A Review of Toxicological Research on Sodium Monofluoroacetate (1080) and its Policy Implications

Sean Weaver
Environmental Studies, School of Earth Sciences,
Victoria University of Wellington
Research Report Number 18.
April 2003

Table of Contents

Abstract

Sodium monofluoroacetate (1080) is used for large-scale pest control operations in New Zealand, to control the brush tailed possum (*Trichosurus vulpecula*) (an introduced marsupial pest). Wide-scale opposition to the use of 1080 has grown in recent years with the development of a substantial "anti-1080" lobby. Concerns for public health and effects on non-target animals among critics of 1080 have prompted the Department of Conservation to seek a review of the chemical by the Environmental Risk Management Authority (ERMA). In 2002 ERMA declared its intention to undertake this review, but in May 2003 announced that the review would be postponed due to impending adjustments to the HSNO Act. This report was prepared in anticipation of this official review and encompasses an independent evaluation of the peer-reviewed scientific literature on the risks associated with the use of 1080, in order to ascertain the degree to which regulations on 1080 reflect current scientific knowledge of the toxicology of this poison. Key areas of concern revealed in the literature include evidence that 1080 could have endocrine disrupting capabilities, and that it is relatively slow to break down at low temperatures (when microbial activity is low). These two issues are yet to be fully resolved through further research and represent significant gaps in current knowledge. If regulations are to take full account of current science on 1080 they will need to acknowledge and reflect what is known, the gaps in this knowledge, and the risks associated with this uncertainty. Recommendations include further targeted research to fill these gaps in current knowledge, regulatory precaution until such research is completed, and explorations of alternative methods to be used either in conjunction with, or (perhaps in certain areas) instead of this toxin.

Summary of Recommendations

It is clear that for acute toxicity there is ample empirical evidence of adverse health effects of 1080 (with a high degree of scientific consensus), and credible explanations of a biological mechanism to explain these effects, and regulations that reflect this consensus. For chronic toxicity (e.g. potential endocrine disruption) there is some (significant) empirical evidence of adverse health effects with animal models, and as yet no clear causal explanations that have led to scientific consensus on the biological mechanisms involved in chronic toxicity (apart from sufficient consensus in California for the EPA to classify 1080 as a male reproductive toxin).

To enable the regulatory framework to be fully informed by science on this matter there is a need to fill the gaps in our current knowledge (where possible), and take appropriate regulatory action during an interim period in order to appropriately deal with the uncertainty associated with chronic toxicity. In terms of research there is a need to:

1. Conduct experiments to determine whether 1080 is an endocrine disrupter, and determine the endocrine disrupting effects (if any) on a variety of aquatic and terrestrial organisms.
2. Conduct experiments to determine the rates of 1080 degradation at temperatures equivalent to those experienced in the winter months in forested mountain areas in New Zealand.

Until the above research has been completed there is a need to re-evaluate the regulatory status of 1080 in the light of these gaps in our knowledge. In particular, there is a need to:

3. Evaluate the risk of 1080 use for the regulatory period prior to the completion of such research, that takes adequate account of this uncertainty; and,
4. Set interim regulations that reflects this uncertainty and the associated risks.
5. Explore the practical and financial feasibility of alternative methodologies for possum control, including the possibility of using 1080 in combination with other methods currently in use (e.g. trapping, other poisons, bounty schemes). As a precautionary measure (prior to the completion of research mentioned in points 1. and 2. above), it would be appropriate to explore the feasibility of using methods other than 1080 in human drinking water catchments, and perhaps restricting 1080 use to areas at some distance from human habitation.

   The financial costs (relative to 1080) of employing non-toxic alternative methods in drinking water catchments could be offset by the political gains in a decrease in the scope of community opposition to the poison. Such measures are unlikely to satisfy recreational hunters, whose geographical area of concern extends to hunting areas located a long distance from drinking water catchments. On the other hand, localised community concern for drinking water quality could be substantially reduced if drinking water catchments and areas close to human habitation (and domestic dog walking areas) became 1080 exclusion zones. It is still important however, to deal with the concerns of recreational hunters, particularly if DOC wants to manage a significant potential liability to the conservation estate in the form of vigilante hunters who may seek to wilfully jeopardise the biosecurity of conservation areas (as became

apparent in the threats made to Kapiti Island Nature Reserve during January 2003). One solution could be to manage possums in recreational hunting areas by intensive trapping and targeted (species specific) poisoning programmes undertaken in partnership with hunting organisations.

Because of the risks associated with the build-up of resistance to 1080 among target populations (as has been reported with rabbits in Australia) it would be prudent to regulate 1080 use to minimise this possibility. As such, increasing the use of other methods for possum control would serve this end as well as a human health precaution.

Once the above research has been completed it will be necessary to:

6. Re-evaluate the calculation of the MAV for 1080 on the basis of the findings of this research and all of the science readily available on acute and chronic toxicity internationally.

Further research should also be conducted as part of the on-going relationship between research, regulation and management for 1080. In particular, two areas of supplementary research warrant investigation:

7. Evaluate the food web effects of fluoride ion release into soil and water as a result of 1080 breakdown; and,
8. Evaluate the effects of on-going 1080 use on the broader ecological functionality of habitats where it is used, including
    a. Potential impacts on food webs;
    b. Chronic toxicity (wildlife), with particular reference to long-term fertility and fecundity studies of native wildlife populations at concentrations below the known or estimated LD_{50} for these species; and,
    c. Chronic toxicity (human), with particular reference to potential adverse health effects other than endocrine disruption at concentrations at and below the current MAV.

It is recommended that the Environmental Risk Management Authority take account of all currently available science on 1080 when it forms recommendations on regulatory issues relating to this chemical. Taking account of available scientific evidence relating to 1080 use

will also mean considering the risks of not continuing with the current regime for the use of 1080. Such risks include:

- The potential loss of conservation management (and bovine Tb control) gains made in recent years as a result of 1080 use (should 1080 use be more heavily restricted as a result of the EMA review); and
- The risks associated with the employment of any alternative methods of possum control (e.g. the risks associated with the use of other poisons).

Introduction

A visit to the Department of Conservation's (DOC) Lake Rotoiti Mainland Island Project at Nelson Lakes provides an inspirational experience in what is possible in conservation management in accessible parts of the New Zealand mainland. The success of this on-going effort is centred on the ability of DOC to control pests in a well-defined area and monitor the management gains that result. Such gains include a dramatic decrease in pest and predator numbers within the control area enabling an increase in native bird numbers (e.g. South Island robin), and recovery of native plant species (Nugent et al 2002) normally browsed by introduced animals such as the possum (e.g. kohekohe). To a large degree this success has been underpinned by the conservation management benefits associated with 1080 poison (sodium monofluoroacetate), which along side other poisons, has enabled the comprehensive (and cost-effective) control of pests in this area.

From the Mt Robert Ridge overlooking the Lake Rotoiti Mainland Island one can gain a view northwards to the mountains of Kahurangi National Park and the Golden Bay area. In January 2003 a community activist in Golden Bay was convicted of burglary and wilful damage for sabotaging a bulk supply of 1080 poison (sodium monofluoroacetate) owned by DOC. The poison was to be used for a pest control operation to control the brush tail possum (an introduced pest marsupial native to Australia), which poses a considerable threat to native vegetation and wildlife in parks and reserves. The Department of Conservation argues that 1080 poison is the most cost effective and efficient form of pest control for this (and other pest) mammalian species and that the conservation benefits of this poison are substantial. The poison is also used in agriculture to control bovine tuberculosis (spread by possums). The above attack cost DOC $12,000 according to its local area manager (Shuttleworth 2003). In defence the activist said that he was trying to protect his community from a "weapon of mass destruction," (ibid) pointing to the threat to domestic water supplies of 1080 contamination.

This political and media drama is merely one episode in a much larger controversy in New Zealand over the widespread use of 1080 poison as a conservation management tool. A search of web-based media publications and print media archives has revealed a broad selection of stories focusing on community concerns relating to 1080 use. They range from fire bombings of Department of Conservation vehicles, to protests, petitions and conferences. In short, a substantial anti-1080 lobby has developed in New Zealand. The concerns focus primarily on

human health risk (acute and chronic health risks), and the non-target effects of the poison in the field. In terms of the latter, the recreational hunting fraternity has become very vocal with complaints that deer populations have been decimated as a result of aerial 1080 applications in hunting areas. Another concern for hunters is the risk to their dogs, which are particularly susceptible to secondary poisoning.

As a consequence of the build up of community disquiet over 1080 use in recent years, the Environmental Risk Management Authority (ERMA) decided in March 2002 that there were sufficient grounds for a full scientific review of the poison (ERMA 2002)[1]. This will be[2] the first official review of the poison since its introduction for pest control in 1964. The review will enable an assessment of the risks, costs, and benefits of 1080 under the provisions of the Hazardous Substances and New Organisms (HSNO) Act (1996), and provide an opportunity for the wider public to raise their concerns.[3] This paper was prepared in response to this review as a contribution to the debate (i.e. as an independent public submission).[4] The central research questions for this analysis are "what can the peer-reviewed scientific literature tell us about the health risks associated with 1080; and, what are the policy implications of this scientific knowledge?"

Science is an integral tool for the setting of regulations relating to public health and environmental protection. Scientific knowledge is not always complete, however, particularly in the complex arena of public health toxicology and the effects of chemicals on biological systems. Where scientific knowledge is incomplete, regulators are compelled to build regulatory bridges over these gaps until they can be filled. One such regulatory bridge is the employment of the precautionary principle which, according to Principle 15 of the 1992 Rio Declaration invites states and regulators to implement cost-effective measures to prevent adverse environmental effects (where there are threats of serious or irreversible damage) even where there is a lack of full scientific certainty (UNEP 1992). A set of issues associated with

[1] In Australia a review of 1080 is currently underway to ensure there is minimal non-target impact and minimal environmental impact. The results of this review are likely to be published in 2004.
[2] At the time of writing (early 2003) the ERMA review had not officially commenced but had been publicly announced.
[3] The purpose of the HSNO Act (1996) is to "protect the environment and the health and safety of people and communities, by preventing the adverse effects of hazardous substances and new organisms" (section 4).
[4] The author regards himself as a conservationist who is acutely aware of the importance of pest control in conserving functional ecosystems (as habitats) that provide for the protection of New Zealand's unique contribution to global biodiversity. He is also aware that pest control comes at a price and that this price needs to fit within the budget of agencies charged with the responsibility to undertake such management. The author is also an environmental health advocate who is concerned for the appropriate management of hazardous substances in the protection of public health.

science, its relationship with regulatory structures, and the theme of precaution is the fact that (a) Scientists do not always agree with each other (there are a variety of different theoretical standpoints and degrees of understanding among scientists in any scientific discipline); (b) There is commonly a lag time between scientific understanding and the incorporation of this understanding into regulations (sometimes regulations never catch up with science); (c) New scientific consensus is commonly preceded by a period where evidence of causal mechanisms build up ahead of conclusive research findings that are capable of verifying such causal mechanisms (this evidence may point to significant potential risks that are relevant to regulatory structures); and, (d) The role of government is to protect the public good whilst also protecting private and other economic interests. For example, section 9 of the (Methodology) Order 1998 of the Hazardous Substances and New Organisms (HSNO) Act (1996) instructs ERMA to "recognise risks, costs, benefits, and other impacts" when registering pesticides. As such, this regulatory authority is responsible for weighing risks against benefits of toxic substances, rather than purely protecting the public good from toxins. As such, ERMA (by definition) is not an advocate for public or environmental health per se, but instead an advocate for balancing risks and benefits of potential hazards. Each of these will be taken into account in the following analysis.

The following sections look into the history of scientific knowledge of the toxin, and its use as a mammalian pesticide. It then establishes a framework for assessing environmental health issues relating to the toxin. This is followed by a summary of scientific understanding of the acute and chronic toxicological effects of the toxin, including research on its effects on non-target organisms, and rates of degradation. The regulatory and policy implications of this knowledge are discussed, which lead to a set of policy recommendations

Naturally Occurring Toxin

Sodium monofluoroacetate is a naturally occurring toxin found in a number of different plant species that may have developed this compound as a chemically mediated defence strategy against browsing animals (Twigg et al 1996). This has led to varying degrees of tolerance among certain herbivores and carnivores preying on tolerant herbivores (King et al 1996; Martin and Twigg 2002). It was first isolated as the toxic component of the African plant *Dichapetalum cymosum* in 1944 and was the first organofluorine compound known to occur naturally (Twigg op cit.). Several other species of this same genus have since been discovered to contain the toxin (Meyer 1994), as well as a South American plant *Palicourea marcgravii* (de-Moraes-Moreau et al 1995), and forty one plant species of legume in Australia (Twigg 1994). de-Moraes-Moreau et al op. cit. showed that sodium monofluoroacetate was present in the water soluble fraction of *Palicourea marcgravii* leaves that had caused deaths in cattle in Brazil.

The manufactured compound '1080' (first synthesised in 1896 in Belgium) has been shown to be chemically identical to the naturally occurring sodium monofluoroacetate, and also exhibits identical symptoms of poisoning in animals (Eason et al 1999). It was first recorded as toxic in the US in 1934, and thereafter patented as a rodenticide in the late 1930s (Rammell and Fleming 1978). It was developed as a pest control agent through the 1940s and 1950s and was used primarily for the control of coyotes (Fagerstone et al 1994). In 1972 the US EPA banned the use of 1080 for predator control except for its use in livestock protection collars (LPC), designed to kill coyotes when they bite the neck of a lamb or kid goat. At that time most of 1080 use was for rodent control and this was not affected by the ban. Subsequently, all rodenticide registrations for 1080 were cancelled in 1990 (Fagerstone et al 1994), leaving the LPC as the only registered form of the pesticide in the United States. The only registration for LPC use (EPA Reg. No. 56228-22) is held by the Animal and Plant Health Protection Service of the US Department of Agriculture (APHIS).

Compound 1080 was first imported into New Zealand in 1954 for the control of rabbits (Rammell and Fleming 1978). It has since become a key pest management tool for the control of brush tail possums and is commonly dispensed in the form of cereal-based pellets and carrot baits, dropped by air, or dispersed by hand. Since 1080 was de-registered in the US for rodenticides up to 90% of world production is now imported to New Zealand according to media reports (Evening Post 2002; The Timaru Herald 2002). An estimated $27 million was

spent in the 1993/4 season on possum control with 1080 being the primary tool for this task, employing 5,000 tonnes of 1080 carrot bait and 1,200 tonnes of 1080 cereal bait (Livingstone 1994). In the 2001/2 year, Animal Control Products produced 3023 kg of 1080, of which 2271 kg was used by the Animal Health Board and 581.30 kg used by the Department of Conservation (Table 1.; Figures 1. and 2.).

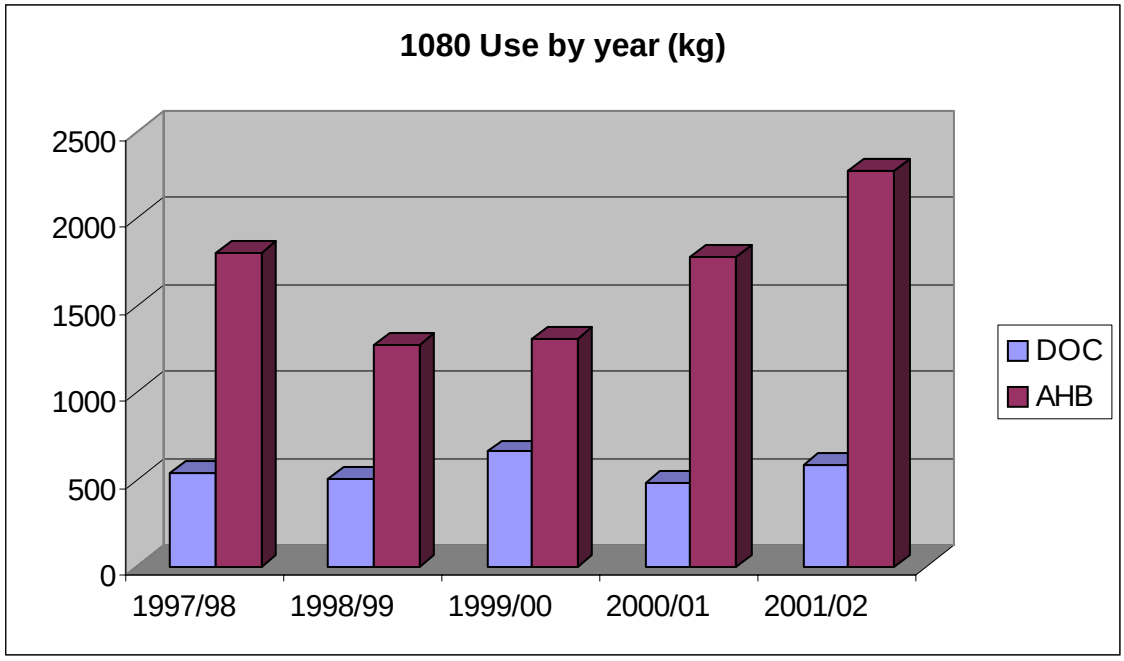
Table 1. 1080 Production and use (kg) by different agencies.

Year	ACP (Production)	DOC (use)	AHB (use)	Other users
1996/97		378.19		
1997/98	2532	534.08	1798	199.92
1998/99	1915	504.12	1270	140.88
1999/00	2111	658.21	1308	144.79
2000/01	2455	481.16	1777	196.84
2001/02	3023	581.30	2271	170.60

(Source: Parliamentary Questions for written answer No. 012822, 012824, 12823 November 2002).

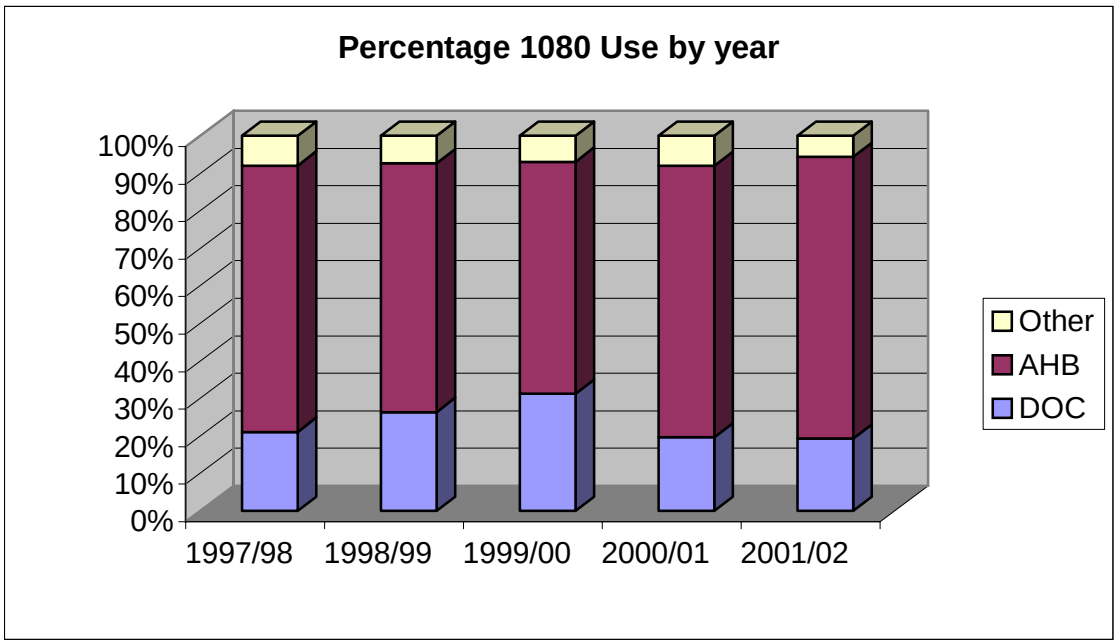
DOC - Department of Conservation
AHB - Animal Health Board
ACP - Animal Control Products

Figure 1. 1080 Use by year (kg).
(Source: Parliamentary Questions for written answer No. 012822, 012824, 12823 November 2002)



As of 2002 $53 million was being spent annually controlling possums and other bovine Tb disease vectors over 8.5 million ha of land. In addition to this $21 million is being spent annually on controlling possum and other mammalian pests on 770,000 ha of publicly owned conservation land. $15 million is spent annually on the possum control component of regional pest management strategies.[5]

Figure 2. Percentage 1080 use by agency.
(Source: Parliamentary Questions for written answer No. 012822, 012824, 12823 November 2002).



Science, Evidence and Policy

In order to make an objective assessment of the health risks of a toxin one needs to consider:

1. Empirical evidence of adverse health effects (where there is scientific consensus).
2. Explanations of the biological mechanism associated with adverse health effects.
3. Empirical evidence of potential adverse health effects (where scientific consensus is currently lacking).
4. Explanations of the biological mechanism for any potential adverse health effect.

Where there is substantial data and scientific consensus on points 1, and 2 above, regulations commonly (but not always) follow as a protection from known risks. Where regulations do

not follow in spite of scientific consensus we simply have a case of (what is often a politically normal) lag time between scientific knowledge and the translation of such knowledge into policy and law. Points 3, and 4 above, on the other hand, are normal components in any (potential) shift in scientific consensus. If both evidence, and credible scientific explanations for any potential health effects are lacking then no shift in scientific consensus is likely and no shift in regulations would be scientifically warranted.

To make a scientifically robust assessment of the established and potential health risks associated 1080 it is also important to consider the various ways in which toxic compounds can affect living systems. These include acute and chronic health effects, exposure pathways, dose response variations, persistence in the environment, and movement pathways for the chemical, variations in vulnerability to the toxin, and potential effects on non-human organisms.

Acute Toxicity

The toxicity of chemical poisons can be understood in terms of short term (acute) and long-term (chronic) toxicity (Corvalan et al 2000). In turn, the severity of toxic effects (in both short and long term toxicity) ranges from minor irritation to death. An example of chronic toxicity leading to death can be seen in arsenic contamination of water, where low doses over a long sustained period can lead to cancer (Corvalan et al op. cit.). Some pollutants have a threshold below which no adverse health effect occurs or is evident. Others have no, or at least very low safety thresholds and can cause adverse health effects even at extremely low doses (e.g. some genotoxins – i.e. those that cause DNA damage, and can lead to malignant tumors, but these would tend to fall under the heading of chronic toxicity)[6] (see Bickham and Smolen 1994).

The vast majority of 1080 toxicity studies available in the published literature focus on acute toxicity in animals, with an emphasis on severe reactions. Its acute/severe toxicity in humans is also documented although for obvious ethical reasons there are no experimental data relating to dose response relationships. The current scientific consensus is that sodium monofluoroacetate is a deadly human poison. According to the EPA (1987) "This material is super toxic. The probable oral lethal dose in humans is less than 5 mg/kg, or a taste (less than

[5] Figures from the National Science Strategy Committee for Possum Bovine TB Control. Draft, June 2002.

7 drops) for a 150-lb. person." Exposure symptoms include nausea, blurred vision, numbness, low blood pressure, hyperactivity, excessive salivation, respiratory depression or arrest, cyanosis (blue tint to the skin and mucous membranes), vomiting, diarrhoea, hyperactive behaviour, convulsions, coma, ventricular fibrillation and heart failure. These are normally observed within 30 minutes of exposure, although evidence of severe effects may not be apparent for up to 20 hours following exposure (EPA 1987). The pathway to toxicity is by ingestion inhalation, dermal absorption, eye and skin contact.

Once fluoracetate has been absorbed or ingested it is converted to fluorocitrate in the body (Peters and Wakelin 1953), which is the toxic form of the chemical, where it accumulates in the foetus and certain organs such as the heart, lungs, kidneys, liver, and testes (McTaggart 1970; Sullivan et al 1979; Twgg et al 1988). Fluorocitrate, in turn, inhibits the tricarboxylic acid cycle in the Krebs cycle (Schofl et al 2000; Eason 1997) by competitively inhibiting the enzyme aconitate hydratase (Ataria et al 2000). Here, citrate would normally be converted to aconitate, but the blocking of this leads to the (toxic) accumulation of citrate. As a result, energy production (a key function of the Krebs cycle) falls, which in turn leads to cellular energy deprivation and death (Twigg 1994; Rammell and Fleming 1978). The accumulation of citric acid causes violent convulsions and death from cardiac or respiratory failure (Chi et al 1999).

The few human studies on the acute toxicity of 1080 available in the scientific literature provide little detail on its human effects. A rabbiter who was repeatedly exposed to 1080 developed kidney failure and showed evidence of other organ damage (Parkin et al 1977). Other human studies have arisen from poisoning cases in hospitals. Chi et al (1996) undertook a retrospective study of 38 cases of 1080 poisoning at National Cheng Kung University Hospital and found that the early onset of metabolic acidosis, and increased serum creatinine were associated with poor long term survival in humans. Chi (op. cit.) and Chi et al (1999) found that hypotension is one of the most important predictors of mortality in 1080 poisoning. Robinson et al (2002) studied the symptomatic response in a 47-year-old male who survived 1080 poisoning, and observed the patient to respond only to noxious stimuli after 34 hours and, was non-responsive to painful stimuli at 48 hours following ingestion.

[6] DNA damage in itself is not sufficient to cause toxicity in all cases, because DNA is also capable of repairing itself (see Wood et al 2001).

Animal Studies

Studies on the metabolism of sodium monofluoroacetate on animals have shown that unmetabolised fluoroacetate and at least seven breakdown products are excreted in the urine (Hagan et al 1950; Sykes et al 1987; Eason et al 1994a). Symptoms such as vomiting, nausea, heart and respiratory failure are usually apparent following a lag period of 0.5 to 3 hours (Eason et al 1994a; Twigg 1994). Herbivores receiving lethal doses tend to respond to intoxication with cardiac failure whereas carnivores tend to experience central nervous system dysfunction and eventually die of respiratory failure (Egeheze and Oehme 1979). The elimination half life for near lethal doses is 11 hours in sheep, 2 hours in mice, 1 hour in rabbits, and 5 hours in goats (Eason et al 1994). Animal studies in the US have shown 1080 to be absorbed through the skin, which has important implications for safety procedures, and regulations for bait handlers and manufacturers (Fagerstone et al 1994).

Toxicology studies conducted by APHIS looked at the effects of absorption of 1080 through the skin and eyes of rabbits. The results of the dermal toxicity tests demonstrated an LD_{50}[7] of 324 mg kg^{-1}, and allowed it to be classified as a Category IV skin irritant. The study of the effects of 1080 on the eyes of rabbits treated with a 1% solution showed only slight conjunctival irritation enabling it to be classified as a Category III eye irritant (Fagerstone et al 1994). Three aquatic toxicity studies were undertaken by APHIS in the early 1990s. One looked into the acute toxicity of variable 1080 concentrations for bluegill sunfish (*Lepomis macrochirus*) where no lethal or sub-lethal adverse effects were observed at any concentration. Another looked into the acute toxicity of 1080 on rainbow trout (*Oncorhynchus mykiss*) using the same test conditions, and found after 96 hours, mortality ranging from 10% (at 23 mg l^{-1}) through 50% to 90% depending on concentration (at concentrations between 39 and 170 mg l^{-1}). The third study looked into the acute toxicity of 1080 on *Daphnia magna*, a freshwater invertebrate. After 48 hours 70 and 100% immobilisation was observed in daphnids exposed to concentrations of 350 and 980 mg l^{-1} respectively (Fagerstone op. cit.). Eason (1997) reviewed experimental and regulatory toxicology studies on 1080 and mentions a study cited in Ramell and Fleming (1978) where fingerling trout were subjected to 1080 concentrations of 500 mg/l and 1000 mg/l without any visible effect on the fish. He also noted that force-feeding pellets containing approximately 4 mg and 8 mg of 1080 to fingerling and adult trout had no visible effect.

[7] The LD_{50} is also known as the median lethal dose. It is the dose of a substance that will kill 50% of a sample population (McIlroy 1994).

Secondary Poisoning

The issue of persistence of 1080 is also relevant to secondary poisoning in the wake of pest control operations with risks associated with meat consumption (humans consuming domestic animals exposed to 1080) and animal carcasses being eaten by scavenging species (e.g. hunting dogs). A study by Meenken and Booth (1997) assessed the risk of secondary poisoning of 1080 in dogs and found that possum carcasses collected after a possum control operation contained concentrations of 1080 high enough to pose a serious hazard to dogs, even up to 75 days after poisoning. There are also studies that observed no ill effects on non-target animals (e.g. ferrets fed prairie dogs that had died from 1080 poisoning) (Hugghins et al 1988).

Other studies into non-target effects have looked into the effects of 1080 in the secondary poisoning of predators, and the potential for 1080 and its breakdown products to persist in meat (e.g. Murphy et al 1999; Hugghins et al 1988; Allender 1990; Savarie et al 1994; Gooneratne et al 1994; Meenken and Booth 1997; Gillies and Pierce 1999; Murphy et al 1999; Gooneratne et al 1995; Eason et al 1994b). In most of these studies the findings showed no evidence for concern for acute adverse effects on non-target species, apart from the effects of secondary poisoning of predators eating carcasses of animals killed by lethal doses of 1080 (Meenken and Booth 1997). For example, stoats can also suffer mortality from secondary poisoning following control operations for possums (Murphy et al 1999), and from taking baits directly (Moller et al 1996).

The location of the poison in carcasses has been shown to be higher in plasma compared with muscle and organ tissue (Gooneratne et al 1995). This tendency of 1080 concentrations to be highest in blood plasma was also shown in a study that looked at the potential for human secondary poisoning. Eason et al (1994b) administered 1080 orally to sheep and goats at a dose of 0.1 mg kg^{-1} body weight to assess the risk to humans of eating meat contaminated with 1080. Poison residues were measured in blood, muscle, kidney and liver. The plasma elimination half-life of 1080 was 10.8 hours in sheep and 5.4 hours in goats. The concentrations of the poison in plasma were significantly higher than in other tissues. Concentrations of 1080 in sheep tissues dropped to <0.002 to 0.008 mg kg^{-1} after 96 hours. They conclude that human secondary poisoning from meat contaminated with 1080 is highly unlikely due to the elimination of the toxin from tissues and the fact that livestock are usually removed from areas near 1080 applications. A minimum withholding period of 5 days is

currently recommended for stock that are suspected to have come into contact with 1080 even when no deaths have been observed. Longer periods of quarantine (prior to slaughter) are recommended when a livestock death has been observed (Eason et al 1994b). Animals have variable sensitivity to 1080 depending on the species, which means that lethal doses will vary and some species are more vulnerable than others. Dogs for example are known to be far more sensitive to the toxin than many other mammals (Eason 1997; Meenken and Booth 1997), which is of particular concern in relation to secondary poisoning when a dog eats a carcass of a poisoned animal. Limited research on the development of an antidote for 1080 has been conducted (e.g. Omara and Sisodia 1990; Gorniak et al 1994; Cook et al 2001).

In regions where fluoroacetate occurs naturally in plants some animal species have developed a tolerance to the compound. Where animals have developed a resistance to sodium monofluoroacetate (e.g. in parts of Australia) the degree of tolerance will tend to be a function of how long they have lived in association with such plants, the degree of reliance on these plants as a food source, their degree of mobility as a species, and the size of their home range (Twigg 1994; King et al 1996; Martin and Twigg 2002). Herbivores tend to have the highest degree of tolerance, followed by omnivores, followed by carnivores. This tolerance has also been observed in pest species targeted with 1080 poison campaigns. According to Twigg (News in Science 2002) the LD_{50} for rabbits was about 0.45 mg kg^{-1} in 1979, but had increased to 1.1 mg kg^{-1}, and that the tolerance was greatest in areas where the poison has been used intensively (ibid.).

Effects on Non-Target Wildlife

Numerous field studies have been conducted on the effects of 1080 on non-target wildlife populations in New Zealand and Australia. Some of these have been undertaken out of concern that rare, endangered or beneficial animals may be adversely affected by the application of 1080 into the environment (Morgan 1999; Hartley et al 1999; Spurr and Drew 1999; Booth and Wickstrom 1999; Powlesand et al 1999; Spurr 1994; Lloyd and McQueen 2000, 2002; Robertson et al 1999; Powlesland et al 2000; McIlroy 1981a; 1981b; 1982a; 1982b; 1983; 1984; 1986; 1994; McIlroy and Gifford 1991; McIlroy et al 1985; McIlroy et al 1986; Perfect 1996). Spurr (1994) reported that dead birds were recorded from 15 possum control operations undertaken between 1978 and 1993. Associated with these operations 34 blackbirds, 15 tomtits, 14 chaffinches, 9 whiteheads, 4 moreporks, 3 fantails, 1 grey warbler, 1 robin, 1 tui, and 1 magpie were found dead following 1080 drops. Significantly more dead

birds were found following carrot based bait drops compared with cereal based baits. While monitoring of common bird species showed that there was no (short term) detrimental effects on these populations, Spurr (op.cit.) did point out that there had (until that time) been less adequate monitoring of the effects of 1080 bait drops on less common native bird species (e.g. kiwi, kaka, kakariki and kokako).

Since then a number of studies have been carried out on less common species and their susceptibility to 1080 poisoning. Robertson et al (1999) studied adult brown kiwi (*Aapteryx mantelli*) three months after being exposed to a 1080 poisoning operation in Northland. They concluded that possum control operations using green-dyed and cinnamon-lured pollard or jam 1080 baits posed a very low mortality risk to kiwi from either primary, secondary poisoning or starvation associated with a loss of large invertebrates. Powlesland et al (2000) investigated the mortality rates of tomtits (*Petroica macrocephala toitoi*) following aerial 1080 poisoning for possum control in Pureora Forest Park. They found that following an August 1997 poisoning operation 11 of the original 14 tomtits "disappeared" from the treatment area. Because no tomtit carcasses were recovered it is not known whether the birds died from 1080 poisoning, died from other factors, or left the area. No tomtits disappeared from either the control or treatment areas in a 1080 control operation a year later (August 1998). They conclude that further research on this topic is warranted before our understanding of tomtit mortality can be verified. An earlier study by Powlesland et al (1999) on North Island robins (*Petroica australis longipes*) following an aerial 1080 poisoning operation in 1996 showed a 43% mortality of territorial birds (banded and unbanded) or a 55% mortality of banded birds. There was no robin mortality in the control area. A subsequent aerial control operation in September 1997 showed 8.6% and 9.7% mortality (using the same criteria as above). The key difference between these two operations was that the latter had far less chaff and fine particles[8] of bait dispersed in the aerial operation. Following both control operations robin breeding success was significantly higher than immediately prior to the 1080 control of possums, and as such the authors concluded that the benefits of the 1080 control operation for the robin populations outweighed any short term mortality costs.

The mortality of short tailed bats was measured in the field following an aerial 1080 possum control operation in the central North Island (Lloyd and McQueen 2002). Mortality rates were

[8] Ataria et al (2000) noted that non-target bird mortality following large-scale 1080 poisoning operations tends to be highest when using undyed, raspberry-lured, unscreened carrot bait and had a high percentage of small fragments.

measured before and after the 1080 drop. None of the 269 bats (held in captivity for 48 hours) showed any signs of 1080 poisoning, but they concluded that more information is needed before conclusive generalisations can be made concerning 1080 risk to these bats. In a study on native ants (*Huberia striata*) Booth and Wickstrom (1999) found acute mortality to be significantly greater in ants exposed to 1080 baits in the laboratory compared with those in a control study. The LD_{50} at 48 hours was 42 mg kg^{-1} (comparable to results found when toxicity experiments were conducted on the native weta – a large flightless forest dwelling cricket). Spurr and Drew (1999) studied invertebrates and 1080 baits in the field. They found that only a few of the invertebrates likely to be found in the forest litter were actually on the baits, and predicted that aerial vertebrate pest control operations were "unlikely to have any long term deleterious impacts on invertebrate populations" (p.172), although this prediction "needs verifying" (ibid.).

Ecological research into 1080 and its effects on native wildlife have tended to focus on single species population studies. One of the difficulties with broader community or ecosystem studies is their overwhelming complexity. If such studies are not conducted, however, the accolade of "the most researched toxin in New Zealand" may be difficult to sustain due to the relatively narrow ecological and environmental scope of these studies. Innes and Barker (1999) looked into the ecological consequences of mammalian pesticide use in New Zealand and concluded that not using such pesticides would probably have a greater detrimental effect on these ecosystems than any side effects of their use, but that such a suggestion "badly needs exploration by researchers" (ibid.:121).

Chronic Toxicity

In the majority of studies (mentioned above) on the risks to non-target animals the focus has centred on acute and severe toxicological effects. As such, they are limited in their scope in terms of the total potential toxicological effects of 1080 poison on animal biology and demography. To cite one example, Perfect (1996) studied the effects of 1080 on New Zealand native frog (*Leiopelma archeyi* and *L. hochstetteri*) populations. The study concluded that a possum control operation in June 1995 did not cause a decline in the monitored *L. archeyi* populations (low statistical test-power for the *L. hochstetteri* population did not enable conclusive results). If, however, 1080 were capable of contributing to a chronic toxicological effect that impacted on the longer tem fecundity of those frog populations (e.g. by altering fertility rates), then short term population monitoring for mortality rates would not be capable

of testing this. The same can be said of the various other native wildlife population monitoring studies mentioned above that focused on short term mortality impacts for these species (e.g. Booth and Wickstrom 1999; Lloyd and McQueen 2000, 2002; Powlesland et al 1999, 2000; Robertson et al 1999; Spurr 1994; Spurr and Drew 1999).

To adequately assess any chronic risks to non-target organisms (including humans) it is necessary to scrutinise any evidence of chronic effects, determine a biological mechanism associated with different forms of chronic effect, and evaluate what is known about the persistence and degradation rates of the toxin. If 1080 were capable of disrupting the reproductive system of animals for example, then chronic effects could lead to adverse effects on a population in the longer term. This can occur even if the degradation rate of the toxin is rapid, because the *effects* of short term exposure can sometimes be long term (e.g. where short-term exposure of a pregnant adult female to a toxin contributes to the infertility of the offspring. Evidence of this effect will not be apparent until the offspring attempt to breed).

In traditional public health toxicology, the relationship between a toxin and an observed increase in mortality has tended to dominate environmental health assessments. Cancer rates and deaths attributable to cancer are a good example. As pointed out by Corvalan et al (2000:89) however, it is not always easy to link mortality data with even well known acute toxins in population studies. The link between tobacco and cancer is a case in point, where, even though the biological mechanism of toxicity was well established, and a well understood source of a toxin, it was extremely difficult to "prove" that smoking caused cancer in public health regulatory debates. In most situations of environmental toxicology "only a small subset of a population experiences high levels of exposure, and the doses received by the general population are so low that only vulnerable high-risk groups are severely affected" (ibid.:89). An editorial of the Lancet in 1992 asserted that relatively few studies have shown clear associations between environmental pollutants and actual increases in death rates (Lancet 1992). Accordingly, mortality data for any population (whether human or wildlife) are a very insensitive measure of toxicity for environmental contaminants, and yet these have formed the basis of many (if not most) regulatory standards for environmental toxins. This (general) relationship between chronic toxicity of environmental contaminants and long-term reproductive success and population viability has been documented in a growing number of studies focusing on the effects of endocrine disrupting chemicals. Examples include the decline in wildlife reproductive success (e.g. in fish-eating bird populations) in the Great Lakes region (Fry and Toone 1981; Fry et al 1987; Kubiak et al 1989; Gilbertson et al 1991;

Giesy et al 1994; Fry 1995; Tryphonas 1995), reproductive disruptions from environmental contaminants in alligator and panther populations in Florida (Woodward et al 1993; Guillette et al 1995; Crain et al 1997; Facemire et al 1995).

Studies on the chronic toxicology of 1080 are beginning to be conducted, although there seems to be many gaps in current knowledge in this area. For example, Ataria et al (2000) studied the sub-lethal effects of 1080 on adult male mallard ducks (*Anas platyrynchos*), and found that skeletal muscle was a target organ in this species for 1080 damage. They suggest that this may be due to the high-energy requirements of avian muscle tissue. They found that changes in biochemical biomarkers were observed at doses equivalent to the consumption of less that one half of a single 1080 bait pellet. There was no indication in the paper that there was any examination of the testes of the birds – a known target organ for 1080 toxicity in other vertebrates including birds (see below). They do, however, suggest (citing Eason et al 1999 and O'Connor et al 1999) that histopathological damage to target organs may occur at extremely low doses, and that monitoring of sub-lethal effects in individuals and populations is needed in order to ensure that there are no long-term adverse effects on non-target wildlife.

Eason et al (1999) reviewed recent research into the chronic toxicology of 1080 and organised these studies into the following categories: mutagenecity, developmental toxicity, and teratogenic potential (birth defects). Three studies into the mutagenicity (genotoxicity) of 1080 were reviewed (Ames et al 1975; Blazak et al 1989; Hoddle et al 1983) each showing no mutagenicity observed at any dose level. Developmental toxicity studies included those conducted by Eason et al (1999) and were split into two – a pilot study and a main study. In the pilot study five female rats per treatment group were dosed orally with 1080 at 0, 0.05, 0.1, 0.5, or 1.0 mg kg^{-1} day^{-1} from day 6 through day 17 of gestation. No gross uterine effects were observed at any dose, although maternal weight loss, 60% maternal mortality and decreased litter size were observed at 1.0 mg kg^{-1} day^{-1}. The foetuses were not examined.

In the main developmental study 26 female rats per treatment group were dosed orally with 1080 at 0, 0.1, 0.33. or 0.75 mg kg^{-1} day^{-1}. Results showed no maternal mortality at any dose, but did show decreased maternal body weight, decreased weight gain, and decreased food consumption at 0.75 mg kg^{-1} day^{-1}. No soft tissue abnormalities were observed in foetuses at any dose. Foetal skeletal abnormalities were observed at doses of 0.33 and 0.75 mg kg^{-1} day^{-1}. Abnormalities in forelimb development were observed in foetuses at the same dose. Bent ribs were observed at doses of 0.33 and 0.75 mg kg^{-1} day^{-1}, and unossified sternebrae were

observed at the 0.75 mg kg^{-1} day^{-1} dose. Although the study did not look into the effects on foetuses beyond gross observable effects, the authors concluded that the No-Observable-Effects-Level (NOEL) for maternal toxicity was 0.33 mg kg^{-1} day^{-1}, and the NOEL for developmental toxicity for rats subjected to 1080 is 0.1 mg kg^{-1} day^{-1}. Accordingly they conclude that 1080 is teratogenic in rats at a dose of 0.75 mg kg^{-1} day^{-1}. The above study is used by the New Zealand Ministry of Health as the basis for deriving the Maximum Acceptable Level (MAV) for 1080, which is set at 0.0035 mg l^{-1} (which includes an uncertainty factor of 500). Given that teratogens are capable of affecting the development of foetuses (e.g. affecting their fertility once they become adults) without giving rise to gross observable abnormalities, this study cannot be considered conclusive. If, for example, 1080 were capable of endocrine disruption at low concentrations (at or below the doses administered in the above study), then no gross observable effects would necessarily be expected in either adult females or their litters. For example, Turck et al (1998) studied developmental toxicity of 1080 on rats and concluded that there was no evidence of developmental toxicity among pregnant rats or their litters. Like the Eason et al (1999) study, the experiment did not adequately test the potential teratological symptoms of 1080 on these rats, but instead focused on acute and gross observable symptoms such as foetal body weight, external foetal abnormalities, maternal mortality and body weight.

Other experimental evidence exists that links subacute 1080 poisoning with reproductive health in animals. The EPA conducted a study on the low level toxicity of sodium monofluoroacetate in Sprague-Dawley rats where the animals were administered doses of 0, 0.05, 0.20 and 0.50 mg/kg/day for 13 weeks (EPA 1988). The study findings included increased sodium flurocitrate (1080 breakdown product), increased heart weight, decreased testes weight and accompanying microscopic lesions of the testes, and central nervous system disruptions. Other studies have shown damage to seminiferous tubules in rat and skink testes (Atzert 1971; Sullivan et al 1979; Twigg et al 1988), and impaired reproduction in mink (Hornshaw et al 1986).

According to Twigg (1994) fluoroacetate is known to cause a reduction in animal fertility and points out that both acute and chronic effects need to be taken seriously, particularly because these effects can lead to selection pressures that disadvantage the populations in question (e.g. they could lead to population decline or local extinctions). Environmental estrogens (e.g. phytoestrogens) consumed in high doses or at critical stages of development in mammals, for example, can lead to reproductive tract and infertility disorders (Adams 1995; Strauss et al

1998; Tou et al 1999). Doses of fluoroacetate significantly lower than the LD_{50} (minimum lethal dose) have shown to interfere with the reproduction system in rats, skinks, starlings, mink and ferrets (Mazzanti et al 1965; Sullivan et al 1979; Twigg et al 1988; Balcomb et al 1983; Hornshaw et al 1986). In a study on albino rats Mazzanti op. cit. found that 1080 gave rise to lesions on the testes consisting of regressive modifications of the seminifierous tubules which caused damage to spermatogonia. They concluded that the action of 1080 is similar to the effects of fluoroacetamide.

An unpublished study cited in Twigg (1994) found that skinks challenged with sublethal doses of 1080 at 23% of the LD_{50} over 4 consecutive days caused a regression in the germinal epithelium in the testes. Twigg et al (1988) administered 1080 to skinks (*Tiliqua rigosa*) tolerant to naturally occurring fluoroacetate, and found that low levels of 1080 at 12.5% of the LD_{50} over 15 days caused a reduction in plasma testosterone concentration which may affect spermatogenesis in males of the species. They pointed out that the relationship between fluoroacetate dose and fertility was unclear, particularly as the dose response was not tested during the entire breeding season (where fluctuations in testosterone coincide with different stages in the breeding cycle). Sullivan et al (1979) found that testicular weight decreased in rats receiving 20 or 6 p.p.m of fluoroacetate, and found morphological damage to the testes of all rats treated in their experiment. At higher concentrations (e.g. 20 and 6p.p.m) damage progressed to marked seminiferous atrophy. Regeneration of the seminiferous tubules was not complete by Day 21 in these rats. Balcomb et al (1983) studied the acute and sub-lethal effects of 1080 on starlings (*Sturnus vulgaris*) with a particular emphasis on testicular morphology. They noted that although there was a 14% reduction in testicular weight development in starlings fed 1080 compared with control birds, this difference was not statistically significant. They concluded that there is likely to be a substantial difference in sensitivity between birds and mammals in terms of the relationship between 1080 dose and its effect on testicular development. According to the Office of Environmental Health Hazard Assessment, of the State of California Environmental Protection Agency sodium fluoroacetate (1080) is a male reproductive toxin (EPA 2003).

Possibilities of Endocrine Disruption

Endocrine disrupting compounds (whether naturally occurring or synthetic), are capable of affecting the balance of normal hormonal functions. A common hormone disrupted by environmental endocrine disrupters (EEDs) is estrogen. There are a number of known

estrogen mimics and disrupters including dioxin, PCBs, and certain plastics (xenoestrogens), as well as those produced by plants (phytoestrogens). Hormones disrupted by EEDs are not restricted to estrogens, and are known to include other steroid hormones, adrenal hormones, pituitary and thyroid hormones (Colborn et al 1993). According to the EPA an endocrine disrupter is *"an exogenous agent that interferes with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis, reproduction, development, and/or behaviour"* (EPA 1997). Such chemicals can disrupt hormonal activity through mimicry (McLachlan 1993), blocking hormone receptors (McLachlan op. cit; Kelce et al 1994, 1995; Gray et al 1994), altering hormone metabolism (Janssen et al 1997), and interrupting hormone control (EPA 1997). EEDs are also suspected of being capable of interrupting cellular Ah receptors[9] (Giesy et al 1994; Safe and Krishnan 1995).

By disrupting reproductive hormones EEDs have the ability to interrupt hormone balances that drive hormone dependent developmental process in animals. Even at extremely low concentrations (e.g. parts per billion and parts per trillion) such chemicals can contribute to significant adverse reproductive effects. These disruptions may not pose too much of a problem to adult animals (as their developmental period is over), but many studies have shown these disruptions to be particularly important in the reproductive cycle. Embryos for instance, respond to hormonal triggers that influence development pathways. If these triggers are disrupted, developmental pathways can be altered.

Research into the influence of EEDs on sex ratios in exposed populations of humans have shed light on the environmental significance of EEDs on reproductive success (Mocarelli et al 1996; James 1997). The sex-linked behavioural characteristics of mice, have shown to be influenced by the levels of estrogen (or estrogen mimics) in the womb (vom Saal and Bronson 1980; vom Saal 1989, 1995). The concentrations of estradiol capable of altering reproductive capacity in rats is as low as thirty five parts per trillion (see vom Saal and Bronson 1980; vom Saal 1989). The feminisation of males and the masculinisation of females are becoming increasingly understood in the science of EEDs. It is already known that estrogenic compounds have contributed to the feminisation of male fish in streams and estuaries in the

[9] An Ah receptor is a cellular gene transcription factor that functions in association with another protein (Arnt) and is associated as a target for dioxin genotoxicity involving alterations in gene expression. See the Endocrine Disruptor Research Inventory for examples of research into EEDs in general, and the role of Ah receptors in particular. <http://endocrine.ei.jrc.it/gedri/pack_edri.All_Page>.

United Kingdom (MAFF 1998; Allen et al 1999a; Allen et al 1999b; Hutchinson et al 1999; BBC 2000).

Endocrine disrupting chemicals capable of altering the sex ratios in a population (rather than causing direct fatalities) can affect the long-term reproductive success of the population as a whole. These disruptions can happen at very low doses (many orders of magnitude lower than the LD_{50}) and yet can have significant longer-term impacts on animal populations. This can occur even when the toxin is not persistent. For example, phytoestrogens (naturally occurring in plants) have been observed to negatively influence the reproductive success of sheep (Bennetts et al 1967; Lightfoot et al 1967; Findlay 1973; Hughes 1988) cattle (Moule et al 1963), quail (Leopold et al 1976) and mice (Leavitt and Wright 1976). It should also be noted that the endocrine system is remarkably similar across great taxonomic divides. Estrogens, for example, influence the development of secondary sex linked characteristics and regulate the female reproductive system in all vertebrates. For this reason the results of animal studies on EEDs cannot be ruled out as inapplicable to humans.

Persistence and Degradation

Toxic substances vary in their rates of degradation, depending on their chemical structure and the availability of conditions that affect degradation rates. In the case of compounds that are biodegradable (e.g. through microbial activity), persistence may be restricted in time, but this can vary in relation to other environmental factors such as temperature. Microbial activity decreases as temperature decreases for example, which means that biodegradable substances may persist for longer periods in the winter and/or cold climates compared with the summer, and/or warmer climates. Persistent synthetic chemicals that have a molecular structure that is new to the environment can be non-biodegradable with degradation rates relating to the molecular breakdown of the chemical. Dioxins for example can take decades to break down chemically.

Studies on 1080 toxicology have shown that this compound breaks down metabolically within animals that have been exposed to the toxin, involving defluorination of fluoroacetate and fluorocitrate (Schaefer and Machleidt 1971; Smith et al 1977; Twigg 1994). Defluorination (detoxification) is also known to occur in plants and bacteria (Twigg 1994). For example, in soils where the toxin does not occur naturally, breakdown is facilitated by several species of bacteria, fungi, and algae (ibid.). In mammals and birds defluorination normally occurs in the

liver, although when concentrations of the toxin are too high for detoxification, poisoning occurs (ibid.).

Numerous studies have also been undertaken to monitor 1080 concentrations in stream water following 1080 control operations (e.g. Meenken and Eason 1995; Parfitt et al 1994; Hamilton and Eason 1994c; Eason et al 1992), in bait dust (Wright et al 2002), in soil (Walker 1994; Parfitt et al 1995; in a landfill (Bowman 1999), and uptake in plants (Olgilvie et al 1998). 1080 has shown to be highly soluble in water and is likely to leach from baits into the environment in the presence of rainfall (the high solubility will also facilitate rapid dilution of the leached toxin). Of concern from an environmental toxicology perspective is the length of time 1080 takes to degrade in streams surface waters, and soils, and the concentrations that may persist (perhaps for a limited period) in these environments. The rates of bio-degradation of 1080 in water and soil have also been subject to laboratory studies (Booth et al 1999; Olgilvie et al 1996).

Ogilvie et al (1996) examined the rates of 1080 degradation at different water temperatures, involving the inoculation of stream water with an initial dose of 0.12 $\mu g\ ml^{-1}$ of 1080. Experiments investigated degradation rates at 21^0C and 11^0C and were designed to test the different rates likely to occur in different seasons. The research showed that the overall rate of degradation was significantly different at different water temperatures. Concentrations of 1080 declined by 25% (at both temperatures) during the first 24 hours. Significant differences in degradation rates became evident between 24 and 48 hours depending on the water temperature. The rate of degradation after the first 24 hours at 21^0C was significantly higher than at 11^0C. These different rates of degradation were also demonstrated over longer time periods (between 48 and 72 hours). After 141 hours no detectable 1080 was found in the warmer water, whereas approximately 30% of the initial dose of 1080 remained in the cooler water (although the degradation trend was continuing). 1080 dissolved in deionised water was also tested for 1080 breakdown at both temperatures. The results showed that there was little or no breakdown at both temperatures in the absence of microbes (ibid.). Experiments by Booth et al (1999) tested 1080 degradation in stream water at 21^0C and showed 1080 to break down into fluorocitrate (as happens in the body), which is likely to be the result of stream microbial activity. Within 17 days of dosing with 1080 there was little or no 1080 or fluorocitrate remaining in the water at that temperature. Eason et al (1999:134) and Eason (undated) state that the breakdown of this toxin occurs rapidly at higher temperatures "but still occurs at 7^0C within 1-2 weeks." In both cases the publication cited in support of this

statement is Ogilvie et al (1996). Nowhere in the Ogilvie (op. cit.) paper is there any mention of any experiment that tested the degradation of 1080 at 7^0C. If there were unpublished experimental evidence showing rapid breakdown of 1080 at 7^0C it would be very valuable to the debate and should be published.

In New Zealand there are very few forested mountain rivers (i.e. where 1080 drops commonly occur) with water temperatures as high as 21^0C. This is particularly true for the winter months when poisoning operations are most commonly undertaken. Water temperatures in mountain streams are generally considerably colder (particularly in winter), and these temperatures will decrease with increasing altitude and latitude. In other research, possum carcasses (killed by 1080) still posed a serious hazard to dogs 75 days after poisoning (Meenken and Booth 1997), which suggests that 1080 or its toxic breakdown product (fluorocitrate) can persist at hazardous levels for lengthy periods in the environment. The evidence provided by both of these studies suggests that 1080 is moderately persistent at colder temperatures. There are a variety of potential hazards associated with any partial persistence of 1080 (which also shows evidence of endocrine disruption – which can happen at very low concentrations) including acute and chronic hazards to dogs, invertebrates, vertebrate wildlife, fish and other aquatic wildlife, aquatic and terrestrial food webs, human drinking water supplies (particularly subterranean water flows), and meat. Further research is needed to test degradation rates at lower temperatures (in water and other substrates) and for longer time periods before conclusions can be made on the issue of persistence.

The biodegradation of 1080 involves the enzymatic cleavage of the carbon-fluorine bond to produce glycolate and free fluoride ions (Wong et al 1992). Accordingly, fluoride in water is a by-product of 1080 breakdown (Eason et al 1994c). The amount of inorganic fluoride ions was measured by Ogilvie et al (1996) in stream water at 11^0C and 21^0C, and showed an increase with time. The highest rate of fluoride ion release occurred between 24 and 72 hours in the warmer water, which corresponded with the period when the highest rates of 1080 breakdown were demonstrated. Whether concentrations of free fluoride ions in solution following the biodegradation of 1080 in water are likely to be high enough to pose any environmental risks remains to be determined. According to Parfitt et al (1994) fluoride ion concentrations in soil solutions might reach 0.0012mg L^{-1} in a worst-case scenario, as a result if 1080 degradation (according to results of their experiments). This would be well below the range of background fluoride concentrations of 0.01-0.03 mg L^{-1} experienced in many natural waters (Parfitt op. cit.). There is some popular concern about the environmental health

implications of fluoridation of water supplies, and additional fluoridation from the breakdown of 1080 may add to this debate. Environmental toxicological concerns relating to fluoride in water supplies range from effects of fluoride on reproductive health in animals (Chinoy and Sharma 2000; Chinoy and Patel 2001; Chinoy et al 1991; Elbetieha et al 2000; Collins et al 1995), reproductive health of humans (Freni 1994; Susheela and Jethanandani 1996), effects on bone development in humans (Gutteridge et al 1990; Brown and Josse 2002; Frazl et al 1994), effects on bone development in animals (Lafage et al 1995; Giavaresi et al 1999), and its potential link with cancer (Takahashi et al 2001). More detailed research on the impacts of any increase of fluoride ions released into the environment as a result of 1080 breakdown (e.g. effects on soil microfauna, and aquatic organisms) would be helpful in clarifying whether or not there is any potential (localised) hazard associated with fluoride release.

Leaching Through Soils

The solubility of 1080 and its partial persistence at low water temperatures raise questions concerning its ability to leach through soils. Soils contain micro-organisms that are capable of biodegrading 1080 and studies have shown such microbes to be capable of breaking down 1080 in isolation from soils and in their soil environment (Walker and Bong 1981; Wong et al 1991; David and Gardiner 1966; Parfitt et al 1994; King et al 1994; Walker 1994). This means that 1080 is able to biodegrade both in water and soil. A study by Parfitt et al (1995) indicated that there is potential for 1080 to leach through soil in association with heavy rainfall events that occur shortly after 1080 applications. The authors point out however, that some of the compound is likely to be retained in soil pores where biodegradation can occur (Parfitt op cit.). They conclude that while some leaching is possible biodegradation and dilution is likely to contribute significantly to detoxification. This still does not address the issue of the effect of low-level contamination (and associated chronic effects among organisms along the exposure spectrum).

A study of ground water 1080 residues from a landfill site where 1080 baits had been disposed (Bowman 1999) found 1080 concentrations to vary depending on distance from the subterranean source. The concentrations of 1080 in groundwater 13m (horizontally) from the source were significantly lower than those at 5m. It took 5 weeks for the 1080 to be detected 5 meters from the source, and 16 weeks to be detected at 13 meters. The detection limit for this study was 0.0001μg ml^{-1}. The concentrations of 1080 detected were very low in relation to acute toxicity thresholds in adult humans, although two of the 28 measurements were above

the (then) Provisional Maximum Acceptable Value for drinking water (0.005µg ml^{-1}). The study concluded that biological activity broke down the 1080 in situ and in groundwater leachate. No measurable 1080 was detected during the last 6 months of sampling with a total sampling period of 14 months from the time of disposal.

Uptake in Plants

It has been known for some time that the high solubility of 1080 allows it to be absorbed by plants once in solution (Negherbon 1959; Atzert 1971; Rammel & Fleming 1978). Negherbon (1959) showed that brassicas inoculated by 1080 solutions were also toxic to aphids. This raised the concern that herbivores may be at risk from systemic poisoning. A study by Ogilvie et al (1998) showed the toxin to be taken up rapidly (0.08 ppm at 3 days) by ryegrass (probably through the roots rather than through the leaves) but rapidly metabolised. In a native broadleaf species (*Griselinia littoralis*) uptake was less rapid but persisted for longer (0.06 ppm at 10 days) (ibid.). Concentrations of the toxin then declined to near the detectible limits by 38 days. This and other studies (e.g. Preuss et al 1968; Ward and Huskisson 1969) provide evidence that plants degrade 1080.

Because 1080 is known to be toxic to nine orders of insect (Notman 1989), there could be problems for insects that eat plant material containing 1080 as it is degrading. Ogilvie et al (1998) concluded however that a weta (for example) would need to eat 150 times its body weight within a 10-day window of toxicity to receive a lethal dose. The authors of this study do not, however, mention or comment on the potential for these levels of 1080 to produce sub-lethal consequences that could for example, affect the fertility of insect or mammalian browsers and therefore affect longer term survival of a population in the face of regular 1080 applications.

Science and Regulation

According to the New Zealand Ministry of Health the concentration of 1080 in drinking water should not exceed 0.005 mg L^{-1}.[10] The Ministry calculated this Maximum Acceptable Level (MAV) for 1080 using a NOEL derived from "a Department of Conservation teratology study

[10] This is equivalent to 5ppb according to a joint statement by the Department of Conservation, the Animal Health Board, and the Ministry of Health in 1998: "New Research Findings on 1080. Joint news release from the Animal Health Board, Department of Conservation and Ministry of Health, 31 March 1998." The molecular weight of sodium fluoroacetate, however, is M_r100, which means that 0.0035 mg L^{-1} is in fact equivalent to 3.5 ppb.

of rats (Eason [et al] 1999)"[11]. This is based on the following equation: [(0.1 mg kg^{-1} x 70kg x 0.5) / (2L x 500)] = 0.0035 mg L^{-1}. This equation is based on a NOEL of 0.1mg kg^{-1} body weight per day; 70kg average weight of an adult; average quantity of water consumed by an adult of 2 litres per day; portion of lowest lethal dose allocated to drinking water of 0.5; and an uncertainty factor of 500. There are a number of problems with this calculation from a toxicological point of view. Firstly, the equation is based on acute severe toxicity (and does not take into account chronic severe or mild toxicity); secondly, it is based on a study that (a) concluded that 1080 is teratogenic in rats at a dose of 0.75 mg kg^{-1} day^{-1} even though it did not test for symptoms other than gross observable teratological effects at any dose, and (b) did not test for other teratological effects (other than gross morphological effects) at concentrations below 0.1 mg kg^{-1} day^{-1}. For this study to be conclusive enough to demonstrate public safety limits for 1080 it would need to more comprehensively test the teratological potential of 1080, by actually looking for symptoms known to be associated with teratogens in general, and teratogenic symptoms known to be associated with 1080 in particular (e.g. male reproductive toxicity). It would need to test for these symptoms at a range of concentrations well below those tested for, particularly because endocrine disrupters are active can cause adverse effects at extremely low concentrations (i.e. well below those that would cause acute severe reactions).

To recap: a teratogen is an agent that can cause malformations of an embryo or foetus. This can be a chemical substance, a virus or electromagnetic radiation that can affect parents and offspring. Symptoms of teratogenic influences (to be tested in parents and offspring) include:

- sperm abnormalities (decreased number/motility, abnormal morphology of sperm)
- sub-fecundity (abnormal gonads/ducts of external genitalia)
- abnormal pubertal development
- infertility of male/female
- delay in conception
- illness during pregnancy/parturition (toxemia; haemorrhage)
- early foetal loss
- late foetal loss (stillbirth, death in the first week)
- decreased birth weight
- premature/ postmature births

[11] See Ministry of Health web site: http://www.moh.govt.nz/moh.nsf/ea6005dc347e7bd44c2566a40079ae6f/9c57904f727879eacc256bb100143184/$FILE/1080datasheet.doc (visited 20 March 2003).

- altered sex ratio of offspring
- chromosome abnormalities
- multiple births
- birth defects
- infant death
- offspring morbidity and,
- offspring malignancies (Amdur et al 1991).

In the Eason et al (1999) study, birth defects were observed[12], but apart from that, none of the above teratological symptoms were tested, and for this reason it failed to determine whether or not 1080 is an endocrine disrupter. This points to a significant toxicological flaw in the rationale for establishing the MAV for 1080 in New Zealand, primarily because the teratological study it is based on was more of an introductory than a conclusive study. Considerable evidence now exists linking 1080 with endocrine disruption potential (Mazzanti et al 1965; Sullivan et al 1979; Twigg et al 1988; Balcomb et al 1983; Hornshaw et al 1986; Twigg 1994). For example, Sullivan et al (1979) found all rats receiving 20, 6.6 or 2.2 ppm of 1080 to exhibit morphological damage to the testes, and decreased numbers of spermatids. At the two higher doses they observed marked seminiferous tubule atrophy. In November 1998 the EPA in California registered sodium fluoroacetate as a male reproductive toxin (EPA 2003).

In secondary poisoning studies 1080 was shown to persist in carcasses for at least 75 days (Meenken and Booth 1997). This is seen as an advantage in conservation management as it can lead to the control of more than one pest species. But it also raises an issue for human secondary poisoning. As with most studies on the direct toxicity of 1080, secondary poisoning studies have tended to focus only on acute severe toxicity, and none found in the peer reviewed literature looked at teratogenic effects. If 1080 were capable of causing *direct* adverse health effects at levels considerably lower than those that would cause acute symptoms (e.g. if it is an endocrine disrupter), then it is also possible that it could cause *indirect* adverse health effects at low levels through secondary poisoning. This could potentially occur through the consumption of meat contaminated by 1080. Of particular concern here is game meat (especially venison), which may be killed following exposure to

[12] Foetal skeletal abnormalities were observed at doses of 0.33 and 0.75 mg kg^{-1} day^{-1}. Abnormalities in forelimb development were observed in foetuses at the same dose. Bent ribs were observed at doses of 0.33 and 0.75 mg kg^{-1} day^{-1}, and unossified sternebrae were observed at the 0.75 mg kg^{-1} day^{-1} dose.

1080 by the animal. Given that 1080 has shown to break down slowly in cold conditions, it is not out of the question that deer could move into and out of areas targeted for possum control operations, be hunted and then eaten by hunters or other consumers of game meat (e.g. tourist facilities) with significant doses of 1080 in the meat (i.e. not high enough to cause severe acute reactions, but enough to contribute to teratogenic effects).

Until the issue of possible endocrine disruption and partial persistence at cold temperatures is properly resolved, a number of public health and environmental questions will hang over 1080 use in New Zealand. If indeed 1080 is not an endocrine disrupter (and it may not be), then it is important that proper experiments are conducted to determine this once and for all. Until that time the anti-1080 lobby in New Zealand may have sufficient (political) grounds to convince lawmakers and local authorities that 1080 should not be used to the same extent in large-scale possum control operations. If 1080 is not an endocrine disrupter, such political pressure could lead to the demise of a highly successful agent of possum control for the Department of Conservation and the Animal Health Board and could seriously jeopardise New Zealand's ability to protect its unique biological diversity, and control bovine tuberculosis. If properly conducted experiments do show 1080 to be an endocrine disrupter then there are some serious risks that need to be considered, including the long term viability of native wildlife populations and ecosystems subject to 1080 poisoning operations. It would be a great tragedy if one of the tools designed to protect our endangered birds, ended up contributing to their demise.

For science to be used with integrity in the regulatory process, it is important that regulators at least take full account of scientific consensus - otherwise we have wasted our research investment and science fails to serve society. Where consensus is not forthcoming, it is important to prudently manage uncertainty, particularly where public health or environmental risks may be real (actually taking place) but are yet to be confirmed by conclusive scientific research.[13] Section 7 of the HSNO Act (1996) states that "all persons exercising functions, powers and duties under this Act… shall take into account the need for caution in managing adverse effects, where there is scientific and technical uncertainty about those effects." Whether regulators choose to err on the side of caution or on the side of negligence is for them and their political managers to decide. History has taught us though, that the negligent option can lead to adverse and sometimes irreversible environmental and public health impacts. Such impacts can also translate into significant financial costs. The current annual

costs of possum control and possum damage[14] in New Zealand are a consequence of a lack of caution in the late 19th century that saw the introduction of possums for a fur trade.

Conclusion and Recommendations

In terms of the relationship between scientific evidence and policy mentioned at the beginning of this report it is clear that for acute toxicity there is ample empirical evidence of adverse health effects with animal and human models (with a high degree of scientific consensus), and credible explanations of a biological mechanism to explain these effects, and regulations that reflect this consensus. For chronic toxicity (e.g. potential endocrine disruption) there is some empirical evidence of adverse health effects with animal models (without scientific consensus), and as yet no explanations that have led to scientific consensus on this matter (apart from sufficient consensus in California for the EPA to classify 1080 as a male reproductive toxin).

To enable the regulatory framework to be fully informed by science on this matter there is a need to fill the gaps in our current knowledge (where possible), and take appropriate regulatory action during an interim period in order to appropriately deal with the uncertainty associated with chronic toxicity. In terms of research there is a need to:

1. Conduct experiments to determine whether 1080 is an endocrine disrupter, and determine the endocrine disrupting effects (if any) on a variety of aquatic and terrestrial organisms.
2. Conduct experiments to determine the rates of 1080 degradation at temperatures equivalent to those experienced in the winter months in forested mountain areas in New Zealand.

Until the above research has been completed there is a need to re-evaluate the regulatory status of 1080 in the light of these gaps in our knowledge. In particular, there is a need to:

3. Evaluate the risk of 1080 use for the regulatory period prior to the completion of such research, that takes adequate account of this uncertainty; and,
4. Set interim regulations that reflects this uncertainty and the associated risks.
5. Explore the practical and financial feasibility of alternative methodologies for possum control,[15] including the possibility of using 1080 in combination with other methods

[13] For example, it may be raining but it remains an anecdote until we set up a rain gauge to record this fact.
[14] According to Eason et al (1994a) possums cause $35 million in damage each year.

currently in use (e.g. trapping, other poisons, bounty schemes). As a precautionary measure (prior to the completion of research mentioned in points 1. and 2. above), it would be appropriate to explore the feasibility of using methods other than 1080 in human drinking water catchments, and perhaps restricting 1080 use to areas at some distance from human habitation.

The financial costs (relative to 1080) of employing non-toxic alternative methods in drinking water catchments could be offset by the political gains in a decrease in the scope of community opposition to the poison. Such measures are unlikely to satisfy recreational hunters, whose geographical area of concern extends to hunting areas located a long distance from drinking water catchments. On the other hand, localised community concern for drinking water quality could be substantially reduced if drinking water catchments and areas close to human habitation (and domestic dog walking areas) became 1080 exclusion zones. It is still important however, to deal with the concerns of recreational hunters, particularly if DOC wants to manage a significant potential liability to the conservation estate in the form of vigilante hunters who may seek to wilfully jeopardise the biosecurity of conservation areas (as became apparent in the threats made to Kapiti Island Nature Reserve during January 2003).[16] One solution could be to manage possums in recreational hunting areas by intensive trapping and targeted (species specific) poisoning programmes undertaken in partnership with hunting organisations.

Because of the risks associated with the build-up of resistance to 1080 among target populations (as has been reported with rabbits in Australia) it would be prudent to regulate 1080 use to minimise this possibility. As such, increasing the use of other methods for possum control would serve this end as well as a human health precaution.[17]

Once the above research has been completed it will be necessary to:

---

[15] Innes and Barker (1999) recommend that more research be conducted on toxin-free pest control methods in New Zealand.

[16] A group of hunters anonymously claimed to have released 11 possums onto Kapiti Island. See http://www.scoop.co.nz/mason/stories/PA0301/S00056.htm for further details.

[17] Research into immuno-contraception methods of possum control are progressing to the point that they may produce cost-effective operational alternatives in the foreseeable future (Duckworth et al 2001; Harris et al 2001; Molinia et al 2001).

6. Re-evaluate the calculation of the MAV for 1080 on the basis of the findings of this research and all of the science readily available on acute and chronic toxicity internationally.

Further research should also be conducted as part of the on-going relationship between research, regulation and management for 1080. In particular, two areas of supplementary research warrant investigation:

7. Evaluate the food web effects of fluoride ion release into soil and water as a result of 1080 breakdown; and,
8. Evaluate the effects of on-going 1080 use on the broader ecological functionality of habitats where it is used, including
    a. Potential impacts on food webs;
    b. Chronic toxicity (wildlife), with particular reference to long-term fertility and fecundity studies of native wildlife populations at concentrations below the known or estimated LD_{50} for these species; and,
    c. Chronic toxicity (human), with particular reference to potential adverse health effects other than endocrine disruption at concentrations at and below the current MAV.

It is recommended that the Environmental Risk Management Authority take account of all currently available science on 1080 when it forms recommendations on regulatory issues relating to this chemical. Taking account of available scientific evidence relating to 1080 use will also mean considering the risks of not continuing with the current regime for the use of 1080. Such risks include:

- The potential loss of conservation management (and bovine Tb control) gains made in recent years as a result of 1080 use (should 1080 use be more heavily restricted as a result of the EMA review); and
- The risks associated with the employment of any alternative methods of possum control (e.g. the risks associated with the use of other poisons).

Alternatives to current practices will always have their impacts, and it is important that the impacts of such alternatives are weighed up against the risks and benefits of the status quo. This can sometimes mean that regulatory change is necessary but costly, or that the status quo provides the least of a selection of evils.

Acknowledgements

The author is grateful for useful comments on the draft by Ben Wheeler, Laurie Jackson, Sara Kindon, Warwick Murray, Phil Lester, Jan Ridley, (Victoria University, of Wellington), Michael Morris, and Peter Russell.

References

Adams, N. R. 1995 Organizational and activational effects of phytoestrogens on the reproductive tract of the ewe. *Proceedings of the Society for Experimental Biology and Medicine 208:* 87-91.

Allen Y.T., Matthiessen P., Scott A.P., Howarth S., Feist S.W. and Thain J.E. 1999b. The extent of oestrogenic contamination in the UK estuarine and marine environment further surveys of flounder. *Science of the Total Environment 233:* 5-20.

Allen Y.T., Scott A.P., Matthiessen P., Howarth S., Thain J.E. and Feist S.W. 1999a. A survey of oestrogenic activity in UK estuarine and coastal waters and its effects on gonadal development of the flounder *Platichthys flesus. Environmental Contamination and Toxicology 18:* 1791-1800.

Allender, W.J. 1990. Determination of sodium fluoroacetate (Compound 1080) in biological tissues. *Journal of Analytical Toxicology. 14(1):* 45-49.

Amdur MO, Doull J, and Klaassen CD. 1991. *Casarett and Doul's Toxicology: The Basic Science of Poisons*, New York: Pergamon Press.

Ames, B.N., McCann, J., and Yamasaki, E. 1975. Methods for detecting carcinogens and mutagens with the Salmonells/mammalian microsome mutagenicity test. *Mutation Research 31:* 347-364. Cited in Eason et al 1999.

Ataria, J. M., Wickstrom, M., Arthur, D., and Eason, C. T. 2000. Biochemical and histopathological changes induced by sodium monofluoroacetate (1080) in mallard ducks. *New Zealand Plant Protection 53:* 293-298.

Atzert, S.P. 1971. A review of monofluoroacetate (compound 1080) its properties, toxicology and use in predator and rodent control. U.S. Dept of Interior, Fish and Wildlife Services, Bureau of Sport Fisheries and Wildlife. Special Scientific Report – Wildlife No. 146, Washington D.C. 1971.

Balcomb, R., Bowen, C.A., and Williams, H.O. 1983. Acute and sublethal effecs of 1080 on starlings. *Bulletin of Environmental Contamination and Toxicology 31:* 692-698.

BBC 2000. 'Gender bender' fish problem widens. Festival of Science, 6 September 2000. http://news.bbc.co.uk/1/hi/in_depth/sci_tech/2000/festival_of_science/913273.stm (viewed March 2003).

Bennetts, H.W., Underwood, E.J. and Shier, F.L. 1967. A specific breeding problem of sheep on subterranean clover pastures in Western Australia. *Australian Journal of Agricultural Research* 18*:* 335-48.

Bickham, J. W. and M. J. Smolen. 1994. Somatic and heritable effects of environmental genotoxins and the emergence of evolutionary toxicology. *Environmental Health Perspectives. 102 (Suppl. 12):* 25-28.

Blazak, W.F., Los. W.F., Rudd,. C.J., and Caspary, W.J. 1989. Chromosome analysis of small and large L5187Y mouse lymphoma cell colonies: comparison of trifluorothymidine-

resistant and unselected cell colonies from mutagen-treated and controlled cultures. *Mutation Research 224:* 197-208.

Booth, L.H. and Wickstrom, M.L. 1999. The toxicity of sodium monofluoroacetate (1080) to *Huberia striata*, a New Zealand native ant. *New Zealand Journal of Ecology 23(2):* 161-165.

Booth, L.H., Olgilvie, S.C., Wright, G.R., and Eason, C.T. 1999. Degradation of sodium monofluoroacetate (1080) and fluorocitrate in water. *Bulletin of Environmental Contamination and Toxicology 62:* 34-39.

Bowman, R.G. 1999. Fate of sodium monofluoroacetate (1080) fololowing disposal of pest bait to a landfill. *New Zealand Journal of Ecology 23(2):* 193-197.

Brown JP, Josse RG. 2002. 2002 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada. *Canadian Medical Association Journal 167(10 Suppl)*: S1-S34.

Chi, C. H., Lin, T. K., abd Chen, K. W. 1999. Hermodynamic abnormalities in sodium monofluoroacetate intoxication. *Human and Experimental Toxicology. 18 (6):* 353-353.

Chi, C.H., Chen, K.W. Chan, S.H., Wu, M. H., and Huang, J.J. 1996. Clinical presentation and prognostic factors in sodium monofluoroacetate intoxication. *Journal of Clinical Toxicology 34 (6):* 707-12.

Chinoy NJ, Patel TN. (2001). Efects of sodium fluoride and aluminium chloride on ovary and uterus of mice and their reversal by some antidotes. *Fluoride* 34: 9-20.

Chinoy NJ, Rao MV, Narayana MV, Neelakanta E. (1991). Microdose vasal injection of sodium fluoride in the rat. *Reproductive Toxicolology* 5(6):505-12.

Chinoy NJ, Sharma A. (2000). Reversal of fluoride-induced alteration in cauda epididymal spermatozoa and fertility impairment in male mice. *Environmental Sciences* 7: 29-38.

Colborn T., vom Saal F.S. and Soto A.M. (1993). Developmental Effects of endocrine-disrupting chemicals in wildlife and humans. *Environmental Health Perspectives 101(5):* 378-384.

Collins TF, Sprando RL, Shackelford ME, Black TN, Ames MJ, Welsh JJ, Balmer MF, Olejnik N, Ruggles DI. (1995). Developmental toxicity of sodium fluoride in rats. *Food and Chemical Toxicology 33(11):* 951-60.

Cook, C.J., Eason, C.T., Wickstrom, M., and Devine, C.D. 2001. Development of Antidotes for sodium monofluoroacetate (1080). *Biomarkers 6(1):* 72-76.

Corvalan, C., Briggs, D., and Zielhuis (eds) 2000. *Decision Making in Environmental Health*. London, E & FN Spon published on behalf of the World Health Organisation.

Crain D.A., Guillette L.J., Rooney A.A. and Pickford D.B. 1997. Alterations in steriodogenesis in alligators (*Alligator mississippiensis*) exposed naturally and experimentally to environmental contaminants. *Environmental Health Perspectives 105(5):* 528-533.

David, W. A., and Gardiner, B.O. 1966. Persistence of fluoroacetate and fluoroacetamide in soil. *Nature 209:* 1367-1368.

de-Moraes-Moreau, R.L., Haraguchi, M., Morita, H, and Palermo-Neto, J. 1995. Chemical and biological demonstration of the presence of monofluoroacetate in the leaves of *Palicourea marcgravii St. Hil. Brazilian Journal of Medical Biological Research 28 (6):* 685-92.

Duckworth, J.; Mate, K.; Scobie, S.; Jones, D.; Buist, J.; Molinia, F.; Glazier, A.; Cui, X.; Cowan, P.; Walmsley, A.; Kirk, D.; Lubitz, W.; Haller, C. 2001: Evaluating zona pellucida antigens and delivery systems for possum fertility control in New Zealand: progress and future directions. www.maf.govt.nz/mafnet/publications/research/biological-management-of-possums (viewed April 2003).

Eason C.T. undated. Evidence for a Hearing on the application for 1080 use in South Westland. Landcare Research.

Eason, C.T., Wright, G.R., and Fitzgerald, H. 1992. Sodium monofluoroacetate (1080) water residue analysis after large-scale possum control. *New Zealand Journal of Ecology 16(1):* 47-49.

Eason, C.T., Gooneratne, R., and Rammell, C.G. 1994a. A review of the toxicokinetics and toxicodynamics of sodium monofluoroacetate in animals. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 82-89.

Eason, C.T., Gooneratne, R., Fitzgerald, H., Wright, G., and Frampton, C. 1994b. Persistence of sodium monofluoroacetate in livestock animals and risk to humans. *Human Experimental Toxicology 13(2):* 119-122.

Eason, C.T., Morgan, A.J., and Wright. G.R. 1994c. The fate of sodium monofluroacetate (1080) in stream water, and the risks to humans. *Human and Experimental Toxicology 13(9):* 640-640.

Eason, C. T. 1997. Sodium monofluoroacetate toxicology in relation to its use in New Zealand. *Australasian Journal of Ecotoxicology* 3: 57-64.

Eason, C.T., Wickstrom, M., Turck, P., and Wright, G.R. 1999. A review of recent regulatory and environmental toxicology studies on 1080: results and implications. *New Zealand Journal of Ecology 23(2):* 129-137.

Egeheze, J.O., and Oehme, F.W., 1979. Sodium monofluoroacetate (SMFA, Compound 1080): a literature review. *Veterinary and Human Toxicology 21:* 411-416.

Elbetieha, A., Darmani, H., Hiyasat, A. (2000). Fertility effects of sodium fluoride in male mice. *Fluoride 33:* 128-134.

EPA 1987. Chemical Identity – Sodium Fluoroacetate http://www.epa.gov/swercepp/ehs/profile/62748p.txt (viewed March 2003).

EPA 1988. Subchronic toxicity study in rats with sodium fluoroacetate. HLA study No. 2399-118. Office of Solid Waste and Emergency Response, Washington D.C.

EPA 1997. Special report on environmental endocrine disruption: An effects assessment analysis. Prepared for the Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, D.C. EPA/630/R-96/012 February 1997. http://www.epa.gov/ORD/WebPubs/endocrine/ (viewed March 2003).

EPA 2003. State of California, Environmental Protection Agency, Office of Environmental Health Hazard Assessment, Safe Drinking Water and Toxic Enforcement Act of 1986. Chemicals known to the state to cause cancer or reproductive toxicity. March 14 2003, p. 16. Chemical Abstract Services number: 62748, Date registered: November 6, 1998. http://www.oehha.ca.gov/prop65/prop65_list/files/31403LSTA.pdf (viewed March 2003).

ERMA (Environmental Risk Management Authority) 2002. Grounds for Reassessment of 1080. Media Release, 19 March 2002.

Evening Post 2002. Myths surround the use of 1080. 09 April 2002, p. 9.

Facemire C.F., Gross T.S. and Guillette J. (1995). Reproductive impairment in the Florida panther: Nature or nurture? *Environmental Health Perspectives 103(4):* 79-85.

Fagerstone, K. A., Savarie, P. J., Elias, D. J., and Schafer, E. W. 1994. Recent regulatory requirements for pesticide registration and the status of compound 1080 studies conducted to meet EPA requirements. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28: 33-38.

Findlay, J.K., Buckmaster, J.M., Chamley, W.A, Cummings, I.A., Hearnshaw, H., and Goding, J.R. 1973. Release of luteinizing hormone by estradiol -l 7,beta and gonadotrophin -releasing hormone in ewes affected with clover disease. *Neuroendocrinology 11:* 57-66.

Fratzl P, Roschger P, Eschberger J, Abendroth B, Klaushofer K. 1994. Abnormal bone mineralization after fluoride treatment in osteoporosis: a small-angle x-ray-scattering study. *Journal of Bone and Mineral Research 9(10):* 1541-9.

Freni SC. 1994. Exposure to high fluoride concentrations in drinking water is associated with decreased birth rates. *Journal of Toxicology and Environmental Health 42:* 109-121.

Fry D.M. 1995. Reproductive effects in birds exposed to pesticides and industrial chemicals. *Environmental Health Perspectives 103(Suppl 7):* 165-171.

Fry, D., Toone, C., Speich, S., and Peard, R. 1987. Sex ratio skew and breeding patterns of gulls: demographic and toxicological considerations. *Studies in Avian Biology 10:* 26-43.

Fry. D. and Toone, M. 1981. DDT-induced feminisation of gull embryos. *Science 213:* 922-24.

Giavaresi G, Fini M, Gnudi S, Mongiorgi R, Ripamonti C, Zati A, Giardino R. 1999. The mechanical properties of fluoride-treated bone in the ovariectomized rat. *Calcified Tissue International 65:* 237-41.

Giesy J.P., Ludwig J.P. and Tillitt D.E. 1994. Deformities in birds of the Great Lakes region: assigning causality. *Environmental Science and Technology 28(3):* 128-135.

Gilbertson, M. Kubiak, T., Ludwig, J., and Fox, G. 1991. Great Lakes embryo mortality, edema, and deformities syndrome (GLEMEDS) in colonial fish-eating birds: Similarity to chick-edema disease. *Journal of Toxicology and Environmental Health 33(4):* 455-520.

Gillies, C.A. Pierce, R.J. 1999. Secondary poisoning of mammalian predators during possum and rodent control operations at Trounson Kauri Park, Northland, New Zealand. *New Zealand Journal of Ecology, 23(2):* 183-192.

Gooneratne,R., Dickson,C., Wallace, D., Eason, C.T., Fitzgerald, H., and Wright, G. 1994. Plasma and tissue 1080 in rabbits after lethal and sub-lethal doses. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. 178p.

Gooneratne, R., Eason, C.T., Dickson, C.J., Fitzgerald, H., and Wright, G. 1995. Persistence of sodium monofluoroacetate in rabbits and risk to non-target species. *Human Experimental Toxicology, 14(2):* 212-216.

Gorniak, S.L., Palermo-Neto, J., and Spinosa, H.S. 1994. Effects of acetamide on experimentally-induced Palicourea marcgravii (St Hill) poisoning in rats. *Veterinary and Human Toxicology 36(2):* 101-2.

Gray L.E., Ostby J.S., and Kelce W. (1994). Developmental effects of an environmental antiandrogen: the fungicide vinclozolin alters sex differentiation of the male rat. *Toxicology and Applied Pharmacology 129:* 46-52.

Guillette, L., Gross, T., Gross, D., Rooney, A., and Percival, H. 1995. Gonadal steroidogenesis in vitro from juvenile alligators obtained from contaminated or control lakes. *Environmental Health Perspectives 103(4):* 31-36.

Gutteridge DH, Price RI, Kent GN, Prince RL, Michell PA. (1990). Spontaneous hip fractures in fluoride-treated patients: potential causative factors. *Journal of Bone and Mineral Research 5 Suppl 1:* S205-15.

Hagan, E.C., Ramsey, L.L., and Woodward, G. 1950. Absorbtion, distribution, and excretion of sodium monofluoroacetate (Compound 1080) in rats. *Journal of Pharmacology and Experimental Therapeutics 99:* 426-411.

Hamilton, D.J. and Eason, C.T. 1994. Monitoring for 1080 residues in waterways after a rabbit-poisoning operation in Central Otago. *New Zealand Journal of Agricultural Research. 37:* 195-198.

Harris, M. S.; Cui, X.; Jones, S.; McCartney, C.; O'Rand, M. G. 2001: Identification of new antigen targets and the molecular dissection of antigenicity for possum immunocontraception. *In*: Biological management of possums : report of a conference held under the auspices of the National Science Strategy Committee for Possum and Bovine Tb Control, 2-4 April 2001 Wellington, Ministry of Agriculture and Forestry. Pp. 20-23. www.maf.govt.nz/mafnet/publications/research/biological-management-of-possums (viewed April 2003).

Hartley, L., O'Connor, C., Waas, J., and Mathews, L. 1999. Colour preferences in North Island Robins (Petroica australis): implications for deterring birds from poisonous baits. *New Zealand Journal of Ecology 23(2):* 255-259.

Hoddle, J.A., Hite, M., Kirkman, B., Mavournin, K., MacGregor, J.T., Newell, G.W., and Salamone, M.F. 1983. The induction of micronuclei as a measure of genotoxicity: A report of the US Environmental Protection Agency GeneTox Programme. *Mutation research 123:* 61-118.

Hornfeldt, C.S., and Larson, A.A. 1990. Seizures induced by fluoroacetic and fluorocitric acid may involve chelation of divalent cations in the spinal chord. *European Journal of Pharmacology 179 (3):* 307-13.

Hornshaw, T.C., Ringer, R. K., Aulerich, R.J., and Casper, H.H. 1986. Toxicity of sodium monofluoroacetate (Compound 1080) to mink and European ferrets. *Environmental Toxicology and Chemistry 5:* 213-223.

Hugghins, E.J., Casper, H.H., and Ward, C.D. 1988. Tissue fluoroacetate residues in prairie dogs dosed with low-level sodium monofluoroacetate. *Journal of the Association of Official Analytical Chemists* 71(3): 579-81.

Hughes, C.L., 1988. Phytochemical mimicry of reproductive hormones and modulation of herbivore fertility by phytoestrogens. *Environmental Health Perspectives 78:* 171-5.

Hutchinson T.H., Pounds N.A., Hampel M. and Williams T.D. (1999). Impact of natural and synthetic steroids on the survival, development and reproduction of marine copepods (*Tisbe battagliai*). *Science of the Total Environment 233:* 167-179.

Innes, J. and Barker, G. 1999. Ecological consequences of toxin use for mammalian pest control in New Zealand – an overview. *New Zealand Journal of Ecology 23(2):* 111-127.

James, W. 1997. The use of offspring sex ratios to detect reproductive effects of male exposure to dioxins. *Environmental Health* 105(2) (letter to editor). http://ehpnet1.niehs.nih.gov/docs/1997/105-2/correspondence.html (viewed March 2003).

Janssen P.A.H., Dalessi D.L.W.M., Lambert J.G.D., Vethaak A.D., van Wezel A.P. and Goos H.J.Th. (1997). Oestrogenic effects in the flounder, *Platichthys Flesus,* after exposure to polluted harbour sediment. (Abstract). Seventh Annual Meeting of SETAC-Europe, Amsterdam, The Netherlands, 6-10 April.

Kelce W.R., Monosson E., Gamcsik M.P., Laws S.C. and Gray L.E. (1994). Environmental hormone disrupters: evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites. *Toxicology and Applied Pharmacology 126 (2):* 276-285.

Kelce W.R., Stone C.R., Laws S.C., Gray L.E., Kemppainen J.A. and Wilson E.M. (1995). Persistent DDT metabolite p,p'-DDE is a potent androgen receptor antagonist. *Nature 375:* 581-585.

King, D. R., Kirkpatrick, W. E., and McGrath, M. 1996. The tolerance of malleefowl *Leipoa ocellata* to 1080. *Emu* 96(3): 198-202.

King, D.R., Kirkpatrick, W.E., Wong, D.H., and Kinnear, J.E. 1994. Degradation of 1080 in Australian soils. In Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. Miscellaneous Series 28. pp.45-49.

Kubiak, T., Harris, H., Smith, L., Schwartz, T., Stalling, D., Trick, j., Sileo, L., Docherty, D., and Erdman, T. 1989. Microcontamination and reproductive impairment of the Forster's tern on Green Bay, Lake Michigan - 1983. *Archives of Environmental Contamination and Toxicology 18:* 706-27.

Lafage MH, Balena R, Battle MA, Shea M, Seedor JG, Klein H, Hayes WC, Rodan GA. (1995). Comparison of alendronate and sodium fluoride effects on cancellous and cortical bone in minipigs. A one-year study. *Journal of Clinical Investigation 95:* 2127-33.

Lancet 1992. Environmental pollution: it kills trees, but does it kill people? (editorial). *Lancet 340:* 821-22.

Leavitt, W.W. and Wright, P.A. 1963. Effects of legumes on reproduction in mice. *Journal of Reproductive Fertility 6:* 115-23.

Leggat, P. (2003) Environmental health: Global initiatives and new analytic approaches. Journal of Rural and Remote Environmental Health 2(2): 36-37.

Leopold, A.S., Erwin, M., Oh, J., and Browning, B. 1976. Phytoestrogens: Adverse effects on reproduction in California quail. *Science 191:* 98-99.

Lightfoot, J.R., Croker, K.P. and Neil, H.G. 1967. Failure of sperm transport in relation to ewe infertility following prolonged grazing on estrogenic pastures. *Australian Journal of Agricultural Research 18:* 755-67.

Livingston, P. G., 1994. The use of 1080 in New Zealand. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28: 1-9.

Lloyd, B.D., and McQueen, S.M. 2000. An assessment of the probability of secondary poisoning of forest insectivores following an aerial 1080 possum control operation. *New Zealand Journal of Ecology 24(1):* 47-56.

Lloyd, B.D., and McQueen, S.M. 2002. Measuring mortality in short tailed bats (mystacina tuberculata) as they return from foraging after an aerial 1080 possum control operation. *New Zealand Journal of Ecology 26(1):* 53-59.

MAFF 1998. Further Ministry research on gender disruptors, News release. http://www.defra.gov.uk/news/newsrel/1998/981113a.htm (viewed March 2003).

Martin, G. R., and Twigg, L. E. 2002. Sensitivity to sodium fluoroacetate (1080) of native animals from north-western Australia. *Wildlife Research 29(1):* 75-83.

Mazzanti, L., Lopez, M. and Berti, M.G. 1965. Atrofia dek testicuko produvutta dal monofluoroacetato sodico vel ratto albino. *Experimenta 21(8):* 446-447. Cited in Twigg, L.E. 1994. Occurrence of fluoroacetate in Australian plants and tolerance to 1080 in indigenous Australian animals. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. 178p.

McIlroy, J.C. 1981a. The sensitivity of Australian animals to 1080 poison I. Intraspecific variation and factors affecting acute toxicity. *Australian Wildlife Research 8:* 369-383.

McIlroy, J. C. 1981b. The sensitivity of Australian animals to 1080 poison II. Marsupial and eutherian carnivores. *Australian Wildlife Research 8:* 385-399.

McIlroy, J. C. 1982a. The sensitivity of Australian animals to 1080 poison III. Marsupial and eutherian herbivores. *Australian Wildlife Research 9:* 487-503.

McIlroy, J. C. 1982b. The sensitivity of Australian animals to 1080 poison IV. Native and introduced rodents. *Australian Wildlife Research 9:* 505-517.

McIlroy, J. C. 1983. The sensitivity of Australian animals to 1080 poison VI. Bandicoots. *Australian Wildlife Research 10:* 507-512.

McIlroy, J. C. 1984. The sensitivity of Australian animals to 1080 poison VII. Native and introduced birds. *Australian Wildlife Research 11:* 373-385.

McIlroy, J. C., King, D. R., and Oliver, A. J. 1985. The sensitivity of Australian animals to 1080 poison VIII. Amphibians and reptiles. *Australian Wildlife Research 12:* 113-118.

McIlroy, J. C. 1986. The sensitivity of Australian animals to 1080 poison IX. Comparisons between the major groups of animals, and the potential danger non-target animals face from 1080-poisoning campaigns. *Australian Wildlife Research 13:* 39-48.

McIlroy, J. C., Gifford, E. J., and Cooper, R. J. 1986. Effects on non-target animal populations of wild dog trail-baiting campaigns with 1080 poison. *Wildlife Research 13:* 447-453.

McIlroy, J. C., and Gifford, E. J. 1991. Effects on non-target animal populations of a rabbit trail-baiting campaign with 1080 poison. *Wildlife Research 18:* 315-325.

McIlroy, J.C. 1994. Susceptibility of target and non-target animals to 1080. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 90-95.

McLachlan J.A. 1993. Functional toxicology: a new approach to detect biologically active xenobiotics. *Environmental Health Perspectives 101(5):* 386-387.

McTaggart, D. R. 1970. Poisoning due to sodium monofluoroacetate ('1080'). *Australian Medical Journal 2:* 641-642.

Meenken, D., and Eason, C.T. 1995. Effects on water quality of a possum (Trichosurua vulpecula) poisoning operation using toxin 1080 (sodium monofluoroacetate). *New Zealand Journal of Marine and Freshwater Research. 29(1):* 25-28.

Meenken, D., and Booth, L.H. 1997. The risk to dogs of poisoning from sodium monofluoroacetate (1080) residues in possum (Trichoaurua vulpecula). *New Zealand Journal of Agricultural Research 40:* 573-576.

Meyer, M.J.J. 1994. Fluoroacetate metabolism of Pseudomonas cepacia. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 54-57.

Mocarelli P., Brambilla P., Gerthoux P.M., Patterson D.G. and Needham L.L. (1996). Change in sex ratio with exposure to dioxin. The Lancet 348: 409.

Molinia, F. C.; Glazier, A. M.; Myers, J. V.; Sidhu, K. S.; Mate, K. E.; Berg, D. K.; Smith, J. F.; Cowan, P. E.; Rodger, J. C. 2001: In vitro and in vivo models of key reproductive events as tools for possum biological control. *In*: Biological management of possums: report of a conference held under the auspices of the National Science Strategy Committee for Possum and Bovine Tb Control, 2-4 April 2001 Wellington, Ministry of Agriculture and Forestry. Pp. 1-5. www.maf.govt.nz/mafnet/publications/research/biological-management-of-possums (viewed April 2003).

Moller H, Showers J, Wright, M. 1996, Sodium monofluoroacetate (1080) poisoned jam bait laid for brushtail possums (*Trichosurus vulpecula*) also kills ferrets (*Mustela furo*). *New Zealand Journal Of Zoology; 23 (2):* 135-141.

Morgan, D.R. 1999. Risks to non-target species from use of a gel bait for possum control. *New Zealand Journal of Ecology 23(2):* 281-287.

Moule, G.R., Braden,A.W.H. and Lamond, D.R. 1963. The significance of estrogens in pasture plants in relation to animal production. *Animal Breeding Abstracts 31:* 139-57.

Murphy, E.C., Robbins, L., Young J.B., and Dowding, J.E. 1999. Secondary poisoning of stoats after an aerial 1080 poison operation in Pureora Forest, New Zealand. *New Zealand Journal of Ecology, 23(2):* 175-182.

Negherbon, W. O. 1959. Sodium fluoroacetate. Pages 694-695 in Negherbon, W. O. (ed) Handbook of toxicology. Volume III. Insecticides. A compendium. WADC Technical Report 55-16. Cited in Ogilvie, S.C., Booth, L.H., and Eason, C.T. 1998. Uptake and persistence of sodium monofluoroacetate (1080) in plants. *Bulletin of Environmental Contamination and Toxicology 60:* 745-749.

News in Science 2002. News in Science 29/8/2002 Rabbits showing tolerance to 1080. http://www.abc.net.au/science/news/stories/s661039.htm (viewed March 2003).

Notman, P. 1989. A review of invertebrate poisoning by compound 1080. *New Zealand Entomology 12:* 67-71.

Nugent, G.; Whitford, J.; Innes, J.; Prime, K. 2002: Rapid recovery of kohekohe (*Dysoxylum spectabile*) following possum control. *New Zealand Journal of Ecology 26:* 73-79.

O'Connor, C. E., Milne, L., M., Arthur, D. G., Ruscoe, W. A., and Wickstrom, M. 1999. Toxicity effects of 1080 on pregnant ewes. *Proceedings of the New Zealand Society for Animal Production 59:* 250-253. Cited in Ataria, J. M., Wickstrom, M., Arthur, D., and Eason, C. T. 2000. Biochemical and histopathological changes induced by sodium monofluoroacetate (1080) in mallard ducks. *New Zealand Plant Protection 53:* 293-298.

Ogilvie, S.C., Hertzel, F., and Eason, C.T. 1996. Effect of temperature on the biodegradation of sodium monofluoroacetate in water and in *Elodea canadensis*. *Bulletin of Environmental Contamination and Toxicology 56:* 942-947.

Ogilvie, S.C., Booth, L.H., and Eason, C.T. 1998. Uptake and persistence of sodium monofluoroacetate (1080) in plants. *Bulletin of Environmental Contamination and Toxicology 60:* 745-749.

Omara, F., and Sisodia, C.S. 1990. Evaluation of potential antidotes for sodium monofluoroacetate in mice. *Veterinary and Human Toxicology 32:* 427-431.

Parfitt, R.L., Eason, C.T., Morgan, A.J., Wright, G.R., and Burke, C.M. 1994 The fate of sodium monofluoroacetate (1080) in soil and water. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 59-65.

Parfitt, R.L., Eason, C.T., Hoff, H., and Heng, L.K. 1995. Sodium monofluoroacetate (1080) leaching through soils. *Bulletin of Environmental Contamination and Toxicology 55:* 162-169.

Parkin P.J., McGiven, A.R., and Bailey, R.R. 1977. Chronic sodium monofluoroacetate (compound 1080) intoxication in a rabbiter. *New Zealand Medical Journal 85(581):* 93-6.

Perfect, A. 1996. Aspects of the ecology of the native frogs *Leiopelma archeyi* and *L. hochstetteri*, and the impact of compound 1080. Unpublished masters thesis, Victoria University Wellington.

Peters, R. A., and Wakelin, R. W. 1953. Fluoroacetate poisoning: Comparison of synthetic fluorocitric acid with the enzymically synthesized fluorotricarboxylic acid. *Nature 171:* 1111-1112.

Powlesland, R.G., Knegtmand, J.W., and Marshall, I.S.J. 1999. Costs and benefits of aerial 1080 possum control operations using carrot baits to North Island robbins (*Petroica australis longipes*), Pureora Forest Park. *New Zealand Journal of Ecology 23(2):* 149-159.

Powlesland, R.G., Knegtmand, J.W., and Styche, A. 2000. Mortality of North Island tomtits (*Petroica macrocephala toitoi*) caused by aerial 1080 possum control operations, 1997-98, Pureora Forest Park. *New Zealand Journal of Ecology 24(2):* 161-168.

Preuss, P. W., Lemmens, A. G., and Weinstein, L. H. 1968. Studies on fluoro-organic compounds in plants. 1. Metabolism of 2-C14 fluoroacetate. *Boyce Thompson Institute Contributions 24(7):* 151-155. Cited in Ogilvie, S.C., Booth, L.H., and Eason, C.T. 1998. Uptake and persistence of sodium monofluoroacetate (1080) in plants. *Bulletin of Environmental Contamination and Toxicology 60:* 745-749.

Rammell, C.G., and Fleming, P.A. 1978. *Compound 1080. Properties and use of sodium monofluoroacetate in New Zealand*. Animal Health Division, Ministry of Agriculture and Fisheries. Wellington.

Robertson, H.A., Colbourne, R.M., Graham, P., Miller, P.J., and Pierce, R.J. 1999. Survival of brown Kiwo exposed to 1080 poison used for control of brushtail possums in Northland, New Zealand. *Wildlife Research. 26(2):* 209-214.

Robinson, R. F., Griffith, J. R., Wolowich, W. R., and Nahata, M. C. 2002. Intoxication with sodium monofluoroacetate (compound 1080). Veterinary and Human Toxicology. 44 (2):93-95.

Safe, S. and Krishnan V. 1995. Chlorinated hydrocarbons: estrogens and antiestrogens. *Toxicology Letters 82/83:* 731-736.

Savarie, P.J., Matschke, G.H., Engeman, R.M., and Fagerstone, K.A. 1994. Susceptibility of prairie dogs to Compound 1080 (sodium monofluoroacetate) baits and secondary poisoning effects in European ferrets under laboratory conditions. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. 178p.

Schaefer, H., and Machleidt, H. 1971. Conversion of fluoroacetic acid to aminl acids in the mammal. *Biochemica at Biophysics Acta 252:* 83-91.

Schofl, C., Borger, J., Lange, S., von zur Muhlen, A., and Brabant, G. 2000. Energetic Requirements of carbachol-induced CA2+ signalling in single mouse beta cells. *Endocrinology 141 (11):* 4065-71.

Shuttleworth, K. 2003. Anti-1080 Activist in Court. Aotearoa Independent Media Centre, 29 January 2003. http://www.indymedia.org.nz/front.php3?article_id3113&group=webcast (viewed February 2003).

Smith, F.A., Gardener, D.E., Yuile, C.L., and De Lopez, O.H. 1977. Defluorination of fluoroacetate in the rat. *Life Sciences 20:* 1131-1138.

Soto A.M., Sonnenschein C., Chung K.L., Fernandez M.F., Olea N. and Serrano F.O. (1995). The E-Screen Assay as a tool to identify estrogens: an update on estrogenic environmental pollutants. *Environmental Health Perspectives, 103(7):* 113-122.

Spurr, E.B. 1994. Impacts on non-target invertibrate populations of aerial application of sodium monofluoroacetate (1080) for brushtail possum control. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 116-123.

Spurr, E.B., and Drew K.W. 1999. Invertebrates feeding on baits used for vertebrate pest control in New Zealand. *New Zealand Journal of Ecology 23(2):* 167-173.

Strauss, L., Makela, S., Joshi, S., Huhtaniemi, I. and Santti, R. 1998 Genistein exerts estrogen-like effects in male mouse reproductive tract. *Molecular and Cellular Endocrinology 144:* 83-93.

Sullivan, J.L., Smith, F.A., and Garman, R.H. 1979. Effects of fluoroacetate on the testes of the rat. *Journal of Reproduction and Fertility 56:* 201-207.

Susheela AK, Jethanandani P. 1996. Circulating testosterone levels in skeletal fluorosis patients. *Journal of Toxicology and Clinical Toxicology 34(2):* 183-9.

Sykes, T.R., Quastel, J.H., Adam, M.J., Ruth, T.J. and Ninjawa, A.A. 1987. The disposition and metabolism of fluorine-18 fluoroacetate in mice. *Biochemical Archives 3(3):* 317-324.

Takahashi K, Akiniwa K, Narita K. 2001. Regression analysis of cancer incidence rates and water fluoride in the U.S.A. based on IACR/IARC (WHO) data (1978-1992). International Agency for Research on Cancer. *Journal of Epidemiology 11(4):*170-179.

The Timaru Herald 2002. 1080 Anger Directed at Sutton. 24 April 2002, p. 1.

Tou, J. C. L., Chen, J. and Thompson, L. U. 1999 Dose, timing and duration of flax seed exposure affects reproductive indices and sex hormone levels in rats. *Journal of Toxicology and Environmental Health 56:* 555-570.

Tryphonas H. (1995). Immunotoxicity of PCBs (Aroclors) in relation to Great Lakes. *Environmental Health Perspectives 103(Suppl 9):* 35-46.

Turck, P. A., Eason, C.T., and Wickstrom, M. 1998. Assessment of the developmental toxicity of sodium monofluoroacetate (1080) in rats. *Toxicologist 42 (1-S):* 258-9.

Twigg, L.E., King, D.R., and Bradley, A.J. 1988. The effect of sodium monofluoroacetate on plasma testosterone concentration in Tiliqua rugosa (Gray). *Comparative Biochemistry and Physiology 91C:* 343-347.

Twigg, L. E., 1994. Occurrence of fluoroacetate in Australian plants and tolerance to 1080 in indigenous Australian animals. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series 28:* 97-115.

Twigg, L.E., King, D.R., Bowen, L.H., Wright, G.R., and Eason, C.T. 1996. Fluoroacetate found in Nemcia spathulata. Australian Journal of Botany. 44: 411-412.

UNEP (1992) Rio Declaration. http://www.unep.org/unep/rio.htm (viewed March 2003).

vom Saal, F., and Bronson, F. 1980. Sexual characteristics of adult female mice are correlated with their blood testosterone levels during prenatal development, *Science 208:* 597-99.

vom Saal, F. 1989. Sexual differentiation in litter bearing mammals: influence of sex of adjacent foetuses in utero. *Journal of Animal Science 67:* 1824-40.

vom Saal F.S., Nagel S.C., Palanza P., Boechler M., Parmigiani S. and Welshons W.V. 1995. Estrogenic pesticides: binding relative to estradiol in MCF-7 cells and effects of exposure during foetal life on subsequent territorial behaviour in male mice. *Toxicology Letters 77:* 343-350.

Walker, J.R.L. 1994 Degradation of sodium monofluoroacetate by soil micro-organisms. *In* Seawright, A.A. and Eason, C.T. eds 1994. Proceedings of the Science Workshop on 1080. Royal Society of New Zealand. *Miscellaneous Series* 28. pp. 50-53.

Walker, J.R.L., Bong, C.L. 1981. Metabolism of fluoroacetate by a soil Pseudomonas and Fusarium solani. *Soil Biology and Biochemistry 13*: 231-235.

Ward, P. F. V., and Huskisson, N. S. 1969. The metabolism of fluoroacetate by plants. *Biochemistry Journal. 113:* 9. cited in Ogilvie, S.C., Booth, L.H., and Eason, C.T. 1998. Uptake and persistence of sodium monofluoroacetate (1080) in plants. *Bulletin of Environmental Contamination and Toxicology 60:* 745-749.

Wong, D.H., Kirkpatrick, W.E., Kinnear, J.E., and King, D.R. 1991. Defluorination of sodium monofluoroacetate (1080) by microorganisms isolated from Western Australian Soils. *Soil Biology and Biochemistry 24:* 9-14.

Wong, D.H., Kirkpatrick, W. E., King, D.R., and Kinnear, J.E. 1992. Environmental factors and microbial inoculum size, and their effect on biodefluorination of sodium monofluoroacetate (1080). *Soil Biology and Biochemistry 24 (9):* 839-843.

Wood, R.D., Mitchell, M., Sgouros, J., and Lindahl, T. 2001. Human DNA Repair Genes**.** *Science* 291: 1284-1289.

Woodward, A., Percival, H., Jennings, M., and Moore, C. 1993. Low clutch viability of American alligators on Lake Apopka. *Florida Science 56:* 52-63.

Wright, GRG, Booth, LH, Morriss, GA., Potts, MD, Brown, L, and Eason, CT. 2002 Assessing potential environmental contamination from compound 1080 (sodium monofluoroacetate) in bait dust during possum control operations. *New Zealand Journal of Agricultural Research, 45:* 57–65.