citrate lyase (Tucek *et al* 1981). ATP-citrate lyase is required to form acetyl-CoA from citrate or glucose. Acetyl-CoA is the 'precursor' of acetylcholine. Hydroxycitrate concentrations of 2.5 mM can inhibit *in vitro* acetylcholine production from citrate by 82–86% (Tucek *et al* 1981), and second, citrate itself has a strong inhibitory effect on the synthesis of acetylcholine. For example, the formation of acetylcholine from glucose and pyruvate *in vitro* can be reduced by 43 and 66% in the presence of 2.5 and 5 mM citrate, respectively (Tucek *et al* 1981). Citrate concentrations of 1–2 mM are often reached in the plasma of animals poisoned with fluoroacetate (Twigg & King 1991; Gooneratne *et al* 1994). Further, the action of acetylcholine was totally inhibited by ~100 mM fluoroacetate over 24 h during *in vitro* studies with fish cell lines (*Poeciliopsis lucida*), with an EC_{50} (half maximal effective concentration) for acetylcholine of 73 mM fluoroacetate (Zurita *et al* 2007). Fluoroacetate blockage of the TCA cycle often completely inhibits acetylcholine-induced mobilisation of intracellular calcium (Schofl *et al* 2000), further indicating the important role of acetylcholine in maintaining homeostasis.

Glutamate is an important neurotransmitter for some nociceptors (pain receptors), particularly those located in the skin and brain (Fonnum *et al* 1997; Fundytus 2001; Platt 2007). Together with acetylcholine, glutamate is also a modulator of memory, and an important neurotransmitter in the spinal cord (Fundytus 2001; Watanabe *et al* 2009). Fluoroacetate poisoning can result in decreased glutamate levels in the striatum (ie brain) with resultant decreased capacity for nocioception (ie registering pain) as glutamine (a precursor of glutamate) synthesis is particularly sensitive to fluorocitrate (Fonnum *et al* 1997). Functional receptors and neurological pathways are required to experience pain.

1080 toxicosis is thought to induce seizures in rats through alterations to neurotransmitter concentrations within the brain (Wickstrom *et al* 1998). The administration of neurotransmitter modulating agents (eg glutamate inhibitors, GABA and serotonergic antagonists) can significantly ameliorate the toxic effects of 1080 (Cook *et al* 2001; Goh *et al* 2005). Nitrous oxide is also involved in the development of pathological pain and hyperalgesia in the spinal cord (Sun *et al* 2009). Sun *et al* (2009) showed that fluorocitrate significantly inhibited the up-regulation of the nitrous oxide system, and the production of nitrous oxide, in rats, with resultant reversible attenuation of the development of pain and hyperalgesia.

Thus, although the modulation/regulation of the nervous system is obviously complex, it is clear that fluoroacetate poisoning results in the dysfunction of at least two major neurotransmitter pathways, the cholinergic and glutamergic systems, and also attenuates the ability to feel pain in the spinal cord through decreased nitrous oxide production. The dysfunction of the cholinergic and glutamergic systems ultimately results in the tremors/tetanic spasms seen in some poisoned animals. It is unclear to what extent fluoroacetate poisoning disrupts other neurotransmitter systems but, because of the ultimate suppression of ATP production occasioned during fluoroacetate intoxication, the effects of fluoroacetate are most pronounced in those cells with high energy demands (Buffa *et al* 1973; Kun 1982; Twigg &

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King 1991). Because all these effects are quite complex, it is not currently possible to assess the extent to which such impairment decreases the ability of animals to experience painful stimuli during 1080 intoxication. However, any disruption to, or malfunction of, neurotransmitter systems must be considered when assessing the ability of animals to experience pain or distress during 1080 intoxication, particularly given that consciousness declines prior to death during fluoroacetate poisoning (Kun 1982). The effect of fluoroacetate on neurological integrity, and how this relates to decreased neurological function and the ability to register pain are important areas which would benefit from future research. For example, exactly when do *in vivo* levels of neurotransmitters change, and by what amount, in relation to the recognised stages of fluoroacetate poisoning.

Time to death as an indicator of humaneness

Sherley (2007) used time to death from laboratory-based toxicity trials as one of the main measures for assessing the humaneness of 1080 baits during pest control operations. Time to death was taken as the time from administration of 1080 to death. However, this approach does not allow for the lag phase associated with 1080 toxicity, the deliberate administration of sub-lethal or just-lethal amounts during toxicity trials, or for how 1080 is used during baiting operations in the field.

Lag phase

The observed and reported clinical signs of 1080 poisoning (McIlroy 1981, 1982a,b, 1984; Twigg 1986; Eason *et al* 1994a; Litton *et al* 2009), together with the known metabolic effects of fluoroacetate during the lag phase of 1080 intoxication (Buffa *et al* 1973; Kun 1982; Goncharov *et al* 2006), suggest that there is minimal discomfort or pain to poisoned animals during this phase. The lag phase is rarely less than 1 h, and can be much longer than this (eg 3–15 h). Thus, the time during which animal welfare has the potential to become compromised will be overestimated unless this characteristic of 1080 poisoning is taken into account. A more accurate estimate of the time that animal welfare may be potentially compromised would be from the time that signs of poisoning appear until death (eg Littin *et al* 2004). Using this definition, and estimating time to death from ingestion to death minus the reported lag phase (eg McIlroy 1981, 1982a,b, 1984; Eason *et al* 1994a; Twigg *et al* 2002; Sherley 2007), death often occurs within 2–4 h of overt signs of poisoning becoming evident, although it can be longer than this with some individuals. However, such values are difficult to estimate for many species because few published studies have recorded time to death using the above, more accurate definition.

Toxicity data vs operational non-target risk

For the following reasons, using data from toxicity trials designed to assess the sensitivity of animals to 1080 as an indicator of the time to death of animals poisoned during pest control operations is not a valid approach. Laboratory-based assessments usually involve liquid-gavage/injection of the active ingredient whereas, during field operations, the active ingredient is presented in a bait matrix. The bioavailability and absorption profiles are likely to differ between these two delivery methods. Sub-lethal and just-lethal amounts of 1080 are also used during the toxicity trials, and yet 1080 baits are deliberately designed to deliver at least 2–3 times an LD_{99} dose. For example, 1080 baits used in fox and wild dog control programmes contain 3 and 6 mg of 1080 (Saunders *et al* 1995; Fleming *et al* 2001), and these concentrations equate to approximately twice the estimated LD_{99} amount required for the largest individuals of each species. Thus, animals ingesting such amounts during pest control operations are likely to be killed more quickly than what would be suggested using the time to death derived from data obtained during laboratory-based toxicity trials. That is, the time to death of an animal is inversely related to the dose of 1080 received, up to an asymptote level which varies with species (McIlroy 1981, 1984; Eason *et al* 1994a).

Nevertheless, it is important that best practice techniques are followed so as to maximise the number of target species exposed to toxic baits before the level of active ingredient declines over time. Loss or degradation of 1080 from baits is dependent upon bait type, rainfall, time of year and the concentration of 1080 but, in the absence of rainfall, baits generally remain toxic for at least four weeks (Wheeler & Oliver 1978; Oliver *et al* 1982; McIlroy *et al* 1986, 1988; Thomson 1986; Fleming & Parker 1991; Eldridge *et al* 2000; Saunders *et al* 2000; Twigg *et al* 2000; Twigg *et al* 2003). 1080 is readily degraded by a range of bacteria, fungi and aquatic micro-organisms (Kelly 1965; Bong *et al* 1979; Wong *et al* 1992; Twigg & Socha 2001; Suren 2006) and does not persist in ground or surface waters (Eason 1993; Twigg *et al* 1996; Suren 2006; Booth *et al* 2007; Eason & Temple 2008), even in the presence of quite high natural concentrations of fluoroacetate in the surrounding environment (Twigg *et al* 1996). Simple dilution is also an important factor in these considerations (Eason 1993; Twigg *et al* 1996; Eason & Temple 2008). Although it is likely to be dose-dependent, should animals ingest a sub-lethal amount of 1080 then they generally do not display obvious signs of poisoning and most 1080 is eliminated within 8–24 h in mammals (eg rabbits, possums, sheep, goats, mice) with few, if any, long-term effects (Mead *et al* 1979; Eason *et al* 1994a; Gooneratne *et al* 1994, 2008).

1080 toxicosis, endocrine systems and other tissues

It has been recently proposed that, because exposure to fluoroacetate can result in decreased gamete and reproductive hormonal production, fluoroacetate acts as an endocrine disruptor (Weaver 2006; Sherley 2007). However, this does not consider that such a response may be simply caused by the marked decrease in the supply of ATP which accompanies fluoroacetate poisoning. Further, in all cases studied, such effects are reversible and not permanent, and this includes birds (Balcomb *et al* 1983), mammals (Mazzanti *et al* 1965; Sullivan *et al* 1979; Hornshaw *et al* 1986; Gooneratne *et al* 2008) and reptiles (Twigg *et al* 1988a). The doses required to induce such a reproductive effect are also

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often well in excess of those levels which could be ingested from 1080 baits during pest control operations (Twigg *et al* 1988a; Twigg & King 1991; Gooneratne *et al* 2008).

Nevertheless, the potential effects of 1080 on endocrine systems are worthy of further discussion as such concern has been raised by the wider community (Weaver 2006; Eason & Temple 2007), and any serious effects have the potential to influence welfare outcomes. Toxicologists specifically refer to endocrine-disrupting chemicals (EDCs) as synthetic chemicals that, once absorbed, have oestrogenic or anti-androgenic activity which is mediated by their ability to bind or block oestrogen or androgen receptors (Colborn *et al* 1996; Tremblay *et al* 2004, 2005; Eason & Temple 2007). In this respect, the ability of fluoroacetate and its toxic metabolite, fluorocitrate, to act as EDCs has been investigated in mammals and fish. Neither chemical had any effect on oestrogenic receptor binding in sheep (Tremblay *et al* 2004; Eason & Temple 2007). Similarly, neither fluoroacetate nor fluorocitrate displayed androgenic activity in rainbow trout (*Oncorhynchus mykiss*), and neither chemical showed androgenic or anti-androgenic, or oestrogenic or anti-oestrogenic, activity in a human reporter gene assay (Tremblay *et al* 2004, 2005). It is therefore quite unlikely that either chemical would promote oestrogenic or anti-androgenic effects (Tremblay *et al* 2004; Eason & Temple 2007), particularly at the level of fluoroacetate exposure likely to result from pest control operations. The observed reversible effect of 1080 on some reproductive tissue is most likely mediated through the direct intracellular effect of fluorocitrate on the production of ATP. The proposition that 1080 baits adversely affect the breeding performance of native animals (Weaver 2006) is not supported by the available evidence, particularly the many studies where native animal populations have responded very favourably to pest control programmes with 1080 baits (eg Twigg & King 1991; Seawright & Eason 1994; Morris *et al* 1995).

1080 is not mutagenic (Eason *et al* 1999; Eason & Temple 2007). Mouse lymphoma and micronucleus bone marrow assays were used to detect chromosome anomalies in mice given oral doses of 0.8, 1.5, 3.0, 6.0 and 7.5 mg 1080 kg^{-1}. No mutagenic activity was observed at any dose level (Eason *et al* 1999). The lack of harmful effects of fluoroacetate on chromosomes suggests, but is not absolute evidence, that fluoroacetate or its metabolites are also unlikely to act as carcinogens.

Organs most affected by fluoroacetate toxicity mainly include those tissues with high energy requirements (Peters 1952, 1957; Buffa *et al* 1973). The effects of a single exposure to fluoroacetate are relatively short-term in endothermic animals, with most 1080 detoxified or eliminated within 8–24 h (Buffa *et al* 1973; Twigg *et al* 1988a,b; Eason *et al* 1993a, 1994a; Gooneratne *et al* 2008; Littin *et al* 2009). For example, in brushtail possums, sub-lethally dosed individuals were often seen grooming and feeding within 19 and 26 h of dosing (Littin *et al* 2009). Further, no adverse long-term effects were seen over two years in those sheep which survived sub-lethal exposure to 1080 (Gooneratne *et al* 2008). Minor damage may occur to heart tissue and some other organs with repeated exposure to sub-lethal doses of fluoroacetate (Buffa *et al* 1973; Eason *et al* 1999; Eason & Temple 2007) but the available evidence suggests that such mild tissue damage does not generally compromise the long-term survival of affected individuals (eg Eason *et al* 1993a; Gooneratne *et al* 2008). However, there are occasional reports that during some accidental human 1080 poisonings some symptoms may persist for several weeks (Gajdusek & Luther 1950). The no observable effects level (NOEL) for adult rats administered 1080 for 90 days was 0.08 mg 1080 kg^{-1} day^{-1}, and around 0.3 to 0.8 mg kg^{-1} when relatively large doses were administered to gestating females over their first trimester (assessed as developmental toxicity to resultant offspring: Eason *et al* 1999). A single dose of 1080 had no obvious abnormal effects on rat teratogenic development (Spielmann *et al* 1973). Bioaccumulation of fluoroacetate is very unlikely because biodegradation or elimination of fluoroacetate occurs at many levels in the food chain and includes micro-organisms, invertebrates, birds, mammals and reptiles (Kelly 1965; Bong *et al* 1979; Wong *et al* 1992; Twigg & King 1991; Eason *et al* 1993a,b, 1994a; Twigg & Socha 2001; Suren 2006; Zurita *et al* 2007).

Thus, the available evidence indicates that fluoroacetate (1080) or its toxic metabolite, fluorocitrate, are not endocrine-disrupting chemicals or mutagenic. Sub-lethal doses are generally rapidly eliminated or detoxified with no obvious persistent harmful effects that are likely to compromise long-term survival. This is particularly so when the level of potential exposure that is likely to result from properly conducted 1080-baiting programmes is considered.

Antidotes to 1080

One potential disadvantage of 1080 use is the current lack of an effective antidote, although effective treatment regimes have been developed for dogs that have been accidentally poisoned. Considerable effort has been undertaken to investigate a range of antidotal compounds, but no compounds have been found to be effective unless they were administered simultaneously with ingested fluoroacetate, although some can alleviate secondary symptoms (Chenoweth *et al* 1951; Mead *et al* 1985; Omara & Sisodia 1990; Cook *et al* 2001; Goh *et al* 2005; Rammell *et al* 2005). However, as noted, clinical treatment of 1080-poisoned dogs can be successful. Poisoned dogs may be heavily sedated to reduce the possibility of tremors, fluid levels are maintained and or specific treatments provided, and the dogs allowed to metabolise and eliminate ingested 1080 (Parton *et al* 2001; Goh *et al* 2005). Such treatment improves survival and welfare outcomes.

Although still experimental, calcium replacement therapy (eg calcium gluconate) may also be effective as hypocalcaemia is common during fluoroacetate poisoning (Roy *et al* 1980; Robinson *et al* 2002; Collicchio-Zuanaze *et al* 2006). Low calcium levels ultimately lead to heart failure (Omara & Sisodia 1990; Goh *et al* 2005), and calcium deficiency is a well-known cause of epilepsy (Fonnum

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et al 1997). Low calcium levels are also implicated as a partial cause of the fluoroacetate-induced tremors seen in some species (Fonnum *et al* 1997; Goncharov *et al* 2006). Plasma ionised calcium levels can be reduced by 27% within 40 min in some poisoned mammals due to its chelation with citrate (Peters *et al* 1972; Roy *et al* 1980; Goncharov *et al* 2006). Such decreases are physiologically significant (eg prolonging QTc intervals in electrocardiograms: Roy *et al* 1980), and depleted calcium levels have been described as the missing link between the biochemistry of fluoroacetate poisoning and its associated clinical manifestations (Roy *et al* 1980). Calcium, acetylcholine, and glutamate replacement therapies would therefore provide additional research areas for potential antidotes for fluoroacetate poisoning.

However, with respect to potential risks to animals that are not intended targets, it needs to be remembered that 1080 use is tightly regulated in both Australia and New Zealand, including prior notification that baiting is to occur, and the erection of warning signs in baited areas (VPC 2002; ERMA 2007; APVMA 2008). This helps to keep accidental poisoning of domestic animals to a minimum (such events often appear to be caused by the dog-owner's failure to see or adhere to warning notifications — see below).

1080 baits and target specificity

The specificity of any poison bait, including 1080 products, is determined by a number of factors which include: i) the sensitivity of target and non-target species to the active ingredient; ii) the body mass of non-target animals relative to that of target-species; iii) the bait medium used; iv) the digestibility of baits; v) whether non-target animals are exposed to the toxic baits or poisoned animals and, if so, whether these are acceptable food items; and vi) the timing of baiting programmes (King *et al* 1981; Calver *et al* 1989; Twigg & King 1991). For instance, while some native animals may remove 1080 baits, few are actually killed during the operational use of 1080 (McIlroy *et al* 1986; King 1989; McIlroy & Gifford 1991; Kortner 2007). This is in part due to the ability of some animals to detect 1080 in their food such that they refuse to consume it (Sinclair & Bird 1984; Calver *et al* 1989; Kortner & Watson 2005). For these reasons, sensitivity alone is not a reliable indicator of the potential risk posed to non-target species during 1080-based control programmes. This is supported by a number of studies such as those with northern (*Dasyurus hallucatus*: King 1989) and spotted-tailed quolls (*D. maculatus*: Kortner & Watson 2005; Kortner 2007). No deaths of radio-collared quolls were attributable to 1080 during control programmes using 6 mg 1080 baits directed at wild dogs.

A number of native Australian animals have enhanced tolerance to 1080 (fluoroacetate) through their evolutionary exposure to fluoroacetate-bearing vegetation, and some species (eg bandicoots [*Isoodon* and *Perameles* spp] and many dasyurids [*Dasyurus* spp]) have a low-level innate tolerance to fluoroacetate which is independent of any prior exposure to these toxic plants (Twigg & King 1991). However, provided best practice procedures are followed, enhanced tolerance to 1080 of non-target species is not a prerequisite for safe and effective baiting programmes. Decreased sensitivity of such species also means that they must find and consume multiple baits to ingest a potentially harmful dose (Twigg & King 1991).

Longfin eels (*Anguilla dieffenbachii*) have been deliberately exposed to 1080 baits, and 1080-poisoned possum tissue, in New Zealand, and although some eels ingested 1080, there were no ill effects (neither mortality nor abnormal behaviour: Lyver *et al* 2005). Similarly exposed freshwater crayfish (*Paranephrops planifrons*) also showed no ill effects (Suren & Bonnett 2004). 1080 had no discernable effects on native New Zealand fish in freshwater streams deliberately treated with 1080 baits for possum control (Suren & Lambert 2004), and there were no recorded detrimental impacts of the transient 1080 concentrations on the 72 invertebrate taxa included in this study. The No Observable Effect Concentration (NOEC) for water fleas (*Daphnia magna*) during USA toxicity trials was 130 mg L^{-1}, and it was concluded that 1080 was practically non-toxic to these water fleas (Fagerstone *et al* 1994). The NOEC for rainbow trout is 13 mg L^{-1} with an LC_{50} of 54 mg L^{-1}, indicating that 1080 was only slightly toxic to these trout (Fagerstone *et al* 1994). These findings, together with the other published studies (eg King & Penford 1946), indicate that properly conducted 1080-based pest control programmes have negligible, if any, detrimental impacts on aquatic organisms. Similarly, several terrestrial invertebrate species (eg weta, flatworms, spiders, amphipods, millipedes, centipedes, cockroaches, beetles, slugs), including some that may be consumed by insectivorous predators, have been monitored before and after 1080-baiting programmes in New Zealand (Eason 1993; Spurr 1994; Eason *et al* 1998; Lloyd & McQueen 2000; Spurr & Berben 2004; Powlesland *et al* 2005). There was no evidence of significant detrimental impacts of 1080 control programmes on terrestrial invertebrate populations, including the potential risk for secondary poisoning, although further research may be required for a few species (Lloyd & McQueen 2000).

Dogs are the most often poisoned domestic off-target species (primary or secondary poisoning) mainly due to their high sensitivity, and because they are often in close proximity to where baiting occurs (Orr & Bentley 1994; VPC 2002; Goh *et al* 2005). However, unintentional/accidental exposure to 1080 can be limited if correct procedures are followed, and dog owners follow the warning notification recommendations regarding baited areas.

For the above reasons, it is misleading to simply develop a list of the sensitivity of various non-target species to 1080, and then assume these species are at risk or will ingest harmful levels of 1080 during baiting operations. Such assessment has been demonstrated to overstate the real risk faced by each species (McIlroy *et al* 1986; King 1989; McIlroy & Gifford 1991; Twigg & King 1991; Booth & Wickstrom 1999; Kortner & Watson 2005; Lyver *et al* 2005).

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Some ethical considerations and the relative humaneness of 1080 use

Ethical pest control has been defined in terms of whether such actions are necessary, that the benefits clearly outweigh potential harmful effects (with the benefits being maximised while any anticipated harms are minimised), there are no other practical options besides lethal control, the most humane, feasible and practical option must be used, the outcomes must be measurable (ie damage mitigation not just a reduction in pest numbers), and steps need to be implemented to maintain the beneficial state (Littin *et al* 2004). With respect to ethical pest control, properly conducted control programmes with 1080 products for reducing the impacts of pest animals can, in our view, meet the above requirements, although there is still some conjecture as to whether 1080 is a humane poison (Oogjes 1997; Sherley 2007).

By their very nature, toxins disrupt physiological processes in poisoned animals so as to induce death. What is at conjecture with 1080 products is whether the disruption of cellular processes results in an unacceptable level of discomfort or pain, and if so, for how long. This is a difficult question because people will have varying opinions depending upon their knowledge, expertise, personal experience and their ability to set aside anthropomorphic-based views. There are several papers which argue that 1080 is humane relative to wider community expectations (eg Kun 1982; Fisher & Marks 1996; Gregory 1996; Williams 1996; Potter *et al* 2006), others which state this is not the case (eg Oogjes 1997; Marks *et al* 2004 [but only for canids]; Sherley 2004, 2007), and still others which present the 'middle ground' in that no control technique should result in *unnecessary* suffering (eg Littin *et al* 2004; Marks *et al* 2004), or that 1080 is intermediate in terms of its impact on animal welfare (at least, for brushtail possums), compared to other poisons (Littin *et al* 2009). However, rather than providing further summaries of the different views surrounding the effects of 1080 here, we instead summarise where there is general agreement and where additional research is needed to clarify points of view.

Following ingestion, three main phases of fluoroacetate toxicity are generally recognised. These can be summarised as a lag phase, a period during which signs of poisoning are apparent, and the terminal phase of 1080 poisoning when animals are unconscious or virtually so with considerable physiological disruption (Peters 1952, 1972; Buffa *et al* 1973; Kun 1982; Mead *et al* 1985; Twigg & King 1991; Chi *et al* 1996; Gregory 1996; Goncharov 2006; Potter *et al* 2006). Since they appear to maintain normal behaviour and physiological function, there is general agreement that animals are unlikely to experience undue discomfort during the lag phase associated with 1080 intoxication (Buffa *et al* 1973; Gregory 1996; Williams 1996; Sherley 2004, 2007; Potter *et al* 2006). Similarly, it is also generally accepted that because of their reduced consciousness and awareness, poisoned animals are unlikely to experience undue levels of pain during the terminal phase of 1080 intoxication (Kun 1982; Gregory 1996; Williams 1996; Potter *et al* 2006; Sherley 2007). Thus, it is the period between the appearance of obvious signs of poisoning and the beginning of the terminal phase where discomfort or pain could be potentially experienced which is of most concern for animal welfare, particularly for some carnivorous mammals.

In 1080-poisoned stoats, the mean time spent in each phase was: lag phase, ~60 min, the period with obvious signs of poisoning was ~26 min (range, 2 to 100 min), and the period of recumbency and non-responsiveness was ~58 min (Potter *et al* 2006). Thus, following the above definitions, the mean period where the welfare of these stoats may have been potentially compromised was ~26 min. Similarly, in foxes, the mean time from dosing to death was 310 min, with a 205-min lag phase. The mean time from overt signs until death was 118 min which, once allowing for the time spent in the terminal phase (~40 min), suggests that the time in which the welfare of foxes could be potentially compromised is around 80 min (Marks *et al* 2000, 2009).

In contrast, the mean time from obvious signs of poisoning to death in lethally poisoned brushtail possums was approximately 5.5–9.5 h, and although possums were often recumbent during this time, some individuals retained their response to some external stimuli. Some possums also displayed classic signs of fluoroacetate poisoning (Littin *et al* 2009). However, because fluoroacetate intoxication results in impaired neurological function, this does not necessarily imply they were experiencing pain or distress, or other negative impacts. In lethally poisoned sheep, severe signs of poisoning, which included tachypnoea, dyspnoea, and tremors, occurred for ~15 min prior to death but mainly during the terminal phase with initial signs of poisoning being very mild (Gooneratne *et al* 2008). Obviously, the time from overt signs of poisoning to death varies between species but the above outcomes provide further support for the argument that time to death should be taken from the time when overt signs of poisoning begin to when death occurs. If the findings for poisoned stoats, foxes, possums and sheep hold for other species, then even this more conservative definition may lead to overestimation of the time in which the welfare of poisoned animals could be compromised, as they do not seem to respond to painful stimuli during the terminal phase (Potter *et al* 2006; Gooneratne *et al* 2008; Littin *et al* 2009; Marks *et al* 2009). Clearly, this is an area for future research as any decrease in the time from overt signs of poisoning to death could benefit animal welfare outcomes (see Littin *et al* 2009).

A range of signs of poisoning can be invoked during fluoroacetate intoxication, including nausea, hypertension, lowered respiratory and heart rates, tetanic muscle spasms, involuntary vocalisation, disorientation, non-responsiveness to stimuli, hyper-excitability, ventricular fibrillation, retching, and vomiting (Buffa *et al* 1973; Kun 1982; McIlroy 1981, 1982a, 1984; Chi *et al* 1996; Gregory 1996; Littin *et al* 2009); inflammatory responses are not major outcomes of 1080 poisoning (Buffa *et al* 1973; Kun 1982; Chi *et al* 1996). However, it can often be difficult to assign cause and response directly to the effects of fluoroacetate poisoning as key neurological, and other systems (eg citrate

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transport, ATP production), are impaired. In brushtail possums, for example, lethally poisoned individuals gradually lost several responses to external stimuli (Littin *et al* 2009), indicating that they were not fully aware for some time before their death. Additionally, awareness or consciousness can comprise a spectrum rather than a clearly defined endpoint, and animals may cycle in and out of this state (Goncharov *et al* 2006; Littin *et al* 2009). Consequently, their ability to recognise pain will also vary over time depending upon the length and severity of each state, and whether their neurological function is maintained.

A further difficulty arises in trying to assess objectively what is an acceptable level of distress or pain before the terminal phase of 1080 toxicosis is reached. In surviving humans, even though many can experience some nausea and discomfort during the early stages of intoxication, few individuals actually reported any experience of associated pain. This was despite some individuals experiencing a number of muscle spasms once the toxic effects became more pronounced (Chi *et al* 1996). Although it can be distressing to observers, because of the accompanying loss of consciousness and/or awareness, the appearance of convulsive muscle spasms which can be associated with 1080 poisoning is not indicative that animals are feeling pain (Kun 1982; Gregory 1996). That is, just because an animal convulses, this does not mean it is aware, is responsive, feels pain, or can become consciously agitated. However, it is not surprising that such responses can make humans feel uncomfortable because of our often deep-seated empathy with other animals. If animals recover consciousness after any convulsion, it is possible that they may regain the ability to experience pain and distress. Thus, additional research which addresses these issues should help to allay such concerns (eg objective measurement of the length of the intermediate phase of 1080 intoxication, more objective assessment of the potential for feeling pain during the intermediate phase, the importance of impaired key neurological systems).

It is also valid ethically to balance the welfare of pest species against the welfare of those species protected by management actions (eg Cooper *et al* 2007; ERMA 2007). Current pest management focuses on reducing the impacts of introduced species on biodiversity and agricultural production but, unfortunately, the extinction of native species is still a real possibility due to the ongoing impacts of these pests (see, for example, Possingham *et al* 2003; Tyndale-Biscoe 2005). However, the judicious use of 1080 products has proven effective in reducing such impacts (see Morris *et al* 1995; Kinnear *et al* 1988, 1998; Possingham *et al* 2003; Cooper *et al* 2007). There is also an obligation on land managers, including the agricultural community, to protect their livestock from harm. 1080 baiting provides an effective means for reducing the level of predation and competition caused by introduced vertebrate pests. However, we are not suggesting that unacceptable or inhumane techniques are justified, but rather that welfare considerations must be balanced with an holistic approach.

Ways to minimise and/or avoid unnecessary suffering are prerequisites of any pest control programme, and only best practice techniques, which are continuously evolving/improving, should be used (Saunders *et al* 1995; Williams *et al* 1995; Choquenot *et al* 1996; Fleming *et al* 2001; Littin *et al* 2004; Saunders & Sharp 2008). To this end, Sharp and Saunders (2008) recently developed a model to assess the relative humaneness of pest animal control methods. However, as their model only considers the humaneness of the actual active ingredient, it does not include the broader considerations required to assess ethical pest control (eg impact of target species, lack of alternatives, the intrinsic and extrinsic costs of the do nothing option). The Australian Animal Welfare Strategy has also been giving particular attention to vertebrate pest control in recent years, actively promoting the development and use of humane and *effective* methods to control pest animals in Australia (Commonwealth of Australia 2008).

Thus, with respect to ethical pest control, and for the above reasons, the use of 1080 products can, in our view, be justified on the following basis: i) on most occasions, there are no other effective options currently available for wide-scale control operations, and/or the use of 1080 baits forms an integral part of co-ordinated pest control programmes and integrated pest management. This is despite considerable time and monies being expended to develop additional control options which would reduce the reliance on 1080 products for wide-scale vertebrate pest control; ii) the overall level of animal welfare would decrease should 1080 products be withdrawn such that the impact of introduced predators and competitors could not be adequately managed; iii) when used correctly, 1080 products are target specific with few demonstrated long-lasting effects on non-target species, either at the population level and for the vast majority of individuals; iv) 1080 is generally considered the most humane vertebrate pesticide currently available for wide-scale control operations. Such assessments need to consider the neurological impairment associated with 1080 intoxication as this suggests that the ability to register pain will be compromised in poisoned animals; v) the active ingredient of 1080, fluoroacetate, is a natural plant product which is readily degraded by several species of micro-organisms in most environments and hence does not bio-accumulate; and vi) although it may not be always easily demonstrated, the use of 1080 products to reduce the detrimental impacts of invasive animals has clear benefits to biodiversity, agricultural production and our cultural heritage (Seawright & Eason 1994, Saunders *et al* 1995; Williams *et al* 1995; Choquenot *et al* 1996; McLeod 2004). This is particularly so given that best practice techniques, codes of practice, and standard operating procedures for vertebrate pest control, including 1080 products, have been developed at national levels, and that these standards are undergoing continual development and refinement (Saunders *et al* 1995; Williams *et al* 1995; Choquenot *et al* 1996; VPC 2002; ERMA 2007; Saunders & Sharp 2008).

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Use of analgesics and sedatives in baits

It has been recently proposed that the use of analgesics or sedatives (eg carprofen or copper indomethacin — both non-steroidal, anti-inflammatory drugs which work by inhibiting the production of prostaglandins) (Hart & Boardman 1963; Nolan & Reid 1993), including anaesthetic agents, may lead to improved animal welfare with some 1080 products (eg foxes: Marks *et al* 2000, 2009; Sherley 2007). However, the choice of drug is important since inflammatory responses are not major outcomes of fluoroacetate intoxication (Buffa *et al* 1973; Kun 1982). Also, these drugs can have adverse side-effects if used incorrectly or over a long period of time (eg ulcers, bone marrow damage: Hart & Boardman 1963; McCann 2006), which has implications for non-target animals that might ingest repeated doses of 1080 products containing these drugs. Any additive would also have to last long enough to persist through the 1080 poisoning lag phase up until death (or unconsciousness) occurs. That is, the analgesic would need to be effective at the time when the effects of 1080 poisoning become most pronounced, and the timing of this can be unpredictable. Further, these agents must not cause additional animal welfare problems. For instance, some analgesics/sedatives can interfere with thermoregulation and/or animal behaviour (Rosow *et al* 1980; Rodgers & Hendrie 1983; Kohn *et al* 1997; Paul-Murphy & Ludders 2001), and the possibility of target and non-target animals losing their ability to adjust to changing temperatures, and to avoid predators, needs to be considered (also see Marks *et al* 2000). The target specificity of such compounds would also need to be determined. Finally, any additive must not interact negatively with the mode of action, or efficacy, of 1080. For example, the administration of diazepam together with 1080 resulted in decreased sensitivity of foxes to 1080 (Marks *et al* 2009). Interestingly, co-administration of diazepam also increased the time to death in treated foxes (Marks *et al* 2000, 2009). Thus, although at face value the addition of such compounds may seem an attractive option, their use may not necessarily result in an overall gain in animal welfare; researchers need to consider these aspects when planning/undertaking such work. The use of such compounds could even result in decreased welfare outcomes as target and non-target animals lose their ability to escape climatic extremes, and to avoid predators.

Reducing pest fertility

Fertility control of pest species is an attractive option as it focuses on decreasing birth rates rather than increasing death rate as do lethal control options. For this reason, the Australian and New Zealand governments have invested considerable monies to examine the possibility of developing target-specific, naturally disseminated, anti-fertility agents for rabbits, house mice, foxes and introduced (New Zealand) brushtail possums (Tyndale-Biscoe 1994; McLeod *et al* 2007; Tyndale-Biscoe & Hinds 2007). However, despite a conservatively estimated $AUD80 million research effort spanning three Co-operative Research Centres over approximately 15 years (T Peacock, personal communication 2008), the technical challenges have proven too great with current technology, and disseminating or bait-delivered fertility control has not been practically developed for any pest species (Tyndale-Biscoe & Hinds 2007). Further, models developed from field-generated data indicate that a sustained, wide-scale, effective reduction in pest numbers could not be achieved when fertility control only is used (Barlow 1997; Barlow *et al* 1997; McLeod & Twigg 2006; McLeod *et al* 2007). That is, the efficacy and benefit-cost of fertility control rarely compares favourably with the outcomes generated from lethal control options such as baiting. Bait-delivered anti-fertility agents also appear to have limited application unless their use is preceded by lethal control to reduce a population to relatively low numbers before anti-fertility baits are used (Barlow 1997; Barlow *et al* 1997; McLeod &Twigg 2006; McLeod *et al* 2007). Substantial damage (eg crop losses, predation) can still be inflicted by those sterile individuals remaining in a population.

Chemical control of the fertility of individuals has been developed for a few mammalian species (eg wild horses, white-tailed deer [*Odocoileus virginianus*], grey kangaroos [*Macropus* spp]). However, this technique requires re-administration/re-injection (usually annually) of the anti-fertility drug to each individual (Miller *et al* 1995; Kirkpatrick *et al* 1997; Herbert *et al* 2006). For this, and other reasons (eg practicality of targeting sufficient individuals, inaccessible terrain), these techniques are not suitable for wide-scale vertebrate pest control programmes, such as those required in Australia and New Zealand.

Other options

Management strategies for reducing the impacts of any pest species require as many options as possible, and the over-reliance on any one option is less than ideal (Seawright & Eason 1994; Saunders *et al* 1995; Williams *et al* 1995; Choquenot 1996; Fleming *et al* 2001). For this reason alone, it would be prudent to develop further options, both lethal and non-lethal, for reducing vertebrate pest impacts. However, new techniques must be efficacious, safe, considered to be humane, practical, and meet registration and regulatory requirements. With respect to 1080 and lethal control, a number of additional options have been examined, but additional products are yet to have been brought to fruition despite considerable effort. Pindone, warfarin, cholecalciferol, coumatetralyl, salicylic acid and several other chemicals, for example, have been assessed for possible control of possums in New Zealand, but for a number of reasons, none has been found suitable (Eason *et al* 1994b). Cyanide has been used for ground control of introduced possums in New Zealand but it is often not the toxin of choice because of poor efficacy and the development of bait/toxicant aversion (Eason *et al* 1994c; Warburton & Drew 1994). The use of 1080 in pest control has undergone significant recent reviews in Australia and New Zealand which recommended continued use of 1080 products but with more focus on uniform labelling and/or directions for use in Australia, and improved community

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notification and reporting procedures for off-target monitoring in New Zealand (ERMA 2007; APVMA 2008).

Several toxins are being currently investigated for vertebrate pest control in Australasia, including encapsulated cyanide, PAPP (p-aminopropiophenone), and sodium nitrite for controlling feral pigs (Marks *et al* 2004; IACRC 2007; Aster & Gentle 2008; Cowled *et al* 2008; Gentle *et al* 2008). However, most still require considerable research before they could be considered for registration and, although some are showing promise (eg PAPP and control of canids: Marks *et al* 2004), it is uncertain whether registered products will eventuate. As mentioned above, considerable effort was also undertaken to develop efficacious anti-fertility agents for several vertebrate pest species but this has proven impossible with current technology. Even if some of the above options can be successfully developed, the number of available options needs to be maximised to ensure that our long-term ability to reduce the impacts of vertebrate pests is maintained. Because of their proven safety and success, this includes the judicious use of 1080 products.

Conclusion

When assessed with appropriate scientific methods we do not believe that the argument that 1080 is an inhumane poison is supported by the evidence presented by Sherley (2007) or by that available elsewhere in the literature. This is particularly so when the neurological effects of 1080 intoxication, and the common field-use patterns for 1080, are considered. Indeed, 1080 is considered more humane than most other pesticides currently available for wide-scale vertebrate pest control operations (Eason *et al* 1994a,b; Fisher & Marks 1996; Gregory 1996; Littin *et al* 2009). Consequently, we believe that the use of 1080 products can be considered ethical when used appropriately, particularly in the absence of viable alternatives for wide-scale pest control, and with the urgent need to reduce the detrimental impacts of pest species (including the detrimental impacts of pest species on the animal welfare of native and domesticated species). However, we do agree that some areas of the effects of 1080 on some target species require further research (eg the amount of time in the various stages which result from fluoroacetate intoxication in some carnivores, the significance of the neurological effects of 1080), and that, as with any toxin, any reduction in the phase where overt signs of poisoning are evident would have potential animal welfare benefits. The available evidence does not support the contention that 1080 is an endocrine disruptor (Weaver 2006), and nor do simple lists of the sensitivity of species to 1080 reflect the practical/real risk faced by each species during the operational use of 1080 products. We also accept that pest management strategies need to include as many options as possible, including lethal control, and that they are implemented within an ethical framework. Any additional control options must be efficacious, safe for the user and the environment, relatively humane and provide cost-effective control, and the welfare assessment framework developed by Sharp and Saunders (2008) will help with this process.

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