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Sodium fluoroacetate (1080): assessment of occupational exposures and selection of a provisional biological exposure index

Michael Beasley, Penny Fisher, Cheryl O'Connor, Charles Eason

Abstract:

Aim Sodium fluoroacetate (1080) is used for control of vertebrate pests in New Zealand. Little is known about chronic effects in humans, but animal studies demonstrate potential for adverse fetal, male fertility, and cardiac effects. We aimed to employ analyses of 1080 to help assess the degree of exposure of bait formulators and distributors, and identify specific tasks where exposure reduction appeared most indicated. We also aimed to utilise the (limited) 1080 toxicity data to assess the significance of the analytical results.

Method Exposures during various activities were assessed by monitoring air levels and blood and urine concentrations. To help evaluate the results, a provisional "biological exposure index" (BEI) was later derived, by extrapolating from experimental data.

Results Early monitoring indicated exposures were highest in relation to (cereal) bait manufacturing and aerial carrot baiting procedures. A provisional BEI of 15 µg/L for 1080 in urine was proposed.

Conclusion Further protective measures and ongoing workplace monitoring are required, particularly in the above situations. Compliance with the current BEI cannot guarantee complete safety. Any information regarding chronic adverse effects in humans, along with the associated urine levels, would assist risk assessment. Further investigation of the human kinetics of fluoroacetate would be helpful.

In New Zealand, introduced vertebrate pests such as brushtail possums cause widespread damage to agricultural land and native forests. Possums are also the most significant wildlife reservoir for (bovine) tuberculosis, so control of their populations remains a priority. In some instances, the aerial application of the vertebrate pesticide sodium fluoroacetate (1080) in baits is considered the most cost-effective method for large-scale possum control operations.[1] However increasing concern has arisen over broad-scale application of 1080, particularly its wider impact on non-target species and possible adverse effects on the environment.[2] Concern extends to possible human risks, especially from aerial operations where contamination of waterways might occur.

While 1080 is highly toxic, the risk of acute human poisoning from environmentally distributed bait is considered low, because of the relatively low concentrations used in bait formulations (up to 0.15% w/w), the size and application rates of baits, and the location of baiting operations.

There are no well validated cases of "exploratory" 1080 poisoning in children in NZ—in contrast to the United States (US) decades ago, where 1080 was used in more concentrated form as a household rodenticide, with occasional severe or tragic consequences.[3,4] Intentional ingestion has also been responsible for serious human poisoning in other countries,[5,6] but very few proven cases have been reported in NZ.

Limited applications as a vertebrate pesticide in the US,[7] and elsewhere,[8] have meant that overseas regulatory requirements for toxicological data have been limited. Given the ongoing unique use patterns in NZ (and Australia), the need for an updated regulatory toxicology database was recognised[7] and relevant studies meeting internationally recognised protocols were commissioned. These included an *in vivo* developmental toxicity study, which estimated a "no observed effect level" (NOEL) of 0.1 mg/kg/day for teratogenic effects,[9] and a 90-day oral gavage dose study;[10] both in rats.

In the latter, a "lowest observed effect level" (LOEL) of 0.25 mg/kg/day was reported, where the heart weight was increased, and (in males) effects observed in the epidiymides and testes, with statistically significant adverse changes in some sperm parameters. A daily dose of 0.075 mg/kg/day was the "no observed effect level" (NOEL) for both these types of effects.[10] A similar, unpublished study of subchronic effects produced a NOEL estimate of 0.05 mg/kg/day for cardiotoxicity and male gonadotoxicity.[11]

Oligospermia and/or aspermia were noted in mink ingesting 0.08 mg/kg/day,[12] suggesting a general mammalian effect on testicular and epididymal function. It is clear both the testis and heart are sensitive target organs; indeed adverse cardiac effects were recognised in livestock from plant sources of fluoroacetate prior to its usage as a pesticide,[13,14] and later studies provided further evidence.[15]

The mechanism underlying these chronic effects are not well established. However it is likely its impairment of aerobic metabolism (due to inhibition of the citric acid or Kreb's cycle), largely responsible for acute 1080 poisoning, is a significant factor. Cellular hypoxia is a recognised cause of adverse cardiac, fetal, and testicular effects.[16,17] Some fluoroacetate is converted *in vivo* to fluorocitrate, which plays a major role in disrupting the citric acid cycle,[8] as well as risking hypocalcaemia.

Given clear laboratory evidence of sublethal effects of oral exposure, there is obvious concern regarding risks of similar effects from human exposures. Pest control industry workers engaged in the preparation and distribution of 1080 baits are the group most likely to be repeatedly exposed, and this paper outlines the initiation of protocols for monitoring such workers in NZ. Our aims were to employ analyses of 1080 as a tool to help identify hazardous situations, where exposure control measures were most indicated.

Here we report the earliest analytical findings, and our subsequent efforts to interpret these in terms of their possible risk, in the face of little previous human data. This involved establishment of a provisional "biological exposure index" (BEI) for 1080, in response to a request for a specific "action" criterion by the regulatory authority.

(A BEI generally indicates a concentration in a biological fluid below which it is considered nearly all workers should not experience adverse health effects from a chemical. Historically, it has often been based on a "threshold limit value" (TLV), which is an average air concentration under which it is believed nearly all workers may be repeatedly exposed (e.g. for 8 hours, 5 days a week) without such effects. The term "workplace exposure standard" (WES) has also been applied to an air level similarly designed to protect workers from the adverse effects of long term exposure).

Method

Identification of subjects and sample collection—After providing information to the pest control industry regarding the proposed monitoring programme, and gaining ethics committee approval (Southern Regional Health Authority Ethics Committee Otago, No. 98/11/088), volunteers from various occupational groups within the industry were obtained. They were classified into groups; workers involved in 1080 cereal bait manufacture at either of two sites (n=9), and applicators involved in either of two (separate) aerial carrot bait (n=9) or aerial cereal bait (n=11) operations. This provided a diverse, if relatively small sample. The details are outlined in Table 1.

Table 1. Monitoring of 1080 operators: work activity, sample type, and timing; numbers sampled

Bait manufacture (*n*=9; 6 at Site 1 and 3 at Site 2)						
Day	***Blood***		***Urine***		***Air***	
	am	pm	am	pm	am	pm
1	9	9	–	9	2	6
2	–	–	–	9	–	6
3	9	9	–	9	2	2
4	–	–	–	9	–	–
5	9	9	–	9	–	–
8	9	9	–	9	–	–
Aerial carrot baiting (*n*=9; 5 at site 1 and 4 at site 2)						
1	9	8	–	8	–	6
2	4	3	–	6	–	–
3	4	3	–	–	–	3
4	–	–	–	5	–	3
5	4	4	–	8	–	–
6	–	–	–	4	–	–
Serial cereal baiting (*n*=11; 6 at Site 1 and 5 at Site 2)						
1	10	10	–	10	–	5
2	5	5	–	1	–	4
3	–	–	–	1	–	–
4	5	4	–	5	–	–
5	5	5	–	5	–	–

Measurement of air levels was targeted to clarify specific tasks presenting inhalation hazards. Workplace contamination at sites of bait manufacture and application was monitored by measuring the concentration in respirable airborne particles <10 µm in Stokes diameter. Gilian air pumps, with intake close to the face, were worn on at least 2 separate days. They were set to sample ~ 2 litres per minute volumetric flow rate- and calibrated at the start and end of each sampling.

The average pump flow rate and sampling duration were used to calculate the total volume of air drawn through each cartridge, and the average air concentration (µg/m^3) was calculated from the mass of 1080 collected on the air filter (0.8 µm mixed cellulose ester filter) divided by the above volume.

Monitoring for larger 1080 particulates was also carried out, as these may be deposited on horizontal surfaces, with risk of inadvertent hand to mouth contact. Swabs were taken from representative sites on the stair and platform rails, desk, taps, and toilet door handle on 2 days during each site visit using the air filters moistened with methanol which were wiped over a small area using a gloved hand.

Blood and urine tests for 1080, being biomarkers of absorption from all relevant tasks and exposure routes, were also undertaken. Blood samples (10 ml) were collected at the start and end of working days (as shown), by professional (Medlab) staff. Plasma were collected, held at 20ºC, and (along with urine samples) delivered to the Landcare Research laboratory for analysis. Total urine for the working day (approx. 12 hours) was collected every day for 6 days, or the length of the field operation. Urine was collected in a 1000-ml sample bottle whenever toilet visits were made.

Analysis of samples for 1080 concentrations—Testing was conducted using a gas chromatography method developed by Landcare Research and based on the work of Ozawa and Tsukioka.[18,19] Plasma (after precipitation of the protein with acetonitrile) and urine (or water) samples were added to 2% sodium chloride solution for derivatisation. The 1080 in aqueous extracts or urine samples was acidified with hydrochloric acid and converted to the dichloroaniline derivative with N,N' dicyclohexylcarbodiimide (DCC) and 2,4 dichloroaniline (DCA) using ethyl acetate as solvent.

The derivative was cleaned on a silica solid-phase extraction cartridge to remove excess derivatising agent, eluted with toluene, and quantified by gas chromatography on a BP-5 capillary column with electron capture detection. The method limit of detection (MLD) was 0.006 µg/ml in blood and 0.0005 µg/ml in urine. The air filter and swab samples were eluted with 50 ml 2% saline solution, then prepared as for a water sample, with a MLD of 0.005 µg 1080.

Initial defining of exposure categories—Initially, three levels of personal exposure were defined (Table 2), on the basis of 1080 concentrations found (or not) in blood and urine.

Table 2. Initial classification of exposure levels

Classification	Measured 1080 concentration in urine and blood
Level 1	below detection limits in blood (<0.006 µg/mL) and urine (<0.0005 µg/mL)
Level 2	not detectable in blood (<0.006 µg/mL), and also <(0.02 µg/mL) in urine
Level 3	blood level ≥(0.006 µg/mL), and/or urine level ≥(0.02 µg/mL)

Derivation of a biological exposure index (BEI) for occupational exposure to 1080—It became clear that a formal, "transparent" guideline value was needed, to more critically evaluate the significance of individual biological monitoring results. A value based on urine sampling was preferred, due partly to its easier detectability than in blood, and greater worker acceptance.

However there is little human data shedding light on what an appropriate biological exposure index would be. One report outlines an incident of excessive exposure from misapplication of 1080 as rat poison in a steel mill, with the generated dusts causing relatively high acute exposures, with several workers becoming seriously ill.[20]

There is also a report of salivation, visual disturbance, paresthesiae, convulsions, and coma after a wind gust blew concentrated powder into one worker's face.[21] However no data were found on chronic, low level human exposures which could indicate minimum daily toxic doses, or the corresponding urine concentrations. Therefore, animal data were utilised to derive an estimated acceptable daily exposure to 1080.

Firstly an appropriate NOEL estimate for 1080 (in rats) was identified; while the lowest reported figure was 0.05 mg/kg/day,[11] the value of 0.075 mg/kg/day, from a more recent study[10] meeting current internationally recognised protocols, was chosen. Then a safety or uncertainty factor (SF, UF) of 10 was applied, in effect allowing for the possibility of a 10-fold greater susceptibility of humans relative to rats. Lastly, the need for further UFs was considered.

In public and environmental health contexts, regulatory agencies routinely incorporate extra UFs, including factors to account for limited data sets and relative lack of chronic studies specifically, which circumstances both applied in the case of 1080.Thus the minimum (mammalian) study requirements

are two chronic, one multigeneration reproductive, and two developmental toxicity studies; so the lack of chronic (lifetime) 1080 studies was a major reason for its adjudgedly inadequate database.

On the other hand, a major purpose of lifetime studies is to assess carcinogenicity, but three complementary toxicity studies had previously indicated that 1080 is not mutagenic, and therefore "not anticipated" to be a carcinogen,[10] or at least not a genotoxic one. Therefore an extra safety factor (of 3) was applied to the chosen NOEL, to derive a so-called reference dose (RfD).

Some approximations and assumptions were then made regarding the likely kinetics of 1080 in humans, to determine the approximate urine concentration to be expected with daily intake of the RfD. The relevant calculations are presented in the Results section.

Results

Air, blood and urine monitoring

Personal air samplers generally showed low levels of airborne 1080 during bait application, with maximum concentrations of 5.54 and 5.62 µg/m^3 respectively for the two aerial carrot operations. Maximum concentrations for the aerial cereal bait operations were lower, at 0.8 and just 0.09 µg/m^3 respectively. However much higher levels were found at times at the factories involved in bait manufacture.

At both sites, a brief but high exposure (~1.9 mg/m^3 over 18 minutes, ~3.5 mg/m^3 over 36 minutes) while weighing out 1080 powder (of technical concentration at least 97%), was sufficient to exceed the NZ workplace exposure standard (WES) of 0.05 mg/m^3 as an 8-hour time weighted average (TWA),[22] even without adding the (much lower) exposures over the rest of the day. However, as these workers were wearing a respirator during the weigh-out period, their effective exposure (inhaled amounts) would have been within that permitted by the WES.

Surface swabs from one cereal bait manufacture site showed a clear relationship to when powder was handled. With the bait distribution operations, less detailed data was obtained (air monitoring was intended primarily to compare the two bait types and to "scope" whether any specific tasks were associated with high airborne levels).

Table 3 summarises the blood and urine results (classified as per Table 2); the maximum concentration found in samples from each worker was used to categorise their 'level' of exposure, with no indication of how many of their samples contained no detectable 1080. Of the nine workers involved in bait manufacture, three had a level 3, and six had a level 2 exposure, detected in at least one sample. Of the nine monitored during aerial carrot baiting operations, four had a level 3 exposure and five a level 2 exposure, on at least one occasion. This latter occurred despite the relatively low air levels noted. Workers in aerial cereal baiting had lower exposure profiles; six having level 2 and five level 1 (no detectable) exposure.

Overall, level 2 exposures were the most common (comprising ~60%).

Table 3. Levels of exposure: monitoring results by occupational activity

Occupational activity	Exposure levels (subject numbers, by site)					
	Level 1		Level 2		Level 3	
	(Site 1)	(Site 2)	(Site 1)	(Site 2)	(Site 1)	(Site 2)
Aerial cereal baiting	2/6	3/5	4/6	2/5	–	–
Aerial carrot baiting	–	–	3/5	2/4	2/5	2/4
Bait manufacture	–	–	4/6	2/3	2/6	1/3

Calculation of a biological exposure index

Derivation of reference dose

- Chosen NOEL: 0.075 mg/kg/day[10]
- Selected total UF or SF: 30 (comprising factors of 10 and 3)
- Therefore derived reference dose (RfD) was 0.0025 mg/kg/day

Estimation of urine concentration expected from daily intake of reference dose— A biological exposure index (BEI) was derived by estimating the likely minimum urine concentration (as a 24-hour average) to be expected following daily intake of the reference dose. The urinary level will depend not only on that dose and body weight, but also the percentage of 1080 excreted in urine and the daily urine output. The steps involved in calculating urine concentrations corresponding to the reference dose are outlined below. (This approach is based on complete absorption of the RfD.)

- Acceptable daily ("reference") dose (RfD) = 0.0025 mg/kg/day
- Acceptable daily urine excretion = RfD × Wt (kg) × (fraction or %ge excreted in urine; F_e)
- Acceptable average urine concentration, C_u = (RfD × Wt × F_e) / (24-hour urine volume, V_{24})
- Therefore general calculation for the mean urine concentration to be expected from the RfD is:
- C_u (mg/L) = 0.0025 mg/kg × Wt (kg) × Fe / V_{24}

The result will depend on individual values for Fe, V_{24}, and body weight. Using the fairly conservative figure of 60 kg for an adult weight, Table 4 indicates the derivation of the selected value.

Table 4. Urine levels (mg/L) corresponding to RfD as modified by urinary excretion and flow

Urine output	Fractional urinary excretion of (unchanged) 1080 in 24 hours (F_e)				
(24 hr, V_{24})	20%	30%	40%	50%	60%
1.5	(0.02)	(0.03)	(0.04)	(0.05)	(0.06)
1.7 L	(0.0175)	(0.0265)	(0.035)	(0.044)	(0.053)
2 L	**(0.015)***	(0.0225)	(0.03)	(0.0375)	(0.045)
2.5	(0.012)	(0.018)	(0.024)	(0.03)	(0.036)

Unfortunately, no data was located shedding light on the typical elimination half life of 1080 in humans, nor, more specifically, the fraction likely to be excreted in urine over any given time. However various experimental data (discussed below) led us to believe that at least 20% of an absorbed dose of 1080 will likely be excreted in urine in unchanged form within 24 hours. Employing also an estimate for daily urine output of 2 litres in adults, it was thus calculated that the average urinary concentration in a 60 kg worker with a daily dose of 0.0025 mg/kg would likely be at least 0.015 mg/L, and this value was selected as a provisional BEI.

Discussion

These monitoring programmes were limited by the relatively small numbers of workers involved, and the self-selected nature of the "sample". (The age, ethnicity and gender mix of volunteers was not examined, partly to preserve confidentiality, and their degree of representativeness of the wider pest control workforce cannot currently be assessed.) There was also limited longitudinal monitoring and tracking of individual workers. However there was sufficient data and consistency therein to identify the more hazardous operations (and occasionally, specific tasks).

Early monitoring indicated a need for improvement in aspects of the cereal bait manufacturing environment and in aerial carrot baiting procedures. The latter (at preparation stage) involves dipping carrots into concentrated solutions of 1080, with risks of splashes to the face and other skin areas; it was not uncommon for operators to be wearing contaminated, damp clothing for prolonged periods.

In contrast, cereal baits were prepared at the formulating factories, and products handled by the "downstream" user contained low levels of 1080. Further monitoring indicated aerial carrot baiting operations remained a significant exposure source, despite increasing use of long water proof gloves and face shields, (and masks in the majority). Likely contributory factors included inconsistent use of and/or substandard protective equipment, and individual hygiene practices (including possible inadvertent urine contamination during sample collection).

It was thought level 1 exposures were unlikely to be harmful, given no detectable 1080, and that level 2 were of relatively low risk, as none was detectable in blood, but the significance of the urine levels became a little more clear after derivation of the BEI.

A BEI should ideally be set by consideration of relevant data relating to the human health experience with chronic exposure. Indeed the most usual, if not always ideal, means of establishing a BEI has been from the threshold limit value (TLV) in air, itself usually derived directly from human experience. However, there was insufficient human data to enable this.

The American Conference of Governmental Industrial Hygienists (ACGIH), in the documentation of its TLV (adopted in NZ as a WES) does not outline in (quantitative) detail any underlying rationale based on human exposures, and while it states the selected TLV should minimise the risk of acute systemic toxicity, it does not explicitly extrapolate from any chronic exposure data.[23] Similarly, LaGoy et al (1992) described excessive exposures following a steel mill contamination incident, but this

resulted in several workers becoming seriously ill, and the report does not shed light on possible more subtle effects from lower level longer term exposure.[20]

Thus neither of these sources are highly informative in terms of establishing a BEI. However it is reassuring to note that our "reference dose" of 0.0025 mg/kg/day is just half that utilised by the above authors in their development of suitable cleanup levels following the mill incident.[20] Similarly, it is somewhat more conservative than the TLV (WES) of 0.05 mg/m^3, in that a 70 kg worker under moderate work load inhaling 10 m^3 of air per work day at the WES would have a respiratory intake of 0.5 mg or ~0.007 mg/kg/day. Moreover, unlike the WES, it also "incorporates" potential doses arising from skin absorption or inadvertent "hand to mouth" ingestion, as opposed to just inhalation.

(Dermal absorption though would seem relatively low, given large disparities between experimental median lethal doses (LD_{50s}) when administered orally versus dermally. Thus summary data[24] indicate dermal LD_{50} values 480 and 253 times higher than oral LD50 values for rats and mice respectively. However these come from different studies and may not be completely comparable, and there was only a 5.3-fold difference between cited dermal and oral LD_{50} values for guinea pigs. Prolonged contact with liquid formulations, or solubilisation of dusts by sweat, could increase absorption, particularly through compromised skin).

Basing a BEI on urine rather than blood levels has advantages besides greater worker acceptability. Urine levels are slower to decline, and hence less likely to "miss" significant exposure, so timing is a little less critical. Additionally, for many industrial compounds, a blood level gives little indication of the daily exposure ("dose") giving rise to it, while the amount excreted in urine is potentially useful for roughly estimating daily (absorbed) doses, though this is more so for compounds with substantial, quantified, prompt urinary excretion in their unchanged form.[25]

This is significant, because of our need to utilise data from experimental animals (given lack of human data). The standard approach in such situations is to extrapolate from adjudgedly safe daily doses in animals to estimate likely safe doses in humans. This is more enshrined than extrapolation from an experimentally derived no-effect blood level to a safe human blood concentration.

However there are several potential imprecisions in this process, including the selection of appropriate safety or uncertainty factors. This approach is well established in public health regulatory practice, where a safety factor (of typically 10) is employed for inter-species extrapolation, but also other precautionary factors are applied, generally in conservative fashion. These include factors to take into account intra-species (human) variation in susceptibility (often 10), an incomplete overall database (up to 10), and to extrapolate from a subchronic to a chronic exposure (up to 10).

Indeed in the regulatory context, the US EPA has applied a total uncertainty factor of 3000 to their chosen NOEL (0.05 mg/kg/day) for 1080, comprising factors of 10 for all but one of the above considerations, the incomplete database, where instead a factor of three was used to adjust for lack of reproductive/developmental studies and toxicity studies in a second species.[26] The same general approach has been taken in

New Zealand in setting a drinking water standard,[27] and further lowering has been proposed., based on a total UF of nearly 3000.[28]

However a formal "safety factor" approach is not typically used in occupational health practice, though when the concept has been employed, emphasis has been on a factor of ten for inter-species differences, with less expressed need for a safety factor for intra-species variability, given the presumed exposure of healthy, working age adults only. Therefore a total UF of 3000 was not considered necessary or appropriate. Having said that, it could be argued that the total UF should be more than 30. It was chosen to limit it to this figure for the time being, partly to ensure reasonable achievability of compliance in the medium term, and not too large a "mismatch" with the WES. However, the proposed BEI should be regarded as provisional and subject to ongoing review.

This is doubly so as the estimate of urine levels corresponding to the RfD also has elements of uncertainty and imprecision. Certainly the chosen figure of 20% for the percentage excreted (as unchanged 1080) in urine over the first 24 hours is a rough estimate (or "guestimate") based on extrapolations from experimental animal data.

The kinetics of fluoroacetate, including its half life, are not well established in humans.[6] Blood levels have not been employed in management of acute poisoning cases, as the test is time consuming and of little clinical utility.[5] Two recent reviews discuss aspects of its toxicokinetics, but indicate there is very little quantitative human data.[29,30] Our monitoring programmes focused on the maximum blood and especially urine levels in individual workers as markers of their "worst case" exposure, rather than the details of rate of change of these parameters, such as to estimate elimination half lives. In the event of opportunity for further study, more detailed kinetic analyses involving multiple serial blood levels could be considered, subject to ethical approval.

Neither is there human data on the fractional elimination of (unchanged) fluoroacetate in urine over time. Relating our raw data on an individual's urine volume to their measured 1080 concentrations in 12-hour urine would provide interesting information on the amount excreted, but this would not provide a fractional elimination estimate without knowledge of the (absorbed) dose.

However in most if not all mammalian species thus far tested, estimated mean plasma elimination half lives have been less than 12 hours. Estimates include 10.8 hrs (sheep), 5.4 hrs (goats), ~1.6 hrs (mice), and 1.1 hrs (rabbits).[31,32] Further, in several studies involving various species, 1080 has been found at higher (or similar) concentrations in plasma than in major organs, including kidney, muscle, heart, liver, and spleen.[31,33,34] In sheep, plasma levels were about twice skeletal muscle levels at 2.5 hours, and levels were virtually the same (and very low) at 96 hours.[31]

Therefore it seems plasma concentrations represent a "worst-case persistence profile"[31] or a conservative indicator of changes in whole body load. Hence it would appear that in the species tested (whose 1080 in plasma half lives were all <12 hours), at least 50% of a dose could be eliminated within 12 hours, and 75% by 24 hours. There is no specific reason to believe the situation in humans is different.

However, experimentally, the percentage excreted in unchanged form in urine is less clear. Eason et al[31] found that in (three) sheep, ~7.5% to 14%, was excreted in "pure" urine samples over the first 24 hours, (and the fraction ranged up to ~34% by 72 hours

when urine contaminated faeces was included). In rats, one study found up to 17% unchanged in urine over 2 days.[33] However, while Gal et al collected 30–35% of a radiolabelled dose from urine within 2 days, the "unchanged" percentage was 60% by 4 hours but only 7.3% of the total 24-hour collection.[35]

These studies involved one-off (sometimes high) doses as opposed to chronic dosing. However a comparison between our human data (on urine levels versus blood levels) and that of a 90-day experimental study[10] suggests that the fraction eliminated unchanged in urine could be higher in humans than rats.

In any case, the more recent data on sheep were considered more relevant to humans. Therefore, we considered a figure of 20% for 24 hour urinary (unchanged) excretion is unlikely to be a significant over-estimate for humans. However we recognise that animal studies are not an ideal basis for establishing a BEI.

Regarding an optimum time for urine testing, it is likely (given experimental kinetic data) that the end of the work day would be preferable to the beginning of the next, and certainly the end of a work "week" preferable to after a weekend. We collected total urine for the working day (~12 hours), but any subsequent programme might involve comparing spot levels at the above times.

Air levels during baiting operations were generally low. However those brief periods of handling concentrated powders during manufacturing are cause for concern. This is particularly so as (unfortunately) only respirable levels were measured, not total inhalable levels, which latter may have been substantially higher.

We have not examined in detail the correlation between personal zone air levels and urine (or blood) levels, partly because this could be misleading, given that operators (particularly in the factories) were often wearing respirators at the most hazardous times, so were not effectively exposed to the air levels measured in their breathing zones, which thus would have little or no impact on their urine levels. However with tasks that had not typically been associated with respirator use, any such correlation would be interesting to explore, (though the TLV for systemic toxins is based on inhalable, not just respirable levels).

Conclusions

Our initial findings indicated there remained a need for further improvements in exposure reduction and ongoing monitoring. The derived BEI should be regarded as provisional and subject to ongoing review in the light of further information, particularly any monitoring results relatable to demonstrable adverse health effects in humans from chronic, low level exposures. Further, the aim should always be to reduce toxic exposures (and markers thereof) to as low a level as possible. The kinetics of fluoroacetate in humans also requires more investigation (though kinetic studies in otherwise non-exposed volunteers are not advocated).

Subsequent to the monitoring reported here, further programmes were undertaken, where the provisional BEI was first used as an "action level," with workers exceeding this value being temporarily suspended while work practices were reviewed and urine tests repeated.

Some progress in exposure reduction was achieved. However these programmes did not include detailed clinical appraisal, and (while there is no clear evidence of harm), more extensive health surveillance should be considered in those exposed long term, given the limitations of our proposed BEI as an indicator of risk. This might include questionnaires assessing fertility parameters,[36] though low subject numbers limit the power of such studies, whose methodology is still evolving.[37]

In 2007, in response to health and ecological concerns, the NZ Environmental Risk Management Authority (ERMA) undertook a reassessment of the role of 1080 in pest control management. The ERMA identified a need for further improvements, including a tightening of mandatory controls, closer monitoring, and further research into its adverse effects.[38]

Since then, there has been increased development and availability of "how-to" guidelines for occupational monitoring of 1080,[39] facilitating the increasing adoption of such monitoring as a routine. It is pleasing in 2009 to hear that at least in some sections of the industry, progress has continued to be made in controlling exposures, to such a degree that workers' urine levels are typically below the lower limit of detection of the test (which at 0.0005 ug/mL, is 30 times lower than our provisional BEI). In such cases adverse effects would be extremely unlikely.

Competing interests: None known.

Author information: Michael Beasley, Medical Toxicologist, National Poisons Centre, University of Otago, Dunedin; Penny Fisher, Toxicologist, Pest Control and Wildlife Toxicology, Landcare Research, Lincoln; Cheryl E O'Connor, Programme Manager, Animal Welfare, Ministry of Agriculture and Forestry, Wellington; Professor Charles Eason, Faculty of Agriculture and Life Sciences, Lincoln University.

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Correspondence: Michael Beasley, National Poisons Centre, University of Otago, Dunedin, New Zealand. Fax +64 (0)3 4770509; email: michael.beasley@otago.ac.nz

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