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A REVIEW OF RECENT REGULATORY AND ENVIRONMENTAL TOXICOLOGY STUDIES ON 1080: RESULTS AND IMPLICATIONS

Summary: Sodium monofluoroacetate (1080) is a highly toxic vertebrate pesticide that has been widely used for possum and rabbit control in New Zealand since the 1950s. Because of its importance in pest control and the highly toxic nature of this compound, its environmental fate, persistence, non-target impacts and general toxicology have been and continue to be extensively studied. A series of *in vitro* (cell culture) and laboratory animal studies (in rats and mice) have recently been undertaken to update the regulatory toxicology database for 1080. Results of three different, complementary tests indicate that 1080 is not mutagenic, and therefore unlikely to cause cancer. Results of developmental toxicity studies indicate that 1080 causes developmental defects in rats when pregnant females are exposed to relatively high doses (0.33 and 0.75 mg kg^{-1} day^{-1}) on a daily basis during the period of organogenesis (from days 6 through to 17 of gestation). The developmental abnormalities observed were mild skeletal effects: slightly curved forelimbs, and bent or "wavy" ribs. These results highlight the highly toxic nature of 1080 and the need for extreme care when handling this pesticide during the manufacture and distribution of bait, but do not preclude its proper use. The morphological changes in foetuses observed in the recently completed rat developmental toxicity studies are likely to raise concern regarding the exposure of humans (particularly pregnant mothers) to 1080 through contamination of waterways after the aerial sowing of 1080 baits. However, ongoing monitoring (1990–98) of waterways from areas where 1080 baits have been aerially sown confirms that there is negligible risk of human contact with 1080 through this route of exposure.

Keywords: Sodium monofluoroacetate (1080); mutagenicity; teratogenicity; human exposure.

Introduction

Large-scale possum control in New Zealand is based on the use of sodium monofluoroacetate (1080). The toxin was first introduced into New Zealand in 1954 for the control of rabbits, and between 1000 and 3000 kg are used for possum control each year (Livingstone, 1994). Sodium monofluoroacetate is highly toxic to a wide range of animals (Atzert, 1971). However, until better methods of large-scale control are developed, 1080 is considered to be an essential tool for reducing possum damage to forests and crops, and containing the spread of bovine tuberculosis for which possums are the major wildlife reservoir in New Zealand. During the last 44 years, but particularly over the last 10 years, the toxicology and environmental effects associated with the widespread use of this compound in New Zealand have come under rigorous community (Parliamentary Commissioner for the Environment, 1994) and scientific scrutiny (Seawright and Eason, 1994).

Manufactured 1080 for use in toxic baits has been shown to be chemically identical to and produce the same signs and symptoms of poisoning in animals as the toxic compound found in many poisonous plants (de Moraes-Moreau *et al*., 1995). Research in the 1940s identified fluoroacetate in the South African plant gifblaar (*Dichapetalum cymosum*). Fluoroacetate has also been identified as the toxic agent in many other poisonous plants, including rat weed (*Palicourea margravii*), native to Brazil (de Moraes-Moreau *et al.,* 1995); and ratsbane (*Dichapetalum toxicarium*), native to West Africa (Atzert, 1971). This toxin also occurs naturally in some 40 plant species in Australia. In toxic bait, which can be cereal, carrot, or paste, the maximum concentration used is 1500 mg kg^{-1} bait. Air-dried leaves of heart-leaf poison (*Gastrolobium bilobum*) and box poison (*G. parviflorum*), for example, can contain up to 2600 mg kg^{-1} fluoroacetate, and seeds of heart-leaf poison can have in excess of 6500 mg kg^{-1} fluoroacetate (Twigg, 1994; Twigg *et al.,* 1996). The highest fluoroacetate concentration so far reported from a plant is 8000 mg kg^{-1} in the seeds of *Dichapetalum braunii* (Meyer, 1994) in South Africa. Fluoroacetate would appear to be a secondary plant toxin that has evolved as a defence mechanism

against browsing animals. Most studies assessing fluoroacetate concentrations in plants have focused on plants which are overtly toxic to mammals, leading to losses of sheep and cattle in northern Australia (Seawright, 1994). However, it would appear that the ability of plants to synthesize fluoroacetate is more widespread than generally supposed, since fluoroacetate occurs at extremely low concentrations in some Finnish plants (Vartiainen and Kauranen, 1980), in tea leaves (Vartiainen and Kauranen,1984; Twigg *et al.,* 1996) and guar gum (Vartiainen and Gynther, 1984).

In response to community and scientific concerns with regard to 1080 use in New Zealand, national and international research conducted on 1080 before 1993 was comprehensively reviewed at a Science Workshop in Christchurch, proceedings of which were published by the Royal Society of New Zealand in 1994 (Seawright and Eason, 1994). These proceedings contain 22 papers which effectively collate all the significant research findings on the environmental fate of 1080 in soil, water, and animals, as well as its toxicology and non-target effects.

Health and safety and environmental concerns were considered a priority by participants at this scientific meeting. It was recognised when assessing research priorities for the 1990s, that it was most important that the database on the potential adverse effects of 1080 should be continually updated.

In this paper we report the key findings from the most recent regulatory toxicology studies and environmental monitoring, and reviewed the implications of this new information. These regulatory studies are identified in Table 1. They were selected as having significant scientific merit for future human health risk assessment.

Evaluation and interpretation of toxicology data in New Zealand is generally in accordance with internationally accepted criteria such as specified by OECD, US EPA, or WHO. These laboratory-based regulatory toxicology studies allow for the characterisation of a chemical in terms of its potential to cause genetic mutations, foetal abnormalities, and target-organ toxicity, as well as defining No Observable Effects Levels (NOELs). The NOELs are needed for setting rigorous acceptable daily intakes (ADI) for 1080, which can form the basis for determining a Maximum Acceptable Value (MAV) in drinking water.

A battery of regulatory studies were completed in the USA before 1995, since 1080 is still used in the USA in livestock protection collars. This included 17 studies on product chemistry, six studies on wildlife hazards, and four studies on human health. The results from these studies were summarised in the Science Workshop Proceedings on 1080 (Fagerstone *et al.,* 1994).

The most important of these studies to the health of those involved in pest control in New Zealand was on acute dermal toxicity of 1080 in rabbits. In this test, five male and five female rabbits for each of four dose levels, were treated dermally with 1080 paste. The estimated LD_{50} was 324 mg kg^{-1} for females and 277 mg kg^{-1} for males. It had long been known that 1080 can be absorbed through the gastrointestinal and respiratory tracts, open wounds, and mucous membranes, but is less readily absorbed through intact skin (Atzert, 1971). However, the results of this study demonstrated that poor dermal absorption of 1080 (Atzert, 1971) does not imply no absorption, and there are obvious implications with regard to enforcing strict codes of practice and appropriate protective clothing for those involved in the manufacture or handling of 1080 baits.

Regulatory toxicology studies are usually conducted before the launch of new drugs or pesticides. Alternatively, they may be conducted on older products, such as 1080, to provide an update to

Table 1: *Toxicology studies on 1080 : current status (* = new studies)*

Study types	Status
Acute toxicity	Extensive database in the literature (see Rammell and Fleming, 1978; Seawright and Eason, 1994; Eisler, 1995)
Skin and eye irritation	Completed (see Fagerstone *et al*., 1994)
Skin sensitisation	Completed (see Fagerstone *et al*., 1994)
*Ames assay**	Completed January 1998
*Mouse lymphoma assay**	Completed January 1998
*Mouse micronucleus test**	Completed January 1998
Developmental toxicity in rats (including pilot study)*	Completed January 1998
3-month feeding study in rats (including pilot study)*	Scheduled for completion in October 1999
Metabolism/pharmacology studies	Extensive published database (see Eason *et al*., 1994)
Environmental studies	Extensive published database (see Parfitt *et al.,* 1994; Spurr, 1990, 1994)

the toxicology data generated before the new standards and data requirements that are now commonplace in the 1990s.

The new regulatory toxicology studies listed in Table 1 were conducted following internationally recognised protocols. Since the methods are routine and described in full elsewhere (Wilson, 1965; Ames, McCann, and Yamasaki, 1975; Hoddle *et al*., 1983; Blazak *et al*., 1989) and the results will be published in full in a toxicology journal in 2001, the methodologies and results are summarised below. These data provide answers to the following general questions: Does 1080 alter genetic material (mutagenic) and therefore have the potential to cause cancer, and does it cause birth defects (developmental toxicant)?

In the rest of this paper we review the key findings from the most recent regulatory toxicology studies and environmental monitoring, and explore the implications of this new information.

Results and Discussion

Mutagenicity studies

When screening for potential mutagenicity, three tests are routinely undertaken (two *in vitro* and one *in vivo*).

(i) ***Ames assay (in vitro bacterial gene mutation assay)***
This test is based on the histidine reversion assay using *Salmonella* to detect point and frame shift mutations (Ames, McCann, and Yamasaki, 1975). Sodium monofluoroacetate (1080) was tested at 10, 31.6, 100, 316, and 1000 μg/plate. No mutagenicity was observed at any dose level.

(ii) ***Mouse lymphoma assay (in vitro mammalian gene mutation assay)***
This test, which is similar to Ames assay, uses a mouse lymphoma L5178Y cell line with the thymidine kinase gene as the endpoint to detect mutations (Blazak *et al*., 1989). Sodium monofluoroacetate (1080) was tested at 5 to 5000 μg ml^{-1}. No mutagenicity was observed at any dose level.

(iii) ***Mouse micronucleus assay (in vivo bone marrow assay to detect chromosomal anomalies)***
In contrast to the two previous tests the mouse micronucleus assay is an *in vivo* rather than *in vitro* test. Mice are dosed with a toxicant and the effects of chemicals on rapidly dividing cells in the bone marrow are determined (Hoddle *et al*., 1985). Sodium monofluoroacetate (1080) was dosed orally to mice at 0.75, 1.5, 3.0, 6.0, and 7.5 mg kg^{-1}. No mutagenicity was observed at any dose level.

The results of these three complementary genetic toxicology studies provide strong support for the hypothesis that 1080 is not genotoxic. They also provide strong, but not conclusive, evidence that it is not carcinogenic. [Some carcinogens, e.g., hormones, heavy metals, and irritant fibres, cause cancer by non-genotoxic mechanisms, but they are relatively uncommon].

Pilot developmental toxicity study

The potential adverse effects of 1080 on foetuses was assessed in rats with a "pilot" dose-ranging study preceding the main assessment.

A total of five female rats per treatment group were dosed orally with 1080 in solution at 0.0 (i.e., water alone), 0.05, 0.1, 0.5, or 1.0 mg kg^{-1} day^{-1} from day 6 through day 17 of gestation (inclusive). All females were euthanased on day 20 (gestation = 21 days).

No effects on uterine parameters (gravid uterine weight, number of implantations, resorptions, and live and dead foetuses) were observed at any dose. Maternal toxicity (weight loss and 60% mortality) and decreased litter size were observed at 1.0 mg kg^{-1} day^{-1}. The no adverse effects dose (NOEL) from the pilot study based on gross pathological examination, was 0.5 mg kg^{-1} day^{-1}, but the foetuses were not examined.

Main developmental toxicity study

A total of 26 female rats per treatment group were dosed orally with 1080 in solution at 0.0 (i.e., water alone), 0.1, 0.33, or 0.75 mg kg^{-1} day^{-1} from day 6 - 17 of gestation, and euthanased on day 20.

No maternal mortality or clinical toxicity was observed at any dose. However, decreased maternal body weight, weight gain, and food consumption was observed at 0.75 mg kg^{-1} day^{-1} during dosing. This was accompanied by decreased foetal body weight at 0.75 mg kg^{-1} day^{-1}.

As is standard practice in these studies, half of the foetuses were fixed for examination of soft tissue. No external or visceral (soft tissue) abnormalities were observed at any dose.

The remaining half of the foetuses were fixed for skeletal examination. Treatment-related skeletal abnormalities were observed at 0.33 and 0.75 mg kg^{-1} day^{-1} (see Table 2). Abnormal development of the forelimb, characterised by bent scapula, humerus, and radius or ulna, was observed in 24%, 12% and 8% of litters, respectively, at 0.75 mg kg^{-1} day^{-1}. The changes were mild, but treatment-

Table 2: *Effects of Oral Administration of 1080 on the Incidence of Skeletal Anomalies in Sprague-Dawley Rats - Main Study (* = within the normal historic incidence for this species, therefore not significant)*

Uterine parameter	Classification	Dose Level (mg kg^{-1} day^{-1})			
		0	0.1	0.33	0.75
No. foetuses/litters examined		160/25	160/25	156/25	151/25
Bent scapula	Malformation	0/0	0/0	1/1	17/6
Bent humerus	Malformation	0/0	0/0	0/0	5/3
Bent radius and ulna	Malformation	0/0	0/0	0/0	2/2
Bent ribs	Variation	0/0	2/2*	10/5	39/13
Rudimentary rib	Variation	36/18	27/13	30/14	22/12
Sternebra unossified	Variation	15/10	17/9	26/13	55/18

related, and classed as malformations, i.e., irreversible alterations of skeletal development. Bent ribs were observed in 20% and 52% of litters at 0.33 and 0.75 mg kg^{-1} day^{-1}, respectively. Unossified sternebrae were also observed in 72% of litters at 0.75 mg kg^{-1} day^{-1}. These developmental abnormalities are classed as variations, as opposed to malformations, because they are considered to be reversible, and may potentially be due to maternal stress rather than a direct effect of the toxin on the foetus.

Summary of findings of developmental toxicity studies

The NOEL for maternal toxicity was determined to be 0.33 mg kg^{-1} day^{-1}. The NOEL for developmental effects was 0.1 mg kg^{-1} day^{-1}, based on observation of dose-related increase in bent ribs (a variation) at ≥ 0.33 mg kg^{-1} day^{-1}. Sodium monofluoroacetate can be considered to be teratogenic in rats at 0.75 mg kg^{-1} day^{-1}, based on an increased incidence of forelimb malformations. It should be noted that this is a significant dose to the female rats, and although no mortality was observed, 60% of females given a higher dose (1.0 mg kg^{-1} day^{-1}) in the pilot study died.

Implications of findings of teratogenic potential of 1080

Spielman, Mayer-Wendecker and Spielman (1973) reported that 1080 at a dose just below the maternal LD_{50} was not teratogenic in rats. The embryos in this study showed no macroscopic nor skeletal abnormalities and the weights of the embryos and placenta were unchanged. However, Spielman *et al.*'s work involved only a single oral dose and the results contrast with the present investigation as well as an earlier report by De Meyer and De Plaen (1964) (Table 3).

Critical evaluation of the results of the study by De Meyer and De Plaen (1964) is not possible because of the lack of detail given in the methods and results sections. Comparison of the study by Spielman *et al.* (1973) and our investigation is more relevant to risk assessment in New Zealand. It is noteworthy that the NOEL derived from the present multiple dose study (0.1 mg kg^{1} day^{-1}) was 10-fold less than the single-dose NOEL (1 mg kg^{-1}) reported by Spielman *et al.* (1973).

The results of the present developmental toxicity study reinforce the need for adequate safety standards in handling and use of 1080, but do not preclude its proper use. Individuals with a potential for repeated exposure to 1080 (e.g., workers in the pest control industry) need to exercise extreme care when handling this compound, both because of its extreme acute toxicity and also a risk of developmental toxicity.

Another commonly used vertebrate pesticide (rodenticide), warfarin, has been found to be both embryotoxic and teratogenic to rats when administered in single or repeated doses during organogenesis. At dose levels of 0.04 to 8 mg kg^{-1}, warfarin causes foetal death or gross structural malformations, including internal hydrocephalus, pes varus, and anomalies of skeletal ossification

Table 3:T*eratogenicity studies on 1080*

Source	Dose regime	Species	Results
1. De Meyer and De Plaen, 1964	unclear	rat	+
2. Spielman *et al.*, 1973	1 mg kg^{-1} single dose	rat	-
3. MPI Research / Landcare Research 1998	0.1, 0.33, and 0.75 mg kg^{-1} day^{-1} for 12 days	rat	+

(Mirkova and Antov, 1983). Human developmental toxicity has been reported when anticoagulants, particularly warfarin, have been administered as therapeutic agents during pregnancy (Hall, Pauli and Wilson, 1980). The mechanism of warfarin-induced foetal toxicity is quite different to 1080. Nevertheless, its effects confirm the need for care when handling anticoagulant poisons.

Other chemicals known to cause human developmental toxicity which are in widespread use include various pharmaceutical agents (including some antibiotics, antihypertensive agents, chemotherapeutic agents, anticonvulsants, and lithium), metals (mercury and lead), and recreational drugs (ethanol, cocaine, and cigarette smoke) (Rogers and Kavloch, 1996).

The likelihood of 1080 causing developmental toxicity in humans is not known. Of the >3300 chemicals tested for teratogenicity worldwide, nearly 1000 have been shown to be teratogenic in at least one species of laboratory animal (Schardein, 1993). By contrast, only 35 chemicals or conditions (including radiation exposure, infection, and metabolic imbalances) are known to alter human pre-natal development (Shepard, 1992). This partly reflects a lack of human data, but also indicates that some chemicals may cause developmental toxicity in laboratory animals without being human teratogens. However, in the absence of data to the contrary, it is prudent to assume that 1080 may pose a risk of human developmental toxicity, and take steps to ensure that pest control workers and the general public are not exposed to developmentally significant doses.

Environmental Fate and Persistence Studies: Results and Discussion

In New Zealand we have been re-assessing the fate of 1080 in water and in non-target species, especially livestock and invertebrates (Eason, Wright, and Fitzgerald, 1992; Eason *et al*., 1993; Rammel, 1993; Eason *et al*., 1994a; Eason, Gooneratne, and Rammell, 1994b). Over 70 studies have been completed on the non-target impacts of 1080 on wildlife in New Zealand (Spurr, 1994). This work is complemented by metabolic studies on the breakdown of fluoroacetate and fluorocitrate in the United States (Kirk and Goldman, 1970; Soiefer and Kostyniak, 1983, 1984; Tecle and Casida, 1989), Canada (Sykes *et al*., 1987), Australia (King *et al*., 1994), and South Africa (Meyers, 1994), and by the first series of regulatory toxicology studies to meet EPA requirements (Fagerstone *et al*., 1994).

Fate of 1080 from baits

Sodium monofluoroacetate derived from baits will be dispersed by water since it is highly water soluble and mobile (Parfitt *et al*., 1995). Cereal baits disintegrate readily, but 1080 is retained in carrot baits and will only slowly leach from carrots into the soil (Bowen, Morgan, and Eason, 1995). If heavy rainfall follows the use of 1080 baits, dilution to unmeasurably small concentrations (<0.0001 ppm) may precede biodegradation. However, control operations are planned to coincide with periods of dry weather, and some defluorination by micro-organisms on the decaying baits and in the soil around baits is probable, particularly if the baits become moist. Under favourable conditions such as 11–28°C and 8–15% moisture, 1080 may be significantly defluorinated in 1–2 weeks (King *et al*., 1994). In less favourable conditions, breakdown might take several weeks, and in extreme cold and drought, 1080 residues might persist in baits or in the soil for several months.

Monitoring 1080 in water

Between 1990 and January 1998, field-water-monitoring programmes for 1080 residues were undertaken after 40 large-scale possum and one rabbit control operation using aerially dispersed 1080 baits. A total of 868 water samples have been collected after control operations and there has been no evidence of significant or prolonged 1080 contamination in surface or ground waters (Eason *et al*., 1992; Hamilton and Eason, 1994; Parfitt *et al*., 1994; Meenken and Eason, 1995; Fowles and Williams, 1997; Booth *et al*., 1997).

Most (94.7%) of the samples contained no detectable 1080. However, residues of 1080 were found in 5.3% of the samples analysed, but in most of these the 1080 was below 1 part per billion (ppb). In some of these instances, small numbers of baits were found in the watercourses near to where the samples were taken. Most of the water sample results presented in Table 4 are derived from samples from stream and waterways from within or adjacent to areas where 1080 baits have been dispersed. Thirty-nine samples have been taken from reticulated water after aerial sowing of 1080 baits; all of these were negative.

A series of laboratory studies have shown that 1080 would be biodegraded by aquatic plants and micro-organisms if small amounts entered waterways. The rate of breakdown is temperature dependent and in fast-running streams dilution of the toxin would be more important in reducing the presence of 1080 to toxicologically insignificant

concentrations. The breakdown of this toxin occurs rapidly at higher temperatures but still occurs at 7°C within 1–2 weeks (Ogilvie, Hetzel, and Eason, 1996).

Conclusion and Risk Assessment

The process of risk assessment typically involves hazard identification and exposure assessment. The risks associated with 1080 to human health (or livestock or non-target wildlife) is determined by the innate toxicity of 1080 and the potential for exposure, i.e.:

Risk = Hazard x Exposure

In a recent review Beasley (1996) pointed out that human exposure to 1080 might arise from drinking contaminated water, ingestion of toxic baits, consumption of food contaminated by contact with

Table 4: *Water analysis after 1080 operations. Further water sampling and residue analyses are anticipated as part of standard operating procedures enforced by Medical Officers of Health when granting approvals for aerial 1080 operations.*

Location	Date	Total number of samples taken in operational area	No. with residues	Highest concentration ($\mu g\ L^{-1}$)
Waipoua	1990	36	0	-
Rangitoto	1991	20	0	-
Blackstone Hill	1992	23	11	0.6
Mt Taranaki	1993	125	15	<0.3
Woodside	1993	55	0	-
Hunua Range	1994	136	7	0.7
Mt Taranaki	1994	63	0	-
Marlborough Sounds	1994	26	5	3.4
Wairarapa	1994	31	0	-
Hawke's Bay	1994	15	0	-
Ohakune	1994	6	1	0.2
Whangarei	1994	18	0	-
Karioi	1994	10	1	0.8
Manawatu	1994	21	0	-
Waimakariri	1995	4	1	0.2
Manawatu	1995	48	0	-
Hawke's Bay	1995	8	1	0.3
Ohakune Erua Forest	1995	3	0	-
Tongariro National Park	1995	8	0	-
Northland	1995	11	0	-
Tararua Ranges	1995	11	0	-
Hawke's Bay	1995	9	0	-
Waimarino Forest	1995	4	0	-
Wairarapa	1996	7	0	-
Pirongia	1996	7	0	-
Raukumara Ranges	1996	37	1	0.2
Waikato	1996	4	0	-
Levin Buffer	1996	8	0	-
Manganuiateao	1996	3	1	3.5
Waitohu	1996	4	0	-
Wairokau Stream	1997	4	0	-
Raukokore Stream	1997	12	0	-
Ohakune	1997	10	0	-
Pareora River, Timaru	1997	2	0	-
Rangataua Forest	1997	40	0	-
Te Whaiau Spillway	1997	3	1	2.4
Opotiki	1997	9	1	0.5
Oronui Stream	1997	12	0	-
Warawara Forest	1997	4	0	-
Mt Bruce/Mikimiki	1998	10	0	-
Kuharua Tb	1998	1	0	-
Totals		868	46	

bait, or by inhalation of bait dust or contact with 1080 solution by pest control operators and bait manufacturers. The most significant potential exposure source to the general public was viewed to be the contamination of surface water in public water system catchments by aerially sown 1080 baits.

As indicated previously, 1080 has never been detected in reticulated water at the point of consumption. The highest concentration measured in surface water within the boundaries of pest control areas following aerial 1080 bait distribution is 3.5 $\mu g\ l^{-1}$ (ppb) (Table 4). If this concentration is chosen as a worst-case exposure scenario, the potential risk of adverse developmental effects from exposure of pregnant women to drinking water following possum control operations can be crudely assessed. The assumptions used in these calculations are those recommended by the Ministry of Health (Drs G. Durham and N. Foronda, *pers. comm.*), and are intended to be very conservative (i.e., protective). If a 50-kg woman consumed water containing 1080 at 3.5 $\mu g\ l^{-1}$ to provide all of her 2-litre daily intake during the first 90 days of pregnancy (the approximate period of organogenesis during which the foetus is most sensitive to toxic insult), she would receive a daily 1080 dose of 0.14 $\mu g\ kg^{-1}\ day^{-1}$. The "safe human exposure" for developmental end points is derived by applying a 1000-fold safety factor to the NOEL from the developmental toxicity study, i.e., 0.1 $mg\ kg^{-1}\ day^{-1} \div 1000 = 0.1\ \mu g\ kg^{-1}\ day^{-1}$. Therefore, the potential dose received under this worst-case scenario is slightly greater than the "safe human exposure" derived from the developmental toxicity study (after application of the 1000-fold safety factor).

In light of these findings, the Ministry of Health recommended in 1998 that potable water from catchments treated with 1080 be monitored to confirm that concentrations do not exceed 2 $\mu g\ l^{-1}$. The likelihood of exceeding this value in drinking water is very small, since it has only rarely (i.e., in three samples out of 868) been exceeded in small water bodies within the operational area **immediately** after aerial 1080 bait distribution (see Table 4). Further, these reported levels were only detected for short periods of time (days). Continuous exposure for the 90 days of the first trimester of pregnancy would be the comparable length of exposure to that experienced by the pregnant rats. The current provisional maximal acceptable value in the New Zealand Drinking Water Standards is 5 $\mu g\ l^{-1}$.

All possible precautions should be taken to prevent contamination of food with 1080, including the use of 1080 pastes that are not attractive to bees to prevent residues in honey. Similarly, low-level livestock exposures should be avoided to prevent residues in meat or milk. Current safety practices at manufacturing plants and for pest control operators should be reviewed, and a study should be conducted to quantify exposure and assess risk to workers in the 1080 bait manufacturing and distribution industries.

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