

Appendix M: Exposure and Risk Assessment (1080 and Cyanide): Human Health

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Key points

Occupational health risks with 1080

The Agency has concluded that the occupational health risks associated with **some** 1080 manufacturing and use activities are **potentially significant**. This relates, in particular, to factory workers manufacturing Stock Solution and cereal-based 1080 baits, and field workers loading 1080 treated carrot and cereal based 1080 pellet baits into aircraft hoppers for aerial application.

Limited occupational monitoring data were available for review by the Agency. The data available suggested some occupational exposures may be unacceptably high. The Agency was unable to determine whether this was due to the need for further controls or whether inadequate compliance with existing controls was responsible.

No specific recommendations for modifications to controls on 1080 technical concentrate, stock solution or the formulated products are made

to address these risks. However, the Agency recommends that the industry, pest control applicators and the Department of Labour review occupational best practice with a view to minimising worker exposures to 1080 particularly during the operations where biological exposure monitoring indicates a health risk.

Assessment thresholds were established for acute, sub-chronic and chronic exposure to 1080.

The acute threshold applied was the estimated minimum lethal dose (MLD) in humans 0.7 mg/kg bw.

The sub-chronic exposure threshold established was the acceptable operator exposure (AOEL) of 0.2 µg/kg bw/day (appropriate only for workers). The Department of Labour's biological exposure index for 1080 in urine was used for analysis of some data.

The chronic exposure threshold was the Acceptable Daily Exposure of 0.02 µg/kg bw/day. This was used to derive separate potential daily exposures for different routes:

PDE_{food} = 0.006 µg/kg bw/day

PDE_{water} = 0.01 µg/kg bw/day

PDE_{inhalation} = 0.002 µg/kg bw/day

PDE_{dermal} = 0.002 µg/kg bw/day

Health risks to the general public

Health risk to the general public from direct exposure to 1080 baits is considered *insignificant*.

Health risk to the general public from indirect exposure to 1080 in drinking water considered *insignificant*

Health risk to the general public from indirect exposure to 1080 in farmed and feral meat (and milk) is considered *insignificant*

Health risk to the general public from indirect exposure to 1080 in plants used for food or medicines (rongoa) is considered *insignificant*

Estimates of some health risk based on comparison of possible conservative intake estimates with derived criteria such as the PDE_{water} and PDE_{food}, in some cases appear unacceptable. The Agency considers an overall assessment of the risks needs to take into account the conservatism of the approach and the extremely unlikely nature of simultaneous exposures via multiple pathways for a prolonged period that would be necessary for an adverse effect. When such an approach is taken the health risk estimates are considered *insignificant*.

Other issues for the ‘without 1080’ scenario (use of cyanide)

The acute health hazard to the public from cyanide baits is substantially higher than for 1080 baits due to the higher toxicity level and the speed of action of the poison.

The fact that cyanide is used only in ground-based operations is likely to result in greater control on the placement of baits (compared with aerial application of 1080) so this reduces the likelihood that members of the public will encounter baits.

The acute and chronic health risks to workers from cyanide are considered lower than for 1080. In the case of the acute risks, the availability of proven effective antidotes is of value, but this is only relevant to worker exposures (not members of the public).

M1 Methodology for health risk assessment

Given the nature of the use of 1080 formulations, it is only feasible to do a qualitative assessment of these risks. None of the models the Agency usually uses for quantitative health risk assessments are suitable for assessing the likely exposures to vertebrate toxic agents. (The models are only suitable for assessing likely exposures from spray application to agricultural and horticultural crops.)

While this means only a **qualitative** risk assessment was performed for most end points, the Agency used historical occupational monitoring information to provide quantitative information on occupational exposures.

M2 Thresholds for determination of human health risk

In the case of 1080, the Agency concluded that it is appropriate to consider the human health risk exposure to 1080 in comparison to three types of threshold depending on the nature of the exposure. The three thresholds used were:

- **An acute (short term) exposure threshold**, suitable for assessing the risk from a single exposure to 1080. The threshold selected was the **lowest median lethal dose (MLD)** in humans. Assessment of exposures against this threshold is relevant for members of the public, bystanders and occupationally exposed persons.

The MLD should be used as the basis to assess acute human health risk. The exposure is assumed to be a single, not repetitive, event, and to consider the risk of acute toxicity. It is possible more than one such exposure could occur to a single individual separated by a length of time. The Agency considers that provided such exposures are separated by at least 5 days, each incident can be considered independent. Nevertheless, the assessment assumes that acute exposures are unlikely, rare events.

- **A sub-chronic (intermediate term) exposure threshold**, suitable for assessing risks to occupational exposed persons from repeated exposures

to 1080. The threshold selected was the *Acceptable Operator Exposure Limit (AOEL)* was used for this assessment. In addition, the **Biological Exposure Index (BEI)** was used for assessing the significance of biological monitoring results.

The AOEL is defined as “the maximum amount of active substance to which the operator may be exposed without adverse health effects. The AOEL is expressed in mg/kg bw (milligrams of the chemical per kilogram of body weight) for the operator as an internal dose (European Communities 2006).

- **A chronic (life time) exposure threshold** suitable for assessing the risk from chronic (long term) exposure to 1080. This is for suitable for assessing the risk the general public (non occupational exposed persons) from repeated exposures to 1080. An *Acceptable Daily Exposure (ADE)* has been derived for as this threshold, together with appropriate *Potential Daily Exposure (PDE)* values.

The ADE is defined in the HSNO (Control) Regulations 2001 and is intended to protect the general population from regular daily exposures to substances over a lifetime.

The basis for selection of these thresholds is discussed below, together with some comments relating to the thresholds used by the applicants.

M2.1 Acute (short-term) exposure threshold

The information available on the acute toxicity of 1080 in humans is discussed in Appendix B (section B17) under acute oral toxicity.

Table M1 sets out various acute toxicity thresholds for 1080 in humans.

Table M1: Acute oral toxicity thresholds for 1080 in humans

Parameter measured* (estimated) (mg/kg bw)	Value (mg/kg bw)	Date of original source	Reference
LD _{Lo}	5.0	1946	AJPEAG Vol 36, 1427, 1946 Sax, 1992
LD ₅₀	2–5	1949	Chenoweth, 1949
LD ₅₀	2.5	1950	Rammell and Flemming, 1978 (citing US Public Health Service)
LD ₁₀₀ [†]	2–10	1959	Rammell and Fleming, 1978 (citing Pattison, et al 1959)
LD ₁₀₀ [†]	5	1975	Rammell and Fleming, 1978 (citing Hashimoto, Y et al 1968 and Reigart et al 1975)
LD ₁₀₀ [†]	0.8–1.5	1966	Rammell and Fleming, 1978 (Dreisbach R H, Handbook of Poisoning, 4th ed. Lange Medical Publications, Los Altos, California, 1966)
LD _{Lo} [†]	0.714	1969	Deichmann, 1969 (p542) (Cited by Fairchild et al 1977 and Sax, 1992)

Parameter measured* (estimated) (mg/kg bw)	Value (mg/kg bw)	Date of original source	Reference
LD ₅₀ [†] (MLD actually)	0.7–2.1	1970	Atzert, 1971, ref 1,2 (1) Arena, 2nd ed, 1970 (2) Kaye, 3rd ed, 1970
Estimated lethal dose ranges	50–100 mg calculated to 0.73–1.46 mg/kg bw 0.15 g for 70 kg person calculated as 2.1 mg/kg bw	1986	Arena, 1986
Estimated lethal dose ranges	50–100 mg calculated to 0.73–1.46 mg/kg bw	1970	Kaye, 1970

Notes

* See text and glossary for explanation of terms.

† Rammel and Fleming erroneously referred to this as the minimum lethal dose

‡ Atzert, 1971 erroneously refers to this as a range for the estimated human LD₅₀. As discussed in the text, consideration of the original source makes it clear this is a range for the estimated human minimum lethal dose (MLD).

The Agency considers that ideally, the most appropriate parameter for assessment of whether or not an adverse effect is likely to occur in humans (whether this is from occupational or non-occupational exposure) would be the lowest toxic dose (TD_{Lo}). The Agency reached this conclusion because the intention is to prevent harm to humans (all toxic effects), not only lethality. However, review of the data (as in Table M1) indicates that the TD_{Lo} in humans has not been established, so the Agency concluded that the minimum lethal dose (MLD) should be used instead. An estimate of the MLD is potentially provided by each fatal 1080 poisoning, but often an accurate estimate of the dose received is not available. As noted in Appendix B17, estimates of the doses of 1080 that have been taken by human cases of 1080 poisoning are rarely reported.

In most cases, the applicants have used an estimated human median lethal dose (LD₅₀), 2 mg/kg bw, for the acute human health risk assessment (for example, in H-A1 through H-A27 of the application). This was based on the lowest value from the range of Chenoweth 1949, which quoted the estimated LD₅₀ in humans as 2–5 mg/kg bw. As the basis for the oral LD₅₀ range of 2–5 mg/kg bw in humans, Chenoweth 1949, cites an anonymous reference from the National Research Council (USA) in 1948. The Agency was not able to further clarify the basis for the stated range.

The other threshold most often cited for acute human risk assessment to 1080 is the lower end of the MLD range listed 0.7–2.1 mg/kg bw and often attributed to Atzert (1971). Atzert referred to this as the oral LD₅₀ range in humans, and cites the references Arena (1970) and Kaye (1970).

Kaye (1970) lists the MLD estimate for 1080 in humans as 50 mg for a 150 lb (68.2 kg) human. Calculation based on the value given shows it is

approximately equivalent to 0.73 mg/kg bw. Kaye (1970) did not state the range as given in Atzert (1971) specifically.

The Agency was not able to locate a copy of *Arena* (2nd edition, 1970) cited by Atzert (1971). *Arena* (1986) appears to contain the more complete basis for range attributed to this source by Atzert (1971). *Arena* (1986) gives the estimated lethal dose range for 1080 as 50–100 mg. No reference was provided in support of these values, nor was a body weight or age range given. The Agency notes that the bottom of this 50 mg lethal dose range gives approximately 0.73 mg/kg bw (as stated above based on a body weight just below 70 kg).

The Agency also found that *Arena* (1986) lists (in Table 3-1 on p 230) an estimated lethal dose for 1080 as 0.15 g/70 kg bw. Direct calculation showed this is equivalent to 2.1 mg/kg bw. Therefore, the Agency concluded that the bottom of the lethal dose range and this value, are most likely to be the source of the range of 0.7–2.1 mg/kg bw attributed to this source by Atzert (1971) even though *Arena* (1986) did not state the range specifically.

Other sources refer to slightly different numerical values, but the Agency considers the resulting human MLD is unchanged. Fairchild et al (1977) and Sax (1992) gave the lowest published lethal dose for 1080 of 0.714 mg/kg bw with a citation of Deichmann (1969). Deichman refers to the “probably lethal” oral dose for a human adult as 50 mg. Therefore, values listed by Fairchild et al (1977) and Sax (1992) were considered by the Agency to be derived as above from the estimated MLD of 50 mg (using a 70 kg average weight for a human adult).

Dreisbach (1966) was cited as the basis for an estimated ‘LD₁₀₀’ range of 0.81–1.5 mg/kg bw by Rammell and Fleming (1978). The original reference stated the estimated fatal dose of 1080 was 50–100 mg, so the description of the value as a minimum lethal dose would appear more appropriate. Dreisbach did not specify whether this was for an adult. The Agency noted that the stated range matched that proposed by Kaye (1970) and *Arena* (1986). The Agency considered the slightly modified range quoted by Rammell and Fleming (1978) most likely reflected a slight variation caused by them having used a different body weight for the calculation. In this instance the ratio of the upper and lower values appears to better reflect the range of fatal values provided in the original source.

The Agency did not use the lowest LD₅₀ value for laboratory test species (0.06 mg/kg bw in dogs) for the acute human health risk assessment, although this value was been used for 6.1 acute oral toxicity classification under the HSNO regulations (see Appendix B19.2). The intention of human health risk assessment is to reasonably assess the actual risk level from the use of 1080 and formulated product containing it to humans. While human data are sparse and there is uncertainty with the quality of the data, there is sufficient evidence to indicate that humans are less sensitive to 1080 than dogs. The Agency considers that use of the dog

LD₅₀ value for assessing acute human risk would overestimate acute toxicity risks to humans and would be overly conservative.

M2.1.1 Conclusion: acute health risk criterion

The Agency concluded that it is the lowest end of the MLD range estimate, **0.7 mg/kg bw** should be used to assess acute human health risk. The Agency does not consider the upper end of the range is of significance from the risk assessment perspective, where a precautionary approach is appropriate.

The Agency emphasises that the value should be cited as a minimum lethal dose (MLD), not a median lethal dose (LD₅₀) value for humans. This value appears to be the most widely cited, recent, MLD estimate for humans, notwithstanding very slight variations between sources. The Agency believes this value is more appropriate for the acute human risk assessment than the median lethal dose LD₅₀ estimate of 2 mg/kg bw (Chenoweth 1949) that has been used by the applicants.

M2.2 Sub-chronic (longer-term) exposure thresholds

In relation to longer-term exposure thresholds, the Agency commonly uses two separate values:

- An Acceptable Operator Exposure Limit (AOEL) is usually used to assess occupational exposures from regular daily exposures to a substance.
- An Acceptable Daily Exposure (ADE) is usually used to assess lifetime exposure to the general public.

M2.2.1 Agency derivation of an AOEL

The approach to establishing AOEL values is set out in European Communities (2006). Key aspects relating to setting of AOEL values that are of relevance are:

- The AOEL should be usually derived from the lowest NOAEL in a sub-chronic, toxicity study in a laboratory species. The duration of study chosen is usually 90 days.
- The total toxicology data package should be reviewed and data from the most sensitive species is usually the starting point, unless reliable human data are available.
- A threshold approach is usually applied, so the starting point is the lowest NOAEL for the most sensitive target effect.

In relation to 1080, Appendix B lists the NOAEL values for the range of studies which may be considered as the basis for setting the AOEL. The studies include 90-day oral exposure studies and reproductive/developmental toxicity studies.

The appropriate conclusions, based on the European Community guidance are given in the Table M2.

Table M2: Criteria for setting the AOEL

Duration
Sub-acute and sub-chronic data are available for rats. The most reliable NOAEL values are from 90-day oral toxicity tests in the rat.
Species
The most sensitive species is the dog, based on acute data indicating dogs are approximately 2–10 times more sensitive than other species laboratory rodents. However, neither sub-acute nor sub-chronic data are available for dogs. The Agency considers that the use of the rat data to model the human is appropriate and notes this is the most commonly used species for this purpose. There is no evidence that primates are more sensitive than rodents to 1080. On the contrary, there is some suggestion primates may be less susceptible, but the Agency does not consider this conclusive.
Inter-species variability
The standard factor of 10 was applied.
Intra-species variability
The standard factor of 10 was applied.
Type of critical effect
The Agency considered whether or not a factor would be appropriate to take into account the severity of effect(s) of 1080. Both heart and testes effects occur at doses that are close to MLD in humans, although these effects have not been demonstrated in humans. The Agency considered whether or not the “severity of effect” factor should apply to either or both of these effects. In the case of the heart, the histological findings and organ weight changes do not appear to be associated with adverse organ function. In contrast, histological findings and organ weight findings in the testes are very clearly related to severe reduction in sperm counts in the animals. The effects on testes were found in several species and appear irreversible, but this has not been proven. The Agency concluded that since irreversibility has not been equivocally demonstrated, and, more significantly, the effects have not been found in humans no severity of effect factor should be applied.
Dose response curve
Since toxic effects occur at doses which are a relatively high proportion of the acutely toxic dose, a steep response curve is assumed to apply (a shallow response is more difficult when deriving exposure criteria).
Use of LOAEL in place of NOAEL
N/A
Quality of data
The overall data package is relatively thin. The Agency considered it is appropriate to use an uncertainty factor for this lack of data and has used a factor of 3 for this. This approach is consistent with that taken by the US EPA (IRIS), (US EPA, 2007) and by Foronda et al (2006b). Note that this factor is applied with respect to gaps referred to in Appendix B which were a multi-generation study and a chronic toxicity/carcinogenicity study. The lack of the carcinogenicity study is not considered crucial since mutagenicity data were negative.
Route of exposure
For 1080 variation due to route of exposure is not likely, and the oral study is likely to represent relevant exposure routes.
Internal dose correction
Absorption of 1080 is rapid and the proportion absorbed is high, with the possible exception of dermal exposure. Due to the lack of data, the Agency considered that a correction factor should apply for dermal exposure route.

Table M3 lists the NOAELs and LOAELs for the adverse effects from sub-chronic exposures to 1080 (from Appendix B) which are suitable to consider as the basis for human risk assessment.

Table M3: Summary of NOAELs, LOAELs and adverse effects

Study type	NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Adverse effect
Developmental toxicity (6.8)			
Rat foetus (Eason et al, 1999)	0.1	0.33	Forelimb abnormalities
Reproductive toxicity (6.8)			
90 day oral toxicity in the rat (Eason and Turck, 2002)	0.075	0.25	Reduced testes weight, reduced or absent spermatozoa in testes and epididymides
90 day oral toxicity in the rat (Wolfe, 1988)	0.05	0.2	Reduced testes weight, reduced or absent spermatozoa in testes and epididymides
Target organ systemic toxicity (6.9)			
90 day oral toxicity in the rat (Eason and Turck, 2002)	0.075	0.25	Cardiomyopathy (Adverse effects on the heart)
90 day oral toxicity in the rat (Wolfe, 1988)	0.05	0.2	Increased absolute and relative heart weights

The lowest NOAEL is 0.05 mg/kg bw/day in the male rat from the 90-day study on the basis of cardiac and testicular effects. from the study by Wolfe, 1988, and this was considered by the Agency as the appropriate value from which to derive the AOEL (and ADE in the absence of chronic data, see section B2.2.2).

The uncertainty factors are:

- 10 for inter-species
- 10 for intra-species
- 3 for incompleteness of the dataset.

$$\text{AOEL} = (0.05 \text{ mg/kg bw/day}) / (10 * 10 * 3) = 0.000166 \text{ mg/kg bw/day}$$

The Agency rounded this to AOEL = 0.0002 mg/kg bw/day.

(It may be convenient to express this as AOEL = 0.2 µg/kg bw/day.)

The Agency concluded (Appendix B13) that the 90-day oral toxicity studies identify the most sensitive target organ are the male reproductive system (the testes and epididymides), so that the most sensitive population group are male adults. The Agency considers that the degree of concern is higher with younger male adults who have not yet started or completed their families, and notes this would be of great concern to families generally. The Agency considers this is likely to be of greatest concern with respect to occupational exposures since workers are most likely to have regular exposure to the substance.

M2.2.2 Derivation of an ADE

The ADE is derived to protect the general population from chronic exposures, and as such the ADE should normally be derived from a

chronic toxicity/carcinogenicity study. As discussed in Table M2, there are no chronic toxicity studies available for 1080.

Therefore, the Agency used the data same 90-day study as for the AOEL and applied an additional uncertainty factor of 10 to account allow for the use of a sub-chronic instead of a chronic toxicity value.

The ADE for 1080 is therefore given by the following calculation:

$$\text{ADE} = (0.05 \text{ mg/kg bw/day}) / (10 * 10 * 10 * 3) = 0.0000166 \text{ mg/kg bw/day}$$

The Agency rounded this to ADE = 0.00002 mg/kg bw/day.

(It may be convenient to express this as ADE = 0.02 µg/kg bw/day.)

The Agency notes that the above ADE is the same as the chronic reference dose (RfD) value set by the US EPA which is 0.02 µg/kg bw/day, using similar uncertainty factors. Also Foronda (2007) proposed a Tolerable Daily Intake (TDI) for 1080 of 0.03 µg/kg bw/day and the Agency understands (section M5.1.6) that the Ministry of Health is proposing to use this as the basis for establishing a new PMAV. The uncertainty factors used by Foronda (2007) were very similar. A slightly different result was obtained due to the use of a different key study. Also, Foronda (2006a) derived a bench mark dose at which a 10% response would occur (BMDL₁₀) to use in place of the NOAEL from the relevant study.

Regulation 23 of the HSNO (6, 8, & 9 Controls) Regulations 2001 provides for fractions of the ADE to derive appropriate PDE values for different exposure routes. The use of the standard values was not considered appropriate for 1080, primarily because the Permissible Maximum Exposure (PMAV) set by the Ministry of Health has used 50% of the Tolerable Daily Intake they derived (which is similar to the ADE). Table M4 lists the standard and proposed factors for each exposure route, and the resulting PDE in each case.

Table M4: Exposure proportions for different exposure routes

Medium	Standard factor ¹	Proposed factor for 1080 ²	PDE for this medium (µg/kg bw/day)
Food	50%	30%	0.006
Water	20%	50%	0.010
Inhalation	10%	10%	0.002
Dermal	10%	10%	0.002
Other	10%	0%	-

Notes

- 1 The standard values are based on World Health Organisation, 1994.
- 2 The Ministry of Health has assigned 50% of its TDI when deriving the current permissible maximum value (PMAV) for drinking water, so it is appropriate for the Agency to allow the same proportion here. The resulting TEL_{water} is compared to the PMAV and the proportion assigned water receives further discuss then.

M2.2.3 Conclusion: Sub-chronic and chronic health risk thresholds

For the assessment of sub-chronic exposure of occupationally exposed person to 1080 the **AOEL is 0.2 µg/kg bw/day**.

For assessment of chronic exposures of the general population to 1080 the **ADE 0.02 µg/kg bw/day has been used**. The associated PDE values for different exposure routes are:

PDE_{food} = 0.006 µg/kg bw/day

PDE_{water} = 0.01 µg/kg bw/day

PDE_{inhalation} = 0.002 µg/kg bw/day

PDE_{dermal} = 0.002 µg/kg bw/day

M3 Occupational exposures

Occupational exposure risks were assessed based on the information relating to the use of 1080 in New Zealand provided by the applicants in the life cycle section of the application (see Section 3 of the application) and material available to the Agency from other sources.

It is very difficult to estimate occupational exposures based on work practices and the nature of the substances that are being handled. The Agency is not aware of any suitable exposure models for doing quantitative estimations which are relevant to either the manufacturing processes or the use of 1080 as a vertebrate toxic agent.

The Agency identified a number of key occupational exposure situations (based on the “lifecycle” of 1080 and its formulations) and lists these under headings so that the types of activity can be referred to succinctly.

- Manufacturing and transportation
 - Import and manufacturing use of technical 1080 to make stock solution
 - Factory manufacture of 1080- containing formulations (cereal pellet baits, pastes and gels)
 - Transportation of Stock Solution and manufactured baits
- Field manufacture
 - Field (remote site) manufacture of 1080-containing carrot, cereal and apple baits (including dilution of Stock Solution and mixing the diluted material with carrier material)
- Aerial loading operations
 - Opening bags of (pellet) bait and emptying into hoppers for helicopter/aircraft loading
- Field bait laying and related activities

- Laying of baits (of all types), includes distribution of pellets, setting out and loading of bait stations, application of paste/gel to vegetation.
- Collection of spent and surplus bait
- Collection or burial of carcasses where relevant.

Exposures of occupational exposed persons, particularly during manufacturing operations, may be higher than for other groups due to the use of more concentrated formulations, but the degree of control of exposures in factory situations is likely to be greater than at remote sites, due to the absence of the influence of weather, and the use of exhaust ventilation to control the factory environment, and the ready availability of personal hygiene facilities. Manufacturing may be sporadic to meet seasonal demand for 1080 products.

The occupational exposures during the ground-laying of 1080 pellet, paste and gel baits are rather different from manufacture, primarily because they only involve exposure to products containing relatively low 1080 concentrations and exposure is likely to be more intermittent.

Some occupational exposure studies have been carried out during:

- manufacture of 1080 cereal baits
- field manufacture of 1080 carrot bait, and
- ground laying of 1080 baits and associated activities.

This information provided the only quantitative estimates of 1080 exposures (whether actual or modelled) available to the Agency for the assessment of occupational exposures, and the results are discussed in considerable detail below (section M3.4).

Other exposures are discussed in general terms and assessed qualitatively. The characteristics of the operations were used to assist in qualitative exposure estimates. Emphasis has been given to considerations such as:

- frequency and duration of exposures
- concentration of the 1080 in the material being handled
- the likelihood that the operation would generate dust or mist
- contamination of hands, face etc (where absorption through broken skin may be possible)
- contamination of clothing
- the extent to which the environment is controlled from an environmental contamination perspective
- the extent to which the use of personal protective clothing can reduce exposures.

M3.1 Transportation

In relation to transportation of technical concentrate, Stock Solution and formulated 1080 products, the Agency considered that the health risk was limited to a packaging failure (essentially a spillage) incident or an accident. Due to the nature of the 1080-containing materials and packaging used, the hazards and health risk differ between the different 1080-containing materials.

M3.1.1 Transportation of 1080 technical grade active

1080 technical grade active is only transported from the wharf at Auckland to the factory at Wanganui. Technical grade active will only be transported in containers which comply with international packaging requirements together with additional outer protection. (see section 4.5 lifecycle). The Agency agrees with the applicants that the packaging should prevent an accidental release of technical grade 1080 in all but the most serious incidents.

Although highly unlikely, the failure of packaging of technical grade active during transportation due to an accident could represent an extremely hazardous situation for the following reasons:

- The powder is in a finely divided form. If it escapes containment, particularly in dry, windy conditions, it could be carried some distance.
- The acute inhalation toxicity hazard is high (see Appendix B5).
- A particularly dangerous characteristic of 1080 is the latency period (at least ½ hour) before serious symptoms develop in exposed persons or animals. (There is an extremely remote possibility that a significant number of people could be exposed to the substance before they were advised of the hazard by the driver or other emergency service personnel.)

Training should ensure that the driver has the technical knowledge and experience to advise members of the public to retreat immediately to a safe distance. In the event that the driver was incapacitated, extensive signage on the vehicle and the 1080 containers, together with the dangerous goods information in the vehicle, should alert bystanders to the high risk. This would not be as reliable as the driver giving this advice in person, as it depends on the alertness and experience of the bystanders. Speed of response by emergency service personnel would also be critical.

The following measures could be useful to enhance public safety and reduce risk to the general public during transportation of 1080 technical grade active:

- Suitable route selection for vehicles carrying 1080 technical grade active to avoid highly populated areas and sensitive sites (such as schools).
- Use of a companion vehicle in convoy with the vehicle carrying 1080 technical grade active. The presence of a knowledgeable person, other than the driver in the event of an incident, could greatly reduce the

impact of any event, particularly if the driver of the vehicle carrying the 1080 technical grade active was incapacitated.

The Agency concluded the addition of such measures as controls would be extremely precautionary, given the extensive packaging requirements already in place, and the low chance of such a serious incident.

M3.1.2 Transportation of stock solution

Stock Solution is transported between the factories and to remote sites prior to the field production of 1080 carrot/cereal baits. Stock solution is packaged in 5 litre bottles.

The Agency notes that transportation of Stock Solution within New Zealand is covered by the requirements of the Land Transport Rule: Dangerous Goods 2005 (Rule 45001/1) and controls in place under the HSNO Act approvals for the substances containing 1080. These requirements require packaging which should prevent an accidental release of the substance in all but the most serious incidents.

The failure of packaging during transportation of Stock Solution would represent a hazardous situation for the following reasons:

- The Stock Solution contains 20% of 1080 in soluble form. If it escapes containment, it could form pools or flow into waterways.
- A person who comes in contact with the Stock Solution would be at risk from acute poisoning (including from skin contact). Thorough decontamination would be required.
- As noted above, a particularly dangerous characteristic of 1080 is the latency period (at least ½ hour) before serious symptoms develop.

Nevertheless, the Agency concludes that the risk from transportation of Stock Solution is not as high as for technical concentrate for the following reasons:

- The concentration of 1080 present is lower, so it is less toxic.
- It is unlikely to be released in a form that could be inhaled (such as a mist).
- The most likely exposure route is via skin contact and 1080 is believed to be less readily absorbed by this route than ingestion or inhalation. This gives some opportunity for decontamination to prevent absorption of the poison.

The drivers' training should result in them being able to advise persons who may be present to retreat immediately to a safe distance. In the event that the driver is incapacitated, the extensive signage on the vehicle and containers, together with the dangerous goods information in the vehicle, should alert bystanders to the risk. This would not be as reliable as if the driver gave the advice, as it depends on the alertness and experience of the

bystanders. The speed of response by emergency service personnel would also be critical.

The Agency concluded that additional controls to address the transportation risks associated with Stock Solution are not required given the packaging requirements already in place and the low chance of such a serious incident.

M3.1.3 Transportation of formulated product

While baits will be much more extensively transported around the country than other 1080-containing substances, this is not considered a particularly high risk activity due to the relatively low 1080 concentration present in 1080 baits. The concentration of 1080 in various baits is set out in Table M3, the most common baits contain much less than 1.0% 1080, but one paste contains 1.0% and gel baits may contain 5% or 10%.

The Agency notes that regardless of the manufacturer, baits containing 1080 are required to be transported in accordance with HSNO requirements and the requirements of the Land Transport Rule: Dangerous Goods 2005 (Rule 45001/1) when transported by road in New Zealand.

The need to avoid escape of the material into the environment is important, both from a human health and environmental perspective. Such a release is only likely to represent a significant human health risk if the release occurred without anyone present (such as the driver) who was able to take appropriate steps to secure the material and advise bystanders of the hazard. Due to the lower hazard of the bait in comparison to 1080 technical grade active or Stock Solution, the likelihood of a driver being incapacitated relates almost entirely to causes unrelated to exposure to 1080 (such as an accident, injury or personal health issue).

In the case of 1080-containing baits the risk to human health from release of the material is very low. Only an unsupervised child is likely to investigate the material and be at risk of significant exposure, and this is very unlikely when material is being transported under the control of specially trained drivers. For discussion of the toxicity of different 1080 baits and the quantity of these baits that may present a health risk, see section M4.1. The Agency concluded that taking into account the transportation requirements, the risk presented by transportation of 1080 containing baits is very low.

M3.2 Manufacturing

M3.2.1 Manufacture of stock solution

The applicants (Section 3.5 of the application) indicate that during the preparation of Stock Solution by the dissolving of technical grade 1080 powder (95–98% 1080) in water, full protective equipment is worn. This operation takes about a week and is carried out typically 3–4 times per year. The Agency has no information on the doses of 1080 that workers

are likely to receive through occupational exposure during this process. Since the technical grade active is a highly concentrated powder a significant health risk may occur during preparation of Stock Solution, unless the appropriate controls are carefully followed, including use of personal protective equipment.

The applicants also indicate (Section 1.3 of the application) that workplace exposure monitoring and quarterly biological exposure testing are carried out. No information on the results relating to the manufacture of Stock Solution was available to the Agency. The Agency concurs with the requirement for biological exposure monitoring of workers and environmental monitoring of the workplace when handling 1080 technical grade active. The Agency expects the results would demonstrate whether or not the precautions taken are sufficient to enable compliance with the Biological Exposure Index (BEI) established by the Department of Labour (Department of Labour 2002).

Assuming the company maintains an on-going review of the adequacy of precautions in place, including a review of the use and efficiency of personal protective equipment, the Agency considers that the controls are adequate to protect workers.

M3.2.2 Manufacture of pellet baits, pastes and gels in factories

According to the life cycle discussion by the applicants in Section 3.5 of the application, this involves the mixing of the relevant ingredients with Stock Solution. Appropriate personal protective equipment is used.

A limited amount of biological exposure testing of persons occupationally exposed to 1080 during the manufacture of cereal pellet baits was available to the Agency and is discussed below in section M3.4.

The data indicate that the manufacture of cereal-based pellets may be associated with non-negligible health risks, which need to be assessed. The Agency considers that this does not necessarily mean the other bait manufacturing activities (manufacture of non cereal-based baits such as pastes and gels) carried out in factories are necessarily free from similar risks, as no data on this were available. Nevertheless, the Agency noted that the toxicological hazards may be higher for operations involving dry ingredients (cereal baits) than for pastes/gels since dust exposure may be more likely.

The Agency concluded that the controls relating to the manufacture of baits are sufficient to control worker exposures to 1080, but draws the attention of the manufacturers to the need for use of personal protective equipment.

M3.2.3 Manufacture of carrot, cereal and apple baits from stock solution at remote sites

This section considers the occupational health risk from preparation of 1080 carrot, cereal and apple baits from Stock Solution at remote sites. This is discussed in section M3.5. The Agency notes that the application states this involves the mixing of the relevant ingredients with Stock Solution after appropriate dilution at the site. Appropriate personal protective equipment is used.

The Agency noted that the Department of Labour (2002b) identified a number of hazards associated with the process of preparation of carrot baits. The Agency assumes these are relevant also to cereal and apple bait prepared at remote sites.

The resulting carrot, cereal and apple when treated with the diluted Stock Solution at the stated rates have nominal 1080 concentrations of 0.2, 0.8 and 1.5 g/kg of bait.

A limited amount of biological exposure testing of persons occupationally exposed to 1080 during carrot bait manufacture and loading is discussed in section M3.4. The data indicate these activities may be associated with non-negligible health risks, which need to be assessed by the Agency.

After reviewing the information relating to the biological exposure in section M3.4, the Agency considers there are some uncertainties relating to the operation which may significantly impact on the risk of exposure. The Agency identified the need for information on:

- whether or not the spraying of baits is a contained process which does not generate any mist as claimed in the application,
- whether or not the use of non-contained bait treatments (such as a “concrete mixer” system) is widespread and presents a higher risk of exposure than the “contained process”.

Despite these uncertainties, the Agency considers that the controls are *adequate* to protect workers, since there are requirements for personal protective equipment. Existing controls assume that there will be an on going review of the adequacy of precautions, including the use of personal protective equipment, undertaken by the industry in association with the Department of Labour. That process can consider the questions raised above without modification to the controls being necessary.

M3.3 Use of 1080-baits

M3.3.1 Aircraft loading with cereal pellet and carrot baits.

The Agency notes that there are aspects of these operations that may result in higher exposure to 1080 than from ground baiting operations, even though the material being handled only contains a relatively low concentration of 1080. These aspects are:

- The operation will always be done in relatively dry weather conditions (when a bait drop is appropriate)
- The process is carried out in proximity to helicopter movements which are likely to generate airborne dust
- Large (25 kg) bags of bait are cut open and emptied into a loading hopper
- There is pressure to get the bait ready for the aircraft as soon as it arrives so that the operation is as efficient as possible
- The work is physically demanding and requires the use of personal protective equipment. Workers may be tempted not to use the degree of protection required, due to the heavy nature of the work, but the Agency understands most operations occur in spring rather than summer.

A limited amount of biological exposure testing of persons occupationally exposed to 1080 during carrot-bait manufacture and loading is discussed below in section M3.4. The data indicate these activities may be associated with *non-negligible* health risks, which need to be assessed. Nevertheless, the Agency considered that the health risks are *acceptable with controls*.

Despite the possible health risks and the uncertainties, the Agency considered that the controls are adequate to protect workers, since there are requirements for personal protective equipment. Existing controls assume that there will be an on going review of the adequacy of precautions, including the use of personal protective equipment, undertaken by the company in association with the Department of Labour. That process can consider the questions raised above without modification to the controls being necessary.

M3.3.2 Ground-laying of 1080 pellets, 1080 paste and 1080 gel

The Agency notes occupational exposures during the ground laying of 1080 pellets, 1080 paste and 1080 gel are substantially different from those associated with other types of work with 1080, and that the nature of the exposures vary depending on the type of bait being used. The Agency notes that:

- Work with the 1080-containing bait is not continuous, but would involve moving through the treatment area, and laying the bait periodically, and is likely to also require replenishing bait supplies over the period of the operation.
- The need to wear protective clothing is likely well known. There is the possibility of protective clothing, particularly gloves, being damaged by contact with the environment (such as with trees trunks, fences, or barbed wire) during field operations. Such damage may reduce the degree of protection provided. It is important that the workers have adequate back up supplies of equipment when they are in the field.

- In the case where ground application uses bait stations, collection of unused bait for disposal occurs (either on site by burial or after returning to the depot). This would be associated with an additional exposure period to bait that is no longer in its original condition. While the poison may be more readily accessible the concentration of poison may also decline due to weathering and leaching.
- Paste baits are usually dispensed using a paste gun which is likely to substantially reduce the likelihood of exposure during application for these bait types.

Therefore, different types of baits are associated with slightly different exposure hazards. Pellet and carrot baits are more likely to generate dusts. Pastes and some of the gel formulations are expected to be damp and sticky so they may adhere to exposed skin. When a gun is used exposure is unlikely, but it may be possible for paste and gel to contaminate skin and be transferred later to food or cigarettes, giving rise to the possibility of ingestion of residues. This is much less likely to occur for a worker employed to lay such material than for a members of the public (discussed in section M4).

A limited amount of biological exposure testing of persons occupationally exposed to 1080 during ground bait operations is discussed below. The data suggest these activities were associated with relatively low exposures to 1080, although due to the limitations of the monitoring this was not unequivocally demonstrated.

The Agency concludes that the health risk from the ground laying of 1080 containing baits are *acceptable with controls*.

M3.3.3 Disposal and spillages

Disposal of off-specification products, packaging materials, surplus baits, retrieved baits from the field and potentially contaminated carcasses represent potential occupational exposures. The Agency has no information on which to assess the exposures of persons involved in these activities.

Most of these materials contain relatively low concentrations of 1080, so the Agency identified the following activities as being those most likely to require particular care to avoid occupational exposures:

- The disposal of containers that have been used to contain technical grade active 1080
- The disposal of sweepings of 1080 technical grade active (the Agency expects very little of this material would need to be disposed of as it could be used in the next batch of Stock Solution).
- The disposal of surplus Stock Solution, and liquid discharge (traces of paste/gel). This is referred to in the application in H-A8 which states the method of disposal is by discharge to sewerage treated plant.

The Agency expects that the disposal of all these materials would be done in accordance with appropriate control procedures with careful identification of the nature of the material and the need for appropriate protective equipment for those involved. Workers involved are trained and aware of the substances they are handling.

The Agency concludes that the health risk from these disposal activities is *acceptable with controls*.

M3.4 Occupational exposure monitoring results for selected 1080 manufacturing and use operations

M3.4.1 Introduction

The best information available to the Agency as a basis for estimating likely worker exposures to 1080 was provided by reports on the monitoring of workers using 1080 in comparison with the Biological Exposure Index (BEI) established by the Department of Labour (Department of Labour 2002a).

The most comprehensive report available to the Agency reviewed results from monitoring carried out between 1998 and 2000 by Landcare Research (Fisher et al 2002). The report was commissioned by the Animal Health Board in response to the BEI established by the Department of Labour.

Appendix C to the Application refers to two reports carried out on groups of occupationally exposed individuals in New Zealand with code references LC0102/087 and LC0102/135. One report is the one cited above (Fisher et al 2002), the other reports on an investigation performed at the Animal Control Products (ACP) Plant at Wanganui. Fisher et al (2002) state in the introduction that one purpose was to review previous data in comparison to what was at that time the newly established BEI. The Agency considers the report (Fisher et al 2002) the most comprehensive summary of such work, although the Agency is aware that other investigations have also been carried out.

The BEI of 15 µg/L listed for sodium fluoroacetate (1080) in urine specifies an “End of shift” sample (Department of Labour 2002a). In the preface the Department of Labour specifies that “End of shift” means sampling in “The last two hours immediately following the end of the working day”. The Agency agrees that this timing is appropriate given the relatively short half-life expected for 1080, although the value is not known in humans (see Appendix B15.)

The report refers to groups of workers carrying out two types of work, but the monitoring was done at two separate manufacturing factories and at a number of field locations (since different operations were involved).

M3.4.2 Background

Bait manufacturers

Workers at two manufacturing plants preparing 1080-containing cereal pellet baits were investigated. Information on the concentration of 1080 in the cereal baits being manufactured was not provided, but cereal pellet baits may contain 0.4–0.8 or 1.5–2.0 g of 1080/kg, based on other information above (see also section 4.5). More significant than the final bait concentration is the fact that manufacture of cereal pellet baits at the factory involves mixing components of the baits with Stock Solution (containing 20% 1080).

Field users of 1080

The second type of work involved the operational distribution of cereal, carrot or paste baits. The Agency notes that due to the range of bait types referred to, the nature of work undertaken by the field workers will be quite variable. The Agency assumes the activities would (or may) have included all the activities listed at the beginning of this section (section M3) in relation to both aerial loading operations and field laying operations.

Detailed description of the subjects was not provided. Usually in occupational health investigations some basic data are provided covering matters such as the:

- workers' ages
- nature of their duties
- nature of the protective clothing worn
- lifestyle aspects which may be relevant to exposure (particularly whether or not they are smokers).

Precise details on the methodology employed are not given, in particular, the time of sampling in relation to the work period suggests a range of sampling times was employed which were not in accordance with the Department of Labour, BEI criteria. The significance of this for interpretation of the results is discussed below.

M3.4.3 Summary of results

Factory employees

- In two factories (Wanganui and Timaru) that manufacture 1080 cereal pellet baits, 54 urine samples from nine workers were tested. 10 urine samples out of a total of 54 (the report incorrectly says 53) exceeded the BEI value (19%). The range of values for samples which exceeded the BEI was 20–3410 µg/litre, equivalent to 1.33–227 times the BEI.
- Four out of nine workers (44%) had at least one sample which exceeded the BEI.

- 36 samples (67%) were below the BEI, but had detectable 1080 concentrations in the range 0.6–9 µg/litre.
- The remaining eight samples (15%) were below the BEI.

Given these proportions, the Agency considers it unlikely that all the positive findings were the result of accidental contamination of samples. Almost half of the workers provided at least one urine sample which exceeded the BEI.

Field workers

Field workers were involved in a variety of different operations, aerial carrot, aerial cereal pellet and manual paste.

Aerial carrot

- Thirty seven urine samples were taken from workers involved in three aerial carrot operations. 11 out of 37 urine samples (30%) exceeded the BEI, and the range of values was 20–68.5 µg/litre.
- Nine out of 14 workers (64%) had at least one sample above the BEI.
- 23 samples (62%) were below the BEI, but had detectable 1080 concentrations in the range 0.6–14 µg/litre).
- In three (8%) of the samples, no 1080 was detectable.

Aerial cereal pellet

- In the two aerial cereal pellet operations, none of 29 urine samples (0%) exceeded the BEI. None (0%) of 11 workers had any urine sample above the BEI.
- Eight samples (28%) were below the BEI, but had detectable 1080 concentrations in the range 0.6–1 µg/litre). In 21 samples (72%) of the samples, no 1080 was detectable.

Ground-based paste bait distribution

- In one ground operation using 1080 paste bait, none of 15 urine samples was above the BEI. None of three workers had any levels of 1080 in their urine samples which exceeded the BEI,
- Fifteen samples (100%) were below the BEI, but had detectable 1080 concentrations in the range 0.6–3.3 µg/litre). In this group none of the samples had an undetectable 1080 concentration.

M3.4.4 Interpretation and health significance

Sample timing

In relation to sampling of workers involved in application of 1080, the samples were said to have been taken “sequentially through the operation and once a day for 5 working days”. This is unclear in relation to the work (exposure) period.

The report refers to sampling of factory workers “during the manufacture of 1080 baits”, which is ambiguous in relation to the time of sampling in the work shift. The report states that workers’ samples were taken:

- “immediately prior to commencing work”
- “during the working day, whenever toilet visits were made”, or
- “on days following work handling 1080 products”.

The first and last approaches, in particular, are not consistent with the Department of Labour advice that “End of shift” means sampling in “The last two hours immediately following the end of the working day”. If a sample was taken the next day, or prior to the next shift, it would be likely that a substantial proportion of the 1080 that the worker had received during the previous work period would have already been excreted before the sample was collected.

For a substance like 1080 which has a short half-life in the body, this makes interpretation of the results uncertain. The Agency notes that this would tend to result in lower 1080 concentrations in urine, so that it certainly does not invalidate the high results reported. The Agency recognises that the researchers may not have had full control on sampling times used in the study.

Contamination of urine samples

The report indicates precautions were taken during sampling to avoid contamination of samples, but does not specify what these were. Elsewhere the report indicates that the possibility of contamination cannot be excluded. This raises considerable uncertainty about the findings reported (particularly the more extreme values discussed further below). Contamination of samples is probably particularly likely if they were provided during a mid-shift toilet break. Removal of contaminated clothing and cleaning of hands before collection may not be practical or feasible, and it would be relatively easy for the sample to become contaminated.

Group rather than individual results

The report gives ranges and does not indicate which individual results were associated with particular work activities. This limits interpretation substantially, and makes it harder to determine the likely influence of work duties, sampling times, and contamination of samples.

This also means that the results cannot be compared against a BEI value derived from the AOEL the Agency derived in section M2.2. The Agency notes that the resulting BEI would be lower, so the overall outcome would therefore be similar, since the results were already high in comparison to the Department of Labour BEI value.

High values

A number of the urinary 1080 concentrations found were high compared with the BEI. The highest value for a factor worker was 3,410 µg/litre which exceeded the Department of Labour BEI by a factor of 227.

The exposure a worker would need to receive to produce such a contaminated urine sample would be very high (unless this was the result of accidental contamination). Since unchanged 1080 is what was measured in urine, there is no way of knowing the source of the material.

The following calculation is done by the Agency just to emphasise the dose that would be required to produce such a urinary concentration and is based on the approach used to derive the BEI (Beasley 2002, personal communication, 2007).

The 1080 exposure during the previous shift would be estimated by the following calculation (using Beasley's parameters):

$$\begin{aligned} \text{Internal dose (mg/kg bw/day)} &= \frac{\{\text{concentration in urine} * 2 \text{ litres}\}}{\{\text{body weight} * f\}} \\ &= (3410 * 2) / (60 * 1/5) \\ &= 568 \mu\text{g/kg bw/day} \\ &= 0.57 \text{ mg/kg bw} \end{aligned}$$

The parameters used in the calculation are:

- 2 litres of urine is produced per day
- Body weight was assumed to be 60 kg
- f = Proportion of 1080 assumed to be excreted in urine = 1/5

There are substantial assumptions in this calculation. It assumes the human half life is short enough that accumulation of 1080 does not occur, which the Agency considers reasonable. The urinary volume of 2 litres per day may be misleading for a person involved in heavy outdoor work, during which a small volume may be produced. The use of one-fifth as the proportion excreted in urine is conservative in comparison with animal data which suggest one-third. (Based on the sample concentration this assumes a higher dose would be required, that is, it may overestimate the worker's dose.)

Despite these uncertainties, the result suggests that to reach such a high urinary concentration, the worker would need to receive a dose of 1080 close to the minimum lethal dose in humans (0.7 mg/kg bw). A similar calculation for the highest urinary value in the field users of 1080 suggests the 1080 intake could be as high as one-tenth of the estimated MLD in humans.

The Agency considers that a person exposed to this amount of 1080 might be expected to experience toxic signs and symptoms of exposure to the

substance. Nevertheless, it must be remembered that the MLD is based on lowest end of a range, for the most sensitive individual.

Other biological monitoring data

The Wellington Regional Council's submission reported that between 1999 and 2006, 41 urine samples and 32 blood samples have been collected from staff and contractors working with 1080. No 1080 was detected in the blood samples and none of the urine samples exceeded the BEI of 15 µg/l. The Agency notes that this is a relatively small number of samples considering the seven year duration and the likely number of personnel involved, nevertheless, these results provide are somewhat reassuring in comparison with the data reported above.

Health significance

Due to the uncertainties around the results, the Agency does not consider that any health significance can be ascribed directly to the high urinary 1080 concentrations in some groups of workers in isolation. Nevertheless the finding of residues of 1080 in urinary samples above an established BEI value is a cause for concern.

Claims that 1080 use is or is not associated with known harm

One submitter reported that two employees who they knew personally had been seriously exposed to 1080. One had died of a brain tumour at 38 years of age. The other also developed cancer. The Agency comments that chronic toxicity/carcinogenicity studies have been done in laboratory animals to test the ability of 1080 to cause cancer in animals, although mutagenicity data are negative. Only by carrying out a detailed epidemiological study involving follow up of the historical workforce would it be possible to assess the significance of such a claim.

Other submitters have made statements along the following lines: "1080 has been used extensively and that if there was a problem it would have been identified". The Agency wishes to make it clear that no credence whatever should be given to such conclusions. Occupational health specialists will be well aware that a thorough investigation is usually needed to identify an occupationally related illness.

Particularly in relation to whether or not 1080 may exert effects on the male reproductive system, a targeted investigation would be needed. Male workers are likely to be particularly reticent to raise or discuss such concerns outside a confidential context. It is noteworthy that in the case of the soil fumigant, dibromochloropropane (DBCP), see <http://toxsci.oxfordjournals.org/cgi/content/abstract/76/2/418>, effects on male fertility were not identified before a thorough investigation was done. This was the case even though investigators found the effect on fertility was quite clear-cut and irreversible. In the light of this example, the Agency emphasises that the absence of reports of adverse effects does not mean that no such effects are occurring.

M3.5 Discussion of controls to address occupational exposures to 1080

Some of the occupational health risks identified for the 1080 application appear high on the basis of biological monitoring results. In particular this applies to the following activities:

- Manufacture in the factory of stock solution and cereal pellet baits.
- Unloading of pellet baits into aircraft hoppers.
- Preparation of carrot (cereal and apple) baits in the field and loading of these baits into aircraft hoppers.

The Agency is concerned that the majority of the workforce is likely to consist of male employees. The adverse health effects associated with sub-chronic exposure to 1080 relate to the male reproductive system. Given this, the Agency concluded that the evidence the occupational exposures may be unacceptably high require careful consideration. It is desirable that controls are applied to better manage these exposures.

M3.5.1 Factory manufacturing processes

The Agency considers that preparation of stock solution and pellet baits within a factory represents a process which should be able to be addressed. Staff at the factories should be experienced in handling hazardous substances and the controls already in place requiring extensive personal protective equipment would be expected to reduce exposures to acceptable levels.

Similarly, general environmental controls such as exhaust ventilation and factory hygiene practices should be well developed.

The Agency concluded that the controls should be adequate to manage the risks from exposure to 1080 but emphasises that this assessment assumes that compliance with the requirements already in place is high. On-going training and retention of an experienced workforce is crucial in maintaining safe operations when handling hazardous substances. Successful operation of these controls needs to be periodically reviewed to ensure they are achieving the level of protection required.

Review of work practices by the company and, from time to time, the Department of Labour is necessary, taking into account the result of biological and environmental monitoring. Depending on the outcome of such reviews, the Agency considers that it may be appropriate for the Department of Labour to update *Guidelines for the Safe use of Sodium Fluoroacetate (1080)* (2002).

M3.5.2 Field loading of pellet baits

The Agency concluded that there is a limited amount that can be done to address the occupational exposures in an outdoor environment where workers cut open and empty bags into a hopper as a manual operation.

Such operations require speed of work to ensure an efficient operation. In the outside environment it is difficult to control dust. This may be particularly hard when these operations are taking place in the vicinity of a helicopter movements. Also, the heavy nature of the work may make adequate compliance with personal protective clothing requirements difficult.

There is reference in one report (Epro 2005) to the practice of unloading 25 kg bags into pre-loaded wool bails before transporting the large bails to the aircraft loading area. The large wool bail is then able to be emptied into the aircraft hopper as a single operation.

The Agency does not know the extent of the use of this practice, but considers that it may have the potential to reduce occupational exposures for the following reasons:

- The unloading of 25 kg bags can be done with less time pressure (in advance)
- The unloading can be done in a warehouse where the environment (temperature and airborne dust levels) are able to be better controlled, and exhaust ventilation may be in place.
- At the aircraft loading area, the unloading of the larger wool bails is likely to take much less time, than the unloading of the equivalent number of 25 kg bags.

M3.5.3 Preparation and loading of carrot, cereal and apple baits

Bait preparation

It is unclear where the exposures to 1080 are most likely to occur during these operations. The treatment of the carrot and other baits matrices is one possibility, although the process is stated to be ‘enclosed’. The Agency considers it would be desirable to better define exposure sources, and try to develop enhancements to reduce exposures. The practice of treating small quantities of baits (using a concrete mixer type of arrangement) also should be investigated.

Aircraft loading

In relation to bait loading of aircraft, the Agency notes that there are some similarities between the occupational exposures here and those for pellet baits. Again, the Agency concluded that there is a limited amount that can be done to address the occupational exposures in an outdoor environment where workers load possibly dusty material into a hopper as a manual operation.

The option of pre-loading of bait, as discussed above, would not appear to be an option for these baits prepared on-site as needed.

The Agency would like to consider the following two scenarios for reducing carrot-bait related occupational exposures:

- 1 Prepare the carrot and other baits in advance in a warehouse environment whether the quality can be better controlled and the occupational conditions enhanced, and then this also enable the pre-loading scenario to be introduced to reduce exposures during loading of aircraft.
- 2 Investigate and develop better work practices for the current approach to ensure occupational exposures are reduced, such as improving protection of workers during carrot treatments, improving bait quality (drying) and improving handling of the poison bait during loading.

By raising these suggested options for additional control to address occupational health risks, the Agency hopes to get the benefit of the industry and personal experience of those involved. The Agency has not made a final decision on whether or not such controls would be effective or whether they are feasible.

The Agency hopes that by identifying these options at this stage of the process, it may be possible to gain more information and stimulate other suggestions, so that effective and efficient controls to address the health risks can be applied.

Only by discussion with the industry and considering options for improving work practice is it likely that occupational health risk can be reduced.

M3.6 Conclusion on occupational exposures to 1080

The Agency concluded that the results available for biological monitoring of exposed workers provided the clearest information relating to the human occupational exposure risk. Despite the uncertainties described, the Agency concluded, based on the above analysis, that the occupational exposure risks are potentially significant to workers involved in:

- the use of Stock solution to manufacture cereal pellet baits
- the use of Stock solution to manufacture carrot bait
- the loading of 1080 carrot for aerial operations.

A number of control measures are discussed in relation to how such exposures may be reduced, but the Agency did not consider that specific controls need to be imposed to achieve measures to mitigate these exposures.

The Agency considers that the health risk are acceptable with controls, on the basis that controls when working as they are intended should be protect workers.

In view of the potential risks that appear to have been demonstrated in some operations, the Agency considers that industry and the Department of Labour should review work practices and consider whether there are options for enhancing the level of protection for workers.

M4 Non-occupational exposures: Direct

The Agency has used “direct exposure” to refer to a member of the public being exposed through direct contact with 1080-containing bait. (In section M5, the Agency considers the possibility of a member of the public 1080 being exposed to 1080 in water (including surface, ground and drinking water), meat and plants (including derived products) which the Agency has termed “indirect exposure”.)

M4.1 Agency risk assessment for public contact with baits

During 1080 treatment operations (whether aerial or ground treatment) it is possible that members of the public may come across 1080-baits during recreational activities. The likelihood of this occurring is reduced by the extensive controls in place as set out in Appendix L. In particular, public advance notification of 1080 operations (especially with notification of identified occupants of adjacent properties), and signage requirements are likely to reduce the likelihood of public exposure. Despite these control and information measures, members of the public may still encounter baits, and the degree of health risk this represents depends on a number of factors, in particular:

- age of the person (it is assumed that only a young child would deliberately put a bait into their mouth or eat it, other than with suicidal intent)
- whether or not they are exposed to bait unknowingly, which essentially relates to whether or not they recognise what the material is.

The greatest hazard of such contact relates to young children encountering a bait when not under immediate supervision by parents or guardians. Young children explore their environment in different ways to adults. They do not know not to consume non-food items. There is likely to be a limited opportunity for such activities within a treatment area. Very young children would be unlikely to be left unattended in reserve area due to a wide range of other risks (such as getting lost, reaching unfenced water or steep slopes).

1080 itself is a highly toxic substance, but it is important to recognise that a member of the public is only likely to be exposed to 1080 when it is contained at relatively low concentrations in formulated 1080-baits. Key information for a health risk assessment is the nature and 1080 content of baits. (Appendix B19 identifies that the only toxic component in the baits is the 1080.) Baits vary by both weight and the concentration of 1080 present. Some baits, such as treated carrot, also have a 1080 loading on the surface, rather than a uniform distribution throughout the carrier.

Table M5 summarises the bait sizes and concentrations based on Sections 3.1 and 3.2 (pp 82–88) from the application. Stock Solution is not included as this is not used outside the factory other than to treat carrot, cereal and apple. (Public exposure to the 1080 Technical Concentrate or Stock Solution should not be possible.)

Table M5: Bait composition, weight and 1080 content

Name of approved substance (g/kg)	Concentration of 1080 (%)	Weight	Total 1080 present/bait
Pellets containing 0.4–0.8 g/kg 1080	0.04–0.08%	2, 4, 6 g ¹	2 g: 0.8–1.6 mg
		12 g	4 g: 1.6–3.2 mg
			6 g: 2.4–4.8 mg
			12 g: 4.8–9.6 mg
Pellets containing 1.0 g/kg 1080	0.1%	2 g	2 mg
Pellets containing 1.5–2.0 g/kg 1080	0.15–0.2%	2, 4, 6, 12 g ¹	2 g: 3–4 mg
			4 g: 6–8 mg
			6 g: 9–12 mg
			12 g: 18–24 mg
Paste containing 0.6–0.8 g/kg 1080	0.06–0.08%	20 kg pail or 500 g tube.	Tube: 300–400 mg
		10–15 g per dose	Dose5: 6–12 mg
Paste containing 1.5 g/kg 1080	0.15%	20 kg pail or 500 g tube	Tube: 750 mg
		10–15 g	Dose6: 15–22.5 mg
Paste containing 10 g/kg 1080	1.0%	400 or 500 g tubes	Tube: 4–5 g
			(4,000–5,000 mg)
			Dose4 50 g (in bait station): 500 mg
Gel containing 1.5 g/kg 1080	0.15%	200, 500 g block ²	200 g: 300 mg:
			500 g: 750 mg
Gel containing 50 g/kg 1080	5%	500 g PE tube	Tube: 25 g
			(= 25,000 mg)
			Dose (0.5 g) 3: 25 mg
Gel containing 100 g/kg 1080	10%	500 g PE tube	Tube: 50 g
			(= 50,000 mg)
			Dose (0.5 g) 3: 50 mg
Carrot containing between 0.2 and 1.5 g/kg 1080	0.02–0.15%	Minimum size of bait recommended 6 g (Appendix F, F2.1)	Dose (6 g): 9 mg
	(typically 0.02–0.04%)		

- The wording of section 3.1 and 3.2 is that the baits are “typically 2, 4, 6 g. This implies they may be different. In H-A13, p235 the applicants refer to 12 g baits, so values for 12 g baits have been included.
- Risk assessment for these large, gel block baits, takes into account that they are used in bait stations. It is most unlikely that a child would gain access to such baits.
- Gel baits are said by the applicants to be applied in small “pea-sized pieces approximately 0.4 g” in H-A18, p239. Since this measuring process is unlikely to be highly accurate the Agency based calculations on 0.5 g.
- Information on the pack size and use is not provided in H-A17, p238 for paste baits. On the ACVM web site (NZFSA 2007), the label for 1.0% 1080 Wasp Paste indicates the tubes contain 400–500 g of bait. The product is used for wasp control in bait stations only and 50 g is applied to each bait station.
- Information on the pack size and use is not provided in H-A17, p238 for paste baits. On the ACVM web site (NZFSA 2007), the label for the Pestoff Professional 1080 Possum Paste 0.08% says apply 10–15 g baits in weatherproof pots, in bait stations, on overturned sods or on tin lids.
- Information on the pack size and use is not provided in H-A17, p238 for paste baits. On the ACVM website (NZFSA 2007), the label for the Pestoff Professional 1080 Possum Paste 0.15% says apply 10–15 g baits in weatherproof pots, in bait stations, on overturned sods or on tin lids. The Agency notes that comparison of this wording with older labels from the Agency files indicates that the quantity of paste applied to vegetation has increased since the 1990s. Older labels refer to use of 5–10 g of bait, but the new labels refer to use of 10–15 g.

In order to assess the poisoning risk to members of the public, in particular, young children, the Agency considered likely effect of exposure to baits containing highest quantities of 1080, as a reasonable conservative estimate. In some cases the baits are only used in ways which very substantially reduce the risk of a child gaining access to the bait, such as using containment in bait stations or attachment to trees out of reach of young children. If the bait is only applied in a bait station or in a bait bag nailed to trees, the likelihood of a child gaining access to the bait is greatly reduced.

The Agency assessed the human health exposure in comparison to the minimum lethal dose (MLD) for humans (0.7 mg/kg bw) from section M2.1. Since the likely 1080 exposure in relation to body weight varies with age and weight, the calculation was carried out separately for children as the conservative estimate. For adults, it was assumed that oral exposure would only occur if the person contaminated their hands inadvertently and then consumed a residue later when eating or smoking. The Agency did not assess the risk from dermal absorption because information on dermal absorption of 1080 is sparse. Transfer of contamination from skin to food represents and oral intake.

The Agency based the human risk assessment of 1080 from bait for a young child based on children aged 3–4. The Agency identified a useful source of data of weights of children at different ages (US CDC, 2007). Although the data are for the population of the USA, they are considered sufficiently accurate for the purposes of this assessment. The dataset indicates that 3–4 year old children are approximately 14.4 kg (boys) and 13.9 kg (girls). The Agency used 14 kg in the calculations.

M4.1.1 Pellet bait

If a 14 kg child consumed a complete bait containing 12 mg (typical) or 24 mg (maximum) of 1080, the dose would be 0.86 mg/kg bw or 1.7 mg/kg bw respectively. This indicates that for a very young child, a large bait could provide a lethal dose of 1080. The above values exceed the lowest estimate for MLD (0.7 mg/kg bw). This also indicates that serious toxic effects may be expected to occur if a significant proportion of the bait was consumed by the child.

M4.1.2 Paste/gel bait

The amount of 1080 present in the approximate “bait” sizes, being the size of “pea sized” blob, indicate a possible exposure to a similar quantity of 1080 as from a pellet bait for the lower concentration materials, but the gel containing the highest concentration, the quantity of 1080 in the “pea sized” blob could be up to 50 mg. Therefore, for the highest concentration gel bait, the health risk is higher. The Agency considers it to be more likely that a child may get this dose from a paste or soft gel, due to the ease of swallowing of a fluid material rather than a dry unpalatable solid. On the other hand, the Agency notes that these baits are only applied by

ground-based pest control operators. The placement of paste and gel bait in relation to public walking track is likely to be under better control than for pellet and carrot baits from aerial applications. This means that the likelihood of encountering such baits should be reduced.

Carrot baits

The Agency notes that the estimated quantity of 1080 in a typical carrot bait as listed in Table M5 is less than that of a pellet bait, so concluded that the risk from these baits would be similar, or lower than for pellet baits.

M4.1.3 Comparison with the applicants' health risk assessment for public contact with baits

The applicants looked at the assessment in a different way, by asking the question, "How many 6 gram baits carrying 0.15% of 1080 would a 60 kg adult or a 20 kg child need to consume to reach the estimated human LD₅₀ (median lethal dose) of 2 mg/kg bw.

As discussed in section M2.1 of this appendix, the Agency preferred not to use this LD₅₀ value as the basis for acute risk assessment. The Agency verified the calculation made by the applicants which indicated that a child would need to consume about four 6 g or two 12 g baits respectively to reach this dose rate of 2 mg/kg bw.

The applicants considered the fatal dose to the child was 2 mg/kg bw (the lowest reported human LD₅₀). To reach this dose a child of 20 kg would need to consume 40 mg of 1080.

$$\text{Weight of child} * \text{LD}_{50} \text{ (mg/kg bw)}$$

$$= 20 \text{ kg} * 2 \text{ mg/kg bw}$$

$$= 40 \text{ mg}$$

Each 6 gram bait containing 0.15% of 1080 contains 9 mg of 1080

$$6 \text{ g} * 0.15/100 = 9 * 10^{-3} \text{ g} = 9 \text{ mg} \text{ (since there are one thousand milligrams in 1 gram)}$$

How many baits dose the child need consume to receive 40 mg?

$$40 \text{ mg}/(9 \text{ mg per bait}) = 4.44 \text{ (about } 4 \frac{1}{2} \text{) 6 gram baits}$$

The applicants rounded the result down to 4 baits

Clearly for a 12 g bait with the same concentration of 1080, the result is half the number for the 6 gram bait, about 2 baits.

Although the applicants' calculation appears correct within the assumptions made, the Agency does not totally agree with the applicants' interpretation of this information. For example, in Section 4, H-A19, of the application, the applicants state "a 60 kg person would need to eat about 13 six gram baits containing 0.15% to be fatally poisoned".

The Agency considers this statement quite misleading for several reasons. The applicants are making their comparison with the estimated median lethal dose (LD₅₀) value estimate for humans. The median lethal dose is the dose at which half of the population might be expected to die. Thus, it is quite possible that an individual adult might die as a result of a dose below this level. Indeed, one would expect that would be the case if the LD₅₀ estimate is correct, since that is what the parameter defines.

A greater concern is that the Agency believes that the controls should prevent not only fatalities, but also serious toxicity. Serious illness may result from a lesser dose than the applicants suggest may be necessary, and clearly this would also be of concern.

It is for these reasons that the Agency used the estimated minimum lethal dose (MLD) as the threshold for carrying out the acute human risk assessment.

M4.1.4 Information from the National Poisons Centre on human poisoning with 1080 in New Zealand

The Agency sought information which would give an indication of the public health risk from such operations, in particular, whether there have been cases of poisoning resulting from 1080 operations, since these operations have been occurring for many years. The National Poison Centre in Dunedin provided some information in this area covering the years July 2002 – March 2007 (Beasley, personal communication, 2007). Due to the nature of the records (calls and enquiries rather than cases) the information is relatively difficult to assess in respect to poisoning. Ideally further analysis of the data would be carried out. The conclusion reached was that none of the “cases” involving symptoms looked likely to be the result of 1080 poisoning. This is qualified by recognition that this is limited to those reports for which the information was sufficient to enable a conclusion to be reached. It is also, of course, assumed that following any serious poisoning a call by a member of the public or the accident and emergency staff carrying out the treatment had been made. There was one case involving apparently deliberate ingestion of a 1080-containing material, but information on the outcome was not available.

This information suggests to the Agency that the number of incidents involving 1080 exposure is very low, and that the above “worst case” assessment overstates the acute health risk. The fact that there are numerous enquiries, though little evidence of poisoning, suggest that there is a high level of concern about direct exposure to 1080 during operations. The submissions also make this clear.

M4.1.5 Overall risk assessment

The Agency notes that the risk to young children from consumption of 1080 baits reduced because they are unlikely to be in the bush unsupervised for any length of time due to other hazards (not related to pest control). The likelihood that a child would find a bait and eat a

substantial proportion of it before they were found and stopped from doing so is highly unlikely.

The controls in place to prevent this happening even within treatment areas also need to be borne in mind. The requirement to check major paths for visible bait after aerial application, is likely to greatly reduce the likelihood of a child finding bait, as the children are most likely to be on or near major walking tracks. Similarly, signage draws the attention of parents and guardians to the need for care when treatment has occurred. Children as young as those for whom the assessment was done (3–4 years old), are likely to be restrained in child carry backpacks or push chairs for a lot of the time that they are passing through public walking tracks.

There should be no realistic risk of an adult consuming a pellet bait, other than deliberately. The risk for adults is more likely to relate to gel/paste bait left on vegetation. It may be possible for someone (whether they are an adult or a child) to get such material on the skin of their hands/legs, because pastes and gels (other than those used in bait stations) that are applied to vegetation are soft and sticky. A member of the public (whether a adult or child) may not be aware that they have been exposed to the material. There is the possibility of the material being transferred to the hands and mouths. The Agency concludes that, this is unlikely, and notes that no poisonings in such situations have been reported. The Agency further concludes this is as a theoretical possibility rather than a likely outcome. Bait recognition is likely to be important to prevent such exposures and this relates to how well advertised and sign-posted the poison drop has been. It also depends on how clear the communication of the type of bait (particularly if it is paste/gel bait left on vegetation or overturned sods) has been. The Agency notes there is a requirement for signage or marking at each application site, which would be clear to people and reduce the risk (see Appendix L). As noted above, paste and gel baits are manually applied, so proximity of baits to public walking tracks should be unlikely.

The Agency has assessed the risk, taking into account the extensive controls in place and concluded that the risk to the general public is acceptable with controls.

M5 Non-occupational exposures: Indirect

The Agency has used “indirect exposure” to refer to a member of the public being exposed to a 1080 via drinking water, meat or plant material, not as a result of exposure directly to 1080 bait, itself.

M5.1 Drinking water exposure

Exposure to 1080 from drinking water has been raised as a concern for several years particularly in relation to aerial application of 1080. This is one of the major issues raised in submissions on this application.

M5.1.1 Definitions

The following terms are used as defined below.

- **Surface water** means the water on the land surface. It can be running (as in streams and rivers) or quiescent (as in lakes, reservoirs, impoundments and ponds). Surface water is produced by run-off of precipitation and by **groundwater** seeping through the top layers of soil. Surface water can also be defined as all water open to the atmosphere and subject to surface run-off.
- **Ground water** is water contained beneath the land surface. More particularly, water contained in the saturated zone of the soil, which can be extracted in usable quantities.
- **Community drinking water supply** is a publicly or privately owned drinking-water supply that serves more than 25 people at least 60 days of the year.
- **Drinking water** means water used as a human drinking water source. (Note that this is **not** the definition used in drinking water standards or guidelines.)

The Agency notes that although not a part of a regular supply, trappers and hunters take water directly from surface water courses for human consumption. This is similar to the taking of surface water directly for use by one or more dwellings or community facilities, except that the person may be within the 1080 drop zone so that the risk of contamination is higher.

M5.1.2 Background

Source data relating to residues in surface water are reviewed in Appendix E.

Collection and storage of samples

There may be some uncertainty associated with the results, when sample storage information is taken into account as discussed in Appendix E. Eason, et al 1994 (cited in Table E1, Appendix E) refers to water samples being frozen “within 5 hours” of collection. The Agency notes this seems a relatively long time before appropriate storage of the analytical sample was carried out, but it reflects the reality of sampling remote water sources and traversing the treatment area on foot.

In relation to the time of analysis and storage stability, the Agency considers that this may not be such a concern for testing of community drinking water supplies or source water sources. This is because the Agency understands that sampling protocols required in conditions by the Medical Officers of Health require testing to be done in a time-dependent fashion to confirm freedom from contamination prior to reconnection of supplies. For these samples, analysis is less likely to be influenced by the decomposition in storage. The Agency also expects that these samples

would be taken from relatively accessible locations (the water supply intake), so that handling of the sample before analysis to prevent 1080 break down (rapid chilling, if not, freezing of the sample) would be possible.

Timing of sampling

Due to water flows, it is possible there may be a small spike of contamination in flowing water, if a small proportion of the bait fell into a stream during the operation. It may be some sampling times were too late to detect whether such contamination had occurred. Analytical findings on later samples would be unable to verify whether or not an earlier spike of contamination had occurred. In respect to public water supplies the intake would generally have been closed during the period of the 1080 drop due to controls in place (as discussed below).

This may be important when considering on-going controls. When the treatment area has involved the catchment for a public water supply, the Agency understands that it has commonly been a condition, that the intake is closed until a negative analysis has been confirmed. The Agency considers it is desirable to keep such controls in place.

These controls are a sensible precaution to guard against the remote possibility of a major contamination incident (such as the dropping of a load into a major stream or reservoir). The Agency understands that another condition commonly applied is that in the event of a major incident, such as the dropping of material in the wrong area, this need to be reported as soon as possible to the Medical Officer of Health.

M5.1.3 Analytical results

Surface water

Only rarely has analysis of the surface water resulted in the finding of detectable residues of 1080, after aerial dropping operations. This is the case, even though inspection has shown that baits are not infrequently visible in streams after aerial 1080 operations (see Table E1, Appendix E).

In the Otago rabbit operation, the water concentration found in one stream one hour after treatment was 0.0006 mg 1080/litre. Two higher surface water values have been reported. The first was 3.4 µg 1080/litre from Marlborough Sounds in 1994 (Booth et al, 1997; Eason et al, 1999) and the second was 3.5 µg 1080/litre, from Manganuiateao in 1996 (Eason et al, 1999).

The Agency notes that the water residue data indicate that 1080 concentrations in surface water are generally below the current detection limit of 0.0001 mg 1080/ litre, as discussed in Appendix E.

Community drinking water supplies

All 39 samples from drinking water supplies at the time of this report (Eason et al, 1999) were negative. Such findings are not surprising given the dilution involved and the fact that the reticulated supply intake would be taken some distance from the treatment area.

M5.1.4 Health risk assessment for drinking water

For the purpose of human health risk assessment, the Agency concluded that the highest concentration found after a treatment operation should be used, and that it is not appropriate to set these aside the higher values. It is desirable that the risk assessment is for the reasonable conservative estimate. In taking this approach, it is recognised that the positive finding within drop zones are more likely to be relevant to persons inside the drop zone or nearby private residential supplies than to larger streams used for reticulated drinking water supplies.

Therefore, the Agency assessed the health risk assessment in relation to the maximum contamination concentration found in a surface water sample 3.5 µg 1080/litre.

Exposure to surface water residues from 1080 is likely to be extremely intermittent. For this reason the initial point of comparison was the acute exposure criteria, the MLD. This assessment is considered relevant to both a direct stream supply and the use of stream water for direct consumption by trampers and hunters.

The residues of 1080 found and used for this assessment was 3.5 µg 1080/litre.

The standard intake assumption for drinking water intake is 2 litres per person per day (Ministry of Health, 2005).

Taking a young child (3 - 4 years, body weight 14 kilograms), the intake from this concentration in water would represent a dose rate of:

$$(3.5 * 2)/14 = 0.5 \text{ µg/kg bw.}$$

This is less than one thousandth of the MLD used for acute exposure assessment above (700 µg/kg bw). The calculation includes conservative assumptions:

- That the child drinks 2 litres of water per day
- That all the water consumed is contaminated at the stated level

The Agency also considered whether a risk assessment in comparison with a chronic exposure criterion should be performed, and concluded the only situation where this could potentially be relevant is where a stream is used to feed a small reservoir (roof tank) for one or a small group of residential properties.

It is clear that in this situation the peak value is likely to be subjected to some dilution as the reservoir would contain water provided from the source prior to the 1080 drop. It is most unlikely that the peak level of 3.5 µg 1080/litre would be sustained in the stream flow for more than a short time. Therefore, for the purposes of health risk assessment the Agency reduced the concentration by a factor of 10 due to this dilution effect, giving a value for assessment of 0.35 µg 1080/litre.

The projected dosage, for the 3–4 year child, as derived above, therefore becomes, 0.05 µg/kg bw. The appropriate threshold for comparison for this dose level is the $PDE_{\text{water}} = 0.01 \mu\text{g/kg bw}$ derived in section 2.2.3.

On the basis of this comparison, the value appears to suggest that the child could receive a dose higher than the PDE_{water} .

It is important when considering this comparison to take into account the basis on which the PDE_{water} has been set. It is derived from the lowest no observed effect level in the laboratory animal, and this value has been divided by a high uncertainty factor (3000). Included in this uncertainty factor is a factor to allow for a lifetime of exposure at this level. The scenario described above to identify a way that water contamination could cause intake over a period is an unlikely one, and it could not generate a lifetime of exposure.

The Agency considers that the health risk is not significant given the small chance of such an event and the fact that the comparison is with a chronic threshold when chronic exposure is most unlikely to occur.

M5.1.5 Controls

Water supplies

The above assessment has taken into account what the Agency understands are “standard” controls required in relation to aerial operations covering areas used to collect of water for a public water supply. The Agency expects that during the immediate period of treatment (when poison is actually being dropped) standard controls will apply to address high risks, such as:

- during the operation, no loaded aircraft will fly over reservoir lakes or major feeding streams
- the intake for any public water supply will be disconnected from any streams arising from the treatment area
- arrangements will be made to ensure any incident involving accidental distribution outside the drop zone will be notified as soon as possible to the appropriate authorities.

The Agency has not separately assessed the health risk from a major contamination incident, such as the implications if a load of 1080 pellets/carrots was dropped into a reservoir. During the drop period, the

intakes are closed and a notification system is in place requiring the pest control operator to advise the authorities of any incidents. If such an event occurred, the drinking water supply would not be re-exposed to the source water until public safety was assured. The risk of a large-scale contamination of a public water supply is, therefore, extremely remote.

If such an event occurred, the source water would not be utilized for the drinking water supply until public safety had been assured. The risk of a large scale contamination of a public water supply is, therefore, extremely remote.

Ministry of Health guidelines to Medical Officers of Health

The Ministry of Health also issued 1080 Guidelines to Medical Officers of Health to assist in decision-making in relation to conditions which might be usefully applied to protect human health and safety. A particular focus of these guidelines was the potential for 1080 to get into drinking water. The Ministry of Health has advised the Agency that the guidelines are still in current use.

Having established the PMAV for 1080 = 0.0035 mg/litre, the Ministry of Health, also recommended that monitoring may be carried out after 1080 drops. It was proposed that the Medical Officers of Health should consider requiring water monitoring showing levels in source waters less than 0.002 mg/litre. This approach was taken to ensure the “true” level was below the PMAV, as it is necessary take into account that only a relatively small number of samples would be analysed and there is statistical variability.

The Ministry of Health made a submission on the application, but expressed no view on the adequacy of the HSNO controls on 1080, nor did they comment on the conditions used by Medical Officers of Health (which the Ministry of Health designate for HSNO enforcement purposes) for protection of public health.

Infant-formula from private supplies

Families living close to the drop area, may have a baby receiving water as part of milk formula. If such a family has a stream fed supply it is undesirable for this water to be used directly given the immediate feed requirements of the child. For such a baby, the water intake in proportion to body weight would be higher, even than the 3–4-year-old (assessed above).

Families with formula-fed children, which have a water supply that may be put at risk during any 1080 aerial operation, need to be identified and special arrangements put in place for the provision of an alternative drinking water supply until any contamination risk has passed. The Agency would expect that the Ministry of Health conditions would address such situations as part of their public health risk reduction assessment.

TEL_{water}

The Agency has included in Appendix Q a detailed discussion of the desirability of establishing a TEL_{water}.

In practice, the Agency notes that the Ministry of Health's Provisional Maximum Value (PMAV) has been used for this purpose (in assessing the health significance of 1080 contamination of surface drinking water). It was in recognition of this that the TEL_{water} established in the Hazardous Substances (Sodium Fluoroacetate) Transfer Notice 2005 (17 June 2005) was the same as the existing PMAV.

M5.1.6 Ministry of Health's provisional maximum value for potable drinking water

The Agency has included a discussion of the PMAV for potable water because:

The Ministry of Health's submission advised that it is intending to review the PMAV for 1080.

Some other submitters have expressed concern about the basis for the current PMAV and water monitoring for 1080 generally.

Existing PMAV

The Ministry of Health published a PMAV for 1080 in a public drinking water supply in the drinking water standards (Ministry of Health 2005a).

The basis of the PMAV is clearly set out in the relevant datasheet for 1080 in the Ministry of Health's draft guidelines (Ministry of Health 2005b). The derivation of the PMAV is given below.

The MAV for 1080 was calculated by the New Zealand Ministry of Health using an NOAEL derived from a Department of Conservation teratology study of rats (Eason 1999) as follows:

$$0.1 \text{ mg/kg bw /day} \times 70 \text{ kg} \times 0.5 = 0.0035 \text{ mg/L}$$

$$2 \text{ L/day} \times 500$$

where:

no observable effect level = 0.1 mg /kg body weight per day

average weight of adult = 70 kg

average quantity of water consumed by an adult = 2 L per day

proportion of lowest lethal dose allocated to drinking-water = 0.5

uncertainty factor = 500 (10 for intra-species variation, 10 for inter-species variation, 5 for the inadequacy of the studies and database).

The Agency notes that after they derived a tolerable daily intake (essentially equivalent to a HSNO acceptable daily exposure (ADE) in this calculation). The Ministry of Health has allowed half of this to be

contributed from drinking water. This is a higher proportion than what is usually permitted for other pesticides (20% is commonly used). Given the nature of use and water solubility of 1080, the Agency considers this was appropriate for the following reasons:

- 1080 is not used in any food crops, and so no food residues should contribute to the total intake on a regular basis,
- The residues in feral meat are very unlikely to be significant (see Appendix H and section M5.2)
- 1080 is highly water soluble, so the likelihood of drinking water residues is relatively high.

The Ministry of Health used an additional uncertainty factor of 5 to take account of the incompleteness of the toxicological database for 1080, in addition to the “standard” uncertainty factor of 100 consisting of 10 for inter-species and 10 for intra-species extrapolation. The above approach to derivation of the PMAV is highly relevant to the discussion of exposure parameters proposed in the document and it is discussed further in Appendix Q).

It is also noteworthy that the datasheet relating to 1080 in the Ministry of Health guidelines (Ministry of Health 2005b) indicates no information was available to the Ministry of Health relating to the removal of 1080 from a source water supply during treatment. Since 1080 is highly water soluble, the Agency assumes that it would be difficult to remove by treatment processes.

Relevance of the PMAV

In the context of the current reassessment, the Agency has assessed the estimated 1080 exposures from the intake of drinking water. While these could have been assessed in comparison to the current PMAV, the Agency considered it preferable to compare these with suitable intake parameters derived from the toxicological information which have been used to assess other 1080 exposures. This also appears particularly appropriate given that the Ministry of Health has indicated an intention to review the PMAV.

The information that the Ministry of Health intends to revise the PMAV for 1080, does not actually change the results of monitoring. It would only affect the assessment of the health significance of the values reported if the Agency was carrying out its comparison against the current PMAV.

Review of the PMAV

The Ministry of Health’s submission advised that it is intending to review the PMAV for 1080. The submission indicates that this review is awaiting the assessment of the PhD Thesis of N Foronda. (The Agency has been advised (Foronda, personal communication, March 2007) that the thesis was submitted for assessment in March 2007.) The Ministry of Health did

not indicate when it anticipated the subsequent policy development work relating to the PMAV would be carried out.

Submissions

Contamination of drinking water was commonly raised as a concern in submissions.

Weaver (2003, p 52) and Weaver (2006, pp 377–378) were cited by some submissions in support of the view that the existing PMAV is not appropriate from a regulatory perspective. Weaver's main criticism was that the developmental effects found in the rat study (which formed the basis of the PMAV, see above) may be due to endocrine disruption. He claims on the basis of endocrine disruption that smaller dose levels may have a significant effect in humans. The relevance of endocrine disruption to the mechanism of action of 1080 and its developmental toxicity is discussed in section B16.3.

The possibility of carcasses reaching waterways has been identified as a higher exposure risk for water contamination. The Agency understands that carcasses can reach waterways particularly after significant rain events and agrees there are some aspects which make this a higher risk in relation to drinking water contamination. In particular:

A single carcass could have a number of baits undigested in stomach material so the 1080 content may be higher than the occasional bait reaching a waterway.

The time at which the carcass reaches the waterway is not directly related to time of the 1080 application (so that the drinking water source may already have been declared free of contamination).

The Agency notes that the results of monitoring have not found 1080 water residues other than within a short period of the 1080 application. The Agency also notes that carcasses are most likely to wash into waterways during a significant rain event. At such periods, dilution of any contamination is likely to be enhanced.

M5.1.7 Drinking water health risk conclusion

The Agency compared both the acute and chronic exposures that could occur from aerial 1080 applications, based on the water sampling data that have been reported and in comparison with conservative assumptions (which tend to overestimate the health risk).

The conclusion is that both the acute and chronic exposures are not significant taking into account the control measures in place to minimise drinking water contamination and the likelihood of such exposures and their duration.

M5.2 Exposure to meat (tissue) contaminated with 1080

M5.2.1 Meat and milk contamination

A potential human health risk that has been raised in the past and by a number of submitters is the possibility of exposure to 1080 residues in meat from animals which have been sub-lethally poisoned with 1080. The Agency identified three main scenarios that may give rise to meat containing 1080 residues.

- Farm animals (sheep, beef, goats etc) may accidentally get access to 1080 (due to incorrect placement of baits outside the intended area or failure of a protection strategy to contain the animals (such as fencing). In this instance, consideration was also given to the potential for contamination of milk from dairy animals.
- Feral animals, deer or pigs taken by hunters may have been poisoned
- Feral animals, possums, rabbits, taken by hunters may have been sub-lethally poisoned as part of the intended target of the operation.

Appendix H reviews the information that is available relating to 1080 residues in the meat of animals that are sub-lethally poisoned with 1080. The key parameters determined in that appendix were as follows.

- 1 Highest likely 1080 concentrations in tissue for human consumption were: offal 0.064 mg 1080/kg, skeletal muscle 0.050 mg 1080/kg. (This is based on tissue residue levels in sheep 2½ hours after a single exposure to 1080.)
- 2 Highest likely 1080 concentration (milk) was estimated to be 0.14 mg 1080/litre. (This was based on the sheep blood plasma concentration 2½ hours after a single exposure to 1080.)

M5.2.2 Farm animals

Acute exposures

The Agency considered the significance of the 1080 exposure from consumption of a large meat meal containing the maximum 1080 residue identified above. The NZFSA advised the Agency that based on what people report they consume at an average sitting an adult is likely to consume approximately 173 g of meat in a day, and approximately 45 g offal (NZFSA, unpublished data, April 2007). For the assessment of the possible intake for skeletal muscle the Agency concluded that a large meat meal could involve the consumption of 250 g of meat by a 70 kg adult. The reason a higher estimate was used was that the assessment should reflect an individual exposure (as may occur after a successful hunt) rather than an average figure. This would give rise to a 1080 dose of:

$$= (0.25 \text{ kg} * 0.05 \text{ mg/kg})/70 \text{ kg}$$

$$\text{Dose rate for a 70 kg adult} = 0.00018 \text{ mg/kg bw}$$

Such a calculation is conservative as the assumptions are:

- that the meat contains the highest 1080 concentration from the sheep studied
- the consumption of a large meat meal containing this high level occurred.

The resulting estimated 1080 intake is low in comparison to the estimated minimum lethal dose (MLD) of 0.7 mg/kg bw for humans. A similar calculation relating to children would generate the same conclusion and is not included.

Another approach to the human risk assessment (Eason et al, 1994) was to estimate how much meat containing the residues it would be necessary for a child to consume to reach the MLD. This gave estimates far in excess of any possible level of meat consumption (400–500 kg of meat) for a 30 kg child. This was based on residue concentration (0.05 mg/kg) slightly lower than those assumed by the Agency above, but clearly there is a large margin of safety in such estimates.

The Agency did a separate calculation for offal. The calculation was based on the consumption of 45 g of offal in a single meal containing a residue of 0.064 mg 1080/kg. The Agency considered larger consumption of offal is less likely than for other meat. The calculation becomes:

$$= (0.045 \text{ kg} * 0.064) / 70$$

Dose rate for a 70 kg adult = 0.00004 mg/kg bw.

The health risk relating to the consumption of offal is even lower than for other meat cuts.

Longer-term exposures

The only scenario that the Agency could envisage that could give rise to repeated exposures to contaminated meat for one or more individuals would be the possibility that a large animal is taken and used for food over a period of a week. If the animal, such as a deer, contained 1080 residues, the family could be exposed to residues on a regular basis until the contaminated meat from the single animal has been consumed.

The appropriate threshold for comparison for this dose level is the $PDE_{\text{food}} = 0.006 \mu\text{g/kg bw}$ derived in section M2.2.3. Using the residue concentration above and the same intake of 250 g of the meat, the adult repeated dose intake greatly exceeds the PDE_{food} . The dose rate in comparable units is for the 70 kg adult is $0.18 \mu\text{g/kg bw}$, about 30 times the PDE_{food} .

It is important when considering this comparison to take into account the basis on which the PDE_{food} been set. It is derived from the lowest no observed adverse effect level (NOAEL) in the laboratory animal, and this

value has been divided by a high uncertainty factor (3000). Included in this uncertainty factor is a factor to allow for a lifetime of exposure at this level. The scenario described above to identify a way that meat contamination could cause intake over a period is an unlikely one. It is most unlikely that a particular hunter would repeatedly shoot contaminated game, so the Agency considers this scenario could not result in a lifetime of exposure as provided for in the setting of the PDE_{food} .

It is also important to understand that the PDE_{food} represents 30% of the ADE and for there to be an excessive intake of 1080 over a lifetime the other possible sources of 1080, such as the 50% from the drinking water intake, also need to be reached. The Agency considers that the health risk is not significant given the small chance of such an event and the fact that the comparison is with a chronic threshold when chronic exposure is most unlikely to occur.

A separate assessment has not been done in relation to offal. The Agency understands that the NZFSA recommends that offal from feral animals are not used for human consumption. Even if the offal was consumed the above calculation indicates a lower risk would apply, than for other meat cuts, due to the lower consumption figure for offal.

Weaver, 2003 raised concern about the implications of meat residues for toxic effects other than acute toxicity due to his concern that developmental effects may occur via endocrine disruption (as discussed in section M5.1). As noted there the question of endocrine disruption is discussed in section B16.3.

M5.2.3 Human health risk from milk consumption

As listed above, a conservative estimate is that milk from a contaminated animal could contain approximately 0.14 mg of 1080/litre. The application (in Section 4, H-A26) suggests that milk residues are actually lower than the conservative estimate used, but the Agency did not have the relevant information. If one litre of this milk was consumed by a 14 kg child (aged 3–4 years as discussed in Section 4), the dose received would be:

$$0.14 \text{ mg}/14 \text{ kg} = 0.01 \text{ mg/kg bw}$$

This value is below the minimum lethal dose estimate for humans 0.7 mg/kg bw, although the margin of safety is low (less than 100).

The Agency notes that the assumptions in this assessment would be that the child received the milk directly from the poisoned animal without dilution, which is most unlikely to occur. The Agency concluded that the human health risk from such contamination is low. (As noted in the Appendix H the estimated milk 1080 residue level is likely to be overestimated)

Since dairy animals are handled in herds, it is highly likely that some animals in a herd would be severely poisoned and would suffer obvious

symptoms. This would alert the farmer so that the milk from these, or the other animals, could be intercepted before processing. The applicant refers to one such incident in H-A26.

In the very unlikely event that interception of the milk was not able to be done, the milk would be diluted with milk from uncontaminated herds before processing, so any slight human health risk would be mitigated. While this would reduce the public health risk, such a situation is extremely unlikely. The Agency expects that any potentially contaminated milk or products from it would be intercepted and destroyed.

M5.2.4 Effect of controls (not limited to HSNO controls) in relation to meat

Appendix H includes (as an annex) some information on the controls in place to prevent the occurrence of 1080 residues in recovered farm animal and feral animals. These controls are under the control of the New Zealand Food Safety Authority (NZFSA).

It is possible to imagine scenarios which could result in residues higher than those estimated due, in particular, to the influence of the latency period after a significant poisoning (before it would be obvious that the animal has been poisoned). There is also the question of the relative sensitivity of human food animals, since if the animal consumed is less sensitive to 1080 than the sheep the residues present are likely to be higher than those in the sheep. This is most likely to be relevant to possum meat, but the Agency notes that there are stringent controls in place relating to commercial hunting operations (as discussed in Appendix H).

The Agency concluded that the greatest risk relates to private hunters taking game for their own use, as the Agency understands that this activity would not be subject to regulatory surveillance. Nevertheless, advice to hunters is widely available in this area, in association with public notices and signage relating to poisoning operations. The Agency expects that hunters would be aware of the need to only hunt in areas which are not currently areas where 1080 bait is present, or has been within the restricted time period set by the NZFSA (see Appendix H). The Agency expects that hunters and farmers would be very careful in relation to exposure of their friends and/or families to poison residues (as noted in some submissions).

The Agency notes that the risk is likely to be substantially higher for substances such as the anticoagulants for which longer withholding periods apply. Members of the public may not understand why such long periods are needed. Given the concern with residues, the Agency actually considers the risk may be higher if 1080 is further restricted resulting in greater use of second generation anti-coagulants as residues for such poisons are more persistent in the meat. (In this context, the Agency disagrees with some submissions received on the application.)

The Agency notes that the likelihood of a hunter taking game that has been poisoned with 1080 before the animal either dies or completes excretion of

the poison (which only takes about 48 hours) is remote. The Agency also notes it is most unlikely that this would happen repeatedly for the same hunter and for their family, so a long-term (lifetime) exposure from this source could not occur.

M5.2.5. Wild aquatic species

Concern has been expressed by some submitters that 1080 residues may occur in aquatic species used for human consumption.

Appendix C includes limited data on residues in species of relevance and these are listed in Table M6. (For details on the nature of the tests and the references consult Appendix C.) The applicant considered this (H-A25) and this indicates the eel were fed contaminated possum meat.

Table M6: Tissue residues in aquatic species used for human food

Species	Tissue	Maximum concentration (mg/kg) wet weight	Time and Nature of sampling
Long-fin eel, <i>Anguilla dieffenbachia</i>	Muscle	0.32	Laboratory (time not stated)
Koura/freshwater crayfish, <i>Paranephrops planifrons</i>	Tail muscle	5	Laboratory at 1 day
	Viscera	3.3	
	Viscera and muscle	7.7	

Other relevant observations in Appendix C are analyses done at different times for the koura tail muscle and viscera. For tail muscle analysis gave ~1.5 mg/kg at Day 1 and ~0.25 mg/kg at Day 8, while for viscera analysis gave ~1.2 mg/kg at Day 1 and ~0.2 mg/kg at Day 8. This suggests a relatively slow loss of residues after contamination (in contrast for example to loss of residues in terrestrial vertebrates).

For the purposes of human health risk assessment the maximum concentrations of 1080 found in aquatic species were used. While a large meat meal (250 g) was used for the assessment of feral and farm meat, in this instance a lower consumption pattern seems more likely, so the Agency used a very generous helping of 200 g of fish. The highest 1080 residue concentration from the viscera and muscle of koura (7.7 mg/kg) was used for the calculation below to estimate the dose that may be received.

$$(0.2 \text{ kg} * 7.7 \text{ mg/kg})/70 \text{ kg}$$

$$= 0.022 \text{ mg 1080 /kg bw}$$

The estimated intake from the above scenario is approximately one-thirtieth of the MLD used to assess acute exposures (0.7 mg/kg bw). If a child consumed a similar quantity of this fish they are likely to receive a higher dose on a per kilogram basis, which suggests an unacceptable risk level in that scenario, might be possible.

The Agency notes that such a meal would require the gathering of a very large number of harvested freshwater crayfish. The information in Appendix C indicates the body weight of a medium sized koura is 25.5 g, and large one is 59 g. The tail weight for the large animal was just 13.2 g. A meal of 200 g of meat would require the harvesting of about seven large animals. It seems unlikely that they would all have high 1080 residues or that they would be consumed by a single individual.

The above calculation suggests that the risk from meat consumption for freshwater species may be higher than for terrestrial meat sources. The Agency considers this conclusion misleading. A prime aim of 1080 operations is to avoid deposition of baits into waterways, and while some deposition does occur, the water concentrations are rarely detectable by current analytical methods.

The Agency considers the consumption of a large meal from freshwater species is more likely from eels which appear from the study to be likely to have lower tissue concentrations.

M5.2.6 Conclusion for human health risk from meat and tissue residues

The Agency concluded that even in the most extreme situations the human risk estimates from consumption of meat or tissues from 1080-poisoned animals or from freshwater human food sources were insignificant.

M5.3 Exposure to plants (food and medicinal) contaminated with 1080

M5.3.1 Terrestrial plants

Several submitters have raised concerns about the use of plant material for food and traditional (Maori) medicines (rongoa). (The assessment below has been assumed by the Agency to also apply to any contamination of crop plants, even though this is assessed separately by the applicants in H-A22.)

Appendix C: Exposure Assessment Non Target includes limited data on residues in plant species. While only some of these are of relevance, the Agency concluded the highest value found in these studies should be used as a basis for human health risk assessment. The results are summarised in Table M7. (For details on the nature of the tests and the references, consult that Appendix C.)

Table M7: Tissue residues in plant species

Plant species	Tissue	1080 concentration mg/kg wet weight (ppm)	Study site
Rye grass, <i>Lolium perenne</i>	Shoots	0.08 at Day 3 LOD at Day 7	Laboratory
Broadleaf, <i>Griselinia littoralis</i>	Whole seedling	0.06 at Day 10 LOD at Day 38	Laboratory

Plant species	Tissue	1080 concentration mg/kg wet weight (ppm)	Study site
Pikopiko, <i>Asplenium bulbiferum</i>	Fronde	<LOD (0.002)	Field
Karamuramu, <i>Coprosma robusta</i>	Leaves	0.005 at Day 7 0.0025 at Day 14 <LOD (0.002) at Day 28	Field

The highest plant tissue level reported was at Day 3 in rye grass at 0.08 mg/kg wet weight. Possibly this sampling time is a bit long after exposure to establish the maximum concentration level, but it has been used in the absence of other data to reflect possible residues in plant used for human food and/or medicine (rongoa). The concentration in rye grass is more than 40 times that in pikopiko which the Agency understands is used as a food source.

Ogilvie et al 2005 concluded pikopiko contamination is of no significance as no uptake was demonstrated. Hence the assessment by the Agency below, which applies the value from rye grass and is likely to be over conservative.

Ogilvie et al 2005 used 2 mg/kg as human LD₅₀, but still calculated that a person would need to consume tonnes of karamuramu to reach such a dose level. The Agency notes there is a huge safety margin. Nevertheless, the Agency performed the following calculation to assess dose levels in comparison to the MLD as used for acute exposure assessment elsewhere. The Agency assumed that food uses are likely to involve higher intakes than medicinal uses, and that a likely maximum intake would be 200 g. The dose received can be calculated as:

$$(0.2 \text{ kg} * 0.08 \text{ mg/kg}) / 70 \text{ kg}$$

$$= 0.00023 \text{ mg/kg bw}$$

The Agency notes these estimated dose levels are well below the MLD.

Ogilvie commented that karamuramu is boiled up to make “tea”, rather than consumed as such. Discussion of this exposure scenario is more appropriate in section M5.3.3.

The estimated dose of 1080 from such an exposure is over 1000 times lower than the MLD, so the Agency concluded that the potential health risks from consumption of plants as food or medicine are insignificant.

M5.3.2 Terrestrial aquatic plants

A separate, but related issue raised as a concern by submitters relates to aquatic plant residues and human consumption of these plants.

In a study designed to determine the influence of aquatic plants on 1080 water concentrations, Wright et al, 2003, studied the effect of *Elodea*

canadensis in water on the water concentrations of 1080. In addition to the question of the effects on water concentrations, the paper also produced data of relevance to plant tissue residues. Wright et al, 2003, found that when exposed to 5 µg/litre (ppb) in water, the plants absorbed the 1080 from the solution to reach a maximum concentration of 2.5 µg/kg, before declining relatively slowly to below the limit of detection (2 µg/kg) at 24 hours.

In the assessment above relating to terrestrial plants (above), the maximum concentration of 1080 used for the assessment of 1080 intake from plant consumption was 80 µg/kg.

Considering the surface water analyses, the absorption of 1080 from water containing 5 µg/litre of 1080 for *Elodea canadensis* represents a relatively unlikely scenario and gave a residue lower than that assessed for terrestrial plants. Consequently, the Agency concluded that the potential health risks from consumption of aquatic plants are insignificant.

M5.3.3 Breakfast tea

One of the earliest investigators of naturally occurring, fluorinated organic compounds, Peters, reported the presence of fluoroacetate and fluorocitrate in commercially available leaf tea. This has been quite widely quoted since, though confirmatory analyses appear to have been sparse. It is assumed that this is naturally-occurring fluoroacetate, which is present in the leaf from the plant.

O'Hagan et al, 1999 cites a reference (Peters, 1972) in support of their statement that commercial tea contained 30 ppm of fluorocitrate (isomer not specified) in addition to fluoroacetate. Unfortunately, this source did not give a concentration of fluoroacetate in tea. The concentration of fluorocitrate was presumably in the leaf, not in the infusion.

Vartiainen and Karuanen, 1984 reported trace concentrations of fluoroacetate in a ranges of plant species and tea samples (presumed to be commercial English breakfast tea). The concentration found was mean 0.19 µg/g (range 0.06–0.48 µg/g). It is of interest that no samples of leaf tea were below the limit of detection 0.005 µg/g. The reproducibility was reported as +/- 9%.

In order to assess the health significance of these values the Agency made the assumptions:

- That 10 g of leaf tea may be used to make a pot of 1 litre of tea.
- That all the 1080 in the tea leaves is extracted by the hot water (a conservative assumption).
- That the tea leaves all contained the maximum concentration found by Vartiainen and Karuanen, 1984. The Agency rounded up the concentration to 0.5 µg/g.

Using these assumptions the concentration in the resulting tea would be:

$$10 \text{ g} * 0.5 \text{ } \mu\text{g/g} = 5 \text{ } \mu\text{g/litre}$$

If a person was to obtain their daily drinking water intake of 2 litres entirely from brewed tea (this is really impossible, since some water intake is assumed to be from cooking sources, eg soup), the intake would be:

$$2 \text{ litres} * 5 \text{ } \mu\text{g/litre} / 70 \text{ kg}$$

$$= 0.14 \text{ } \mu\text{g/kg bw/day}$$

Since this represents a long term exposure to which the population is known to be exposed (although the estimates are uncertain), comparison with the $\text{PDE}_{\text{food}} = 0.006 \text{ } \mu\text{g/kg bw/day}$ is appropriate.

Such a comparison suggests that heavy tea drinker could possibly obtain from that source, about 24 times the PDE_{food} . This estimate illustrates that the PDE_{food} as derived represents a very conservative figure. In relation to the assessment of the health risk from 1080 from other sources, such as drinking water, meat and plant contamination, this estimate highlights how low the ADE and PDE values are due to the use of a large uncertainty factor, in part to reflect that incompleteness of the database. Further work may enable the uncertainty factors to be reduced. In the meantime, it should be noted that values in excess of these values would only be of concern if they were they occurred from all routes (water and food) simultaneously and if the exposure was for a significant proportion of the lifetime.

In relation to the use of karamuramu to make “tea”, the 1080 concentrations found in the Table M7 are much lower than naturally occur in leaf tea, which is consumed much more commonly.

The Agency concludes that the health risks from the consumption of tea, whether from 1080 naturally occurring in breakfast tea or from 1080 contamination of karamuramu are insignificant.

M5.4 Honey

From time to time concerns have been raised about the possibility that honey bees may forage on 1080-bait materials and contaminate honey for human consumption.

The only detailed study on the honey residues of 1080 of which the Agency is aware is that carried out in Taranaki (Lowe, 1994) One honey sample was found with 15 ppb (ug/kg) on 5 April 1993 and this subsequently declined to 5 ppb and 3 ppb respectively, the last value being samples on 19 May 1993 (after 59 days). The Agency notes that this conclusion was the result of the decline in a single honey sample, and this rate of decline has not been verified independently.

Information is provided in Appendix C relating to attractiveness of non-poisonous baits to honey bees, and this identified that some types of bait are attractive to bees and accessible for feeding. However, BB13 paste has been identified as very attractive to bees and replaced with a formulation which is significantly less attractive to bees (Morgan 2000).

The Agency concluded that in relation to 1080 honey residues, this is an issue of historical significance only as the formulation of products now takes into account attractiveness to bees. Also, the presence of hives close to a treatment area is an issue which the Agency would expect the Medical Officer of Health to consider when issuing an approval.

The Agency concludes that the health risks from consumption of contaminated honey are insignificant.

M6 Summary of human risk assessment for 1080

Assessment thresholds were established for acute, sub-chronic and chronic exposure to 1080.

The acute threshold applied was the estimated minimum lethal dose (MLD) in humans of 0.7 mg/kg bw.

The sub-chronic exposure threshold established was the acceptable operator exposure (AOEL) of 0.2 µg/kg bw/day (appropriate only for workers). The Department of Labour's biological exposure index for 1080 in urine was used for analysis of some data.

The chronic exposure threshold was the Acceptable Daily Exposure of 0.02 µg/kg bw/day. This was used to derive separate potential daily exposures for different routes:

$$\text{PDE}_{\text{food}} = 0.006 \text{ } \mu\text{g/kg bw/day}$$

$$\text{PDE}_{\text{water}} = 0.01 \text{ } \mu\text{g/kg bw/day}$$

$$\text{PDE}_{\text{inhalation}} = 0.002 \text{ } \mu\text{g/kg bw/day}$$

$$\text{PDE}_{\text{dermal}} = 0.002 \text{ } \mu\text{g/kg bw/day}$$

M6.1 Occupational health risks with 1080

The Agency has concluded that the occupational health risks associated with some 1080 manufacturing and use activities are potentially significant. This relates, in particular, to factory workers manufacturing Stock Solution and cereal-based, 1080 baits, and field workers loading 1080 treated carrot and cereal based 1080 pellet baits into aircraft hoppers for aerial application.

Limited occupational monitoring data were available for review by the Agency. The data available suggested some occupational exposures may be unacceptably high. The Agency was unable to determine whether this

was due to the need for further controls or whether inadequate compliance with existing controls was responsible.

No specific recommendations for modifications to controls on 1080 technical concentrate, Stock Solution or the formulated products are recommended to address these risks. However, the Agency has recommended that the industry, pest control applicators and the Department of Labour review occupational best practice with a view to minimising worker exposures to 1080 particularly during the operations which biological exposure monitoring indicates may represent a health risk.

M6.2 Health risks to the general public

Health risk to the general public from direct exposure to 1080 baits is considered *insignificant*.

Health risk to the general public from indirect exposure to 1080 in drinking water considered *insignificant*

Health risk to the general public from indirect exposure to 1080 in farmed and feral meat (and milk) is considered *insignificant*

Health risk to the general public from indirect exposure to 1080 in plant used for food or medicines (rongoa) is considered *insignificant*

Estimates of some health risk based on comparison of possible conservative intake estimates with derived criteria such as the PDE_{water} and PDE_{food} , in some cases appear unacceptable. The Agency considers an overall assessment of the risks needs to take into account the conservatism of the approach and the extremely unlikely nature of simultaneous exposures via multiple pathways for a prolonged period that would be necessary for an adverse effect. When such an approach is taken the health risk estimates are considered *insignificant*.

M7 Health risk assessment for the 'without 1080' scenario

M7.1 Introduction

This is a health risk assessment for cyanide products used as vertebrate toxic agents. Unlike 1080 which is only used as a vertebrate toxic agent or as an insecticide to control wasps, cyanide-containing substances are quite widely used in industrial processes. Common industrial uses of cyanides include electroplating, chemical manufacturing processes, including of rubber and plastics.

In addition to is in solid baits for control of vertebrate pests, cyanide may used use to control the same pests by means of fumigation and these types of product are not discussed here. In that case the cyanide is in the form of solid pellets which release hydrogen cyanide (HCN) gas, to fumigate structures such as ships, warehouses and stores.

M7.2 Classifications of cyanide which drive the health risks assessment

The classification of cyanide and cyanide containing formulations used as vertebrate toxic agents are given in section 5.2 of this Evaluation and Review Report.

The Agency has not carrying out a full risk assessment of the WITHOUT 1080 scenario, so a full consideration of the health risk of the cyanide products has not been carried out. In particular, the Agency has not carried out a comprehensive review of the literature with respect to cyanide salts and hydrocyanic acid.

The Agency has focused on the most important aspects which are likely to inform a comparison of the health risk assessment of cyanide products to the comprehensive assessment done for 1080 and products containing it.

From a human health risk assessment perspective the important outcome from these cyanide classifications are broadly similar across all the cyanide-based products, and are the following:

- **Acute toxicity:** The acute toxicity classifications are high ranging from 6.1A down to 6.1B for the Feratox and to 6.1C for the bait containing encapsulated cyanide. In this respect they are similar to the 1080-based products.
- **Reproductive/developmental toxicity:** All the products are also classification as reproductive/developmental toxicants 6.8B which is driven by the cyanide active ingredient and applies to all the products.
- **Target organ toxicity:** The majority of the products are 6.9A target organ toxicants but due to the low concentration in the bait containing encapsulated cyanide, this classification is reduced to 6.9B.
- **Other class 6 classifications:** Some of the cyanide products trigger other classifications, such as skin/eye irritation and sensitization. Whether or not these classifications are triggered is not considered to significantly influence any outcome from a health risk assessment point of view. Such effects can be addressed by controls.

M7.3 Nature of the effects and mechanism of action of cyanide

The discussion of the effects and mechanism of action of cyanide is limited to:

- acute toxicity
- reproductive/developmental effects, and
- target organ systemic toxicity.

Particular attention has been given to:

- the nature of the reproductive/developmental effects of cyanide in comparison to those of 1080, and

- an assessment of whether or not cyanide is responsible for sub-chronic or chronic toxicity.

The reason for focusing on these areas was that this is where the Agency believes there may be significant points of difference between the two active ingredients. Consequently this may influence the resulting health risk assessments.

M7.3.1 Assessment of acute risk to public health acute toxicity

For the transfer of products containing these substances, and the approval of the substances as commodity chemicals, the Agency used the following LD₅₀ values in rats.

Sodium cyanide	4.8 mg/kg bw	IUCLID, 2000
Potassium cyanide	5.0 mg/kg bw	Lewis, 1992

These values can be used to estimate the acute toxicity of the formulated products containing these actives. The Agency was not able to locate any oral data for the dog, but there is an intravenous, LD_{Lo} (lowest lethal dose) for the dog of 1300 µg/kg bw (=1.3 mg/kg bw).

Table M8 lists toxicity values for sodium and potassium cyanide, in various laboratory species and humans.

Table M8: Toxicity of cyanide salt in humans and animals

Species	Criterion	Value (mg/kg bw)	Route	Reference
Sodium cyanide				
Human	TD _{Lo} ¹	0.714	Oral	Lewis, 1992
Human	LD _{Lo}	6.557	Oral	Lewis, 1992
Human	LD _{Lo}	2.857	Oral	Lewis, 1992
Rat	LD ₅₀	6.440	Oral	Lewis, 1992
Dog	Lethal dose	2.25	Oral	HSDB, 2007
Dog	Lethal dose	1.2	Oral	HSDB, 2007
Potassium cyanide				
Human	LD _{Lo}	2.857	Oral	Lewis, 1992
Human	TD _{Lo}	14 (inconsistent)	Oral	Lewis, 1992
Rat	LD ₅₀	5	Oral	Lewis, 1992
Mouse	LD ₅₀	8.5	Oral	Lewis, 1992
Rabbit	LD ₅₀	5	Oral	Lewis, 1992
Rabbit	LD ₅₀	4	SC	Lewis, 1992
Rat	LD ₅₀	6	SC	Lewis, 1992

Note

1 The TD_{Lo} is the lowest toxic dose

Human data are needed for the assessment of the acute toxicity of cyanide. The lowest lethal dose (LD_{Lo}) value is the most similar to the MLD used for assessment of 1080 (0.7 mg/kg bw, see section M1.2). For both sodium and potassium cyanide the LD_{Lo} value is about 3 mg/kg bw (rounded to one significant figure).

From a human risk perspective, the key point of comparison of cyanide and 1080-based products relates to the toxicity to humans of a “standard” cyanide bait. As for the 1080 baits, the key issue then is what quantity of the active ingredient does each bait contain. The quantities of sodium or potassium cyanide in the various cyanide baits of relevance are listed in Table M9.

Table M9: Quantity of cyanide in various cyanide baits

Name of Product	Concentration (g/kg)	Concentration (%)	Bait size	Amount of active in “standard” bait
Cyanide paste for possum destruction	500–550 g/kg of sodium cyanide	55%	Pea sized portion ¹	0.275 g sodium cyanide
Trappers cyanide paste	600 g/kg	60%	Pea sized portion	0.30 g sodium cyanide
Feratox	475 g/kg potassium cyanide	47.5%	Pellets are not used directly for pest control. First they are incorporated with food to make the bait. Typical baits available commercially or as made would contain: 0.055–0.92% KCN in a 12–20 g bait 1.1–1.85% KCN in a 12–20 g bait	Only if the pellet embedded in the bait is chewed strongly and broken up, is the cyanide released. 0.07–0.18 g 0.13–0.37 g
Cyanara (paste bait)	500g/kg of potassium cyanide	50%	Pea sized portion*	0.25 g potassium cyanide

Note

* A pea-sized portion is assumed to be 0.5 g, as in Table M5.

The applicants indicate that a human adult would need to eat a single Feratox bait to reach the estimate of the human LD₅₀. Their estimate is based on an LD₅₀ of about 1.5 mg/kg, since they say a 60 kg person needs to consume about 100 mg of “cyanide”. (The label refers to the content as potassium cyanide (NZFSA 2007).)

The consumption of a single Feratox bait by an adult is not likely, but this estimate is of concern, since this means that a child need to consume proportionately less in relation to their body weight. The Agency used a 14 child in the 1080 assessment. That would mean in this case the child would need to eat only approximately one quarter of a Feratox bait for this

to represent a potentially fatal dose. This suggests that the cyanide baits are more toxic than the 1080 baits.

The Agency also assessed the amount of sodium or potassium cyanide in the pea-sized portion of cyanide paste. Since the applicants stated that the 60 kg person needs about 100 mg of cyanide, it is clear from Table M6 that the quantity of cyanide in the pea-sized portion is approximately equal to this amount.

For example, the pea-size portion of Trapper's Cyanide paste contains approximately 300 mg of sodium cyanide (about 150 mg of cyanide ion).

Again the pea-size portion of this and the other pastes contains approximately enough to provide a lethal dose to an adult, and clearly this means the quantity of cyanide present is a significant hazard to children and is almost certain to represent a lethal dose if consumed. Since the cyanide acts very quickly, unless a parent is very quick and able to get the child to vomit, this represents a serious risk. The Agency also understands that the National Poisons Centre usually considers that the induction of vomiting is not successful in removing the poison and may introduce other hazards for the victim (Beasley, Personal Communication, 2007).

It is useful to contrast this with the situation for 1080. Only with the largest of the 1080 baits was the very young child likely to receive a lethal dose from one bait.

M7.3.2 Mechanism of action of cyanide

The high acute toxicity of cyanide is very well known and understood. The toxic action of cyanide is very rapid, particularly when it is in the form of hydrocyanic acid which is fatal in a few minutes (Arena, 1986). For cyanide containing salts, the process is slightly slower. When large doses are taken death may occur in several minutes, but usually occurs within an hour (if the dose is fatal).

The main mechanism of toxicity of cyanide ion is that it binds to the oxygen-binding site of the cytochrome oxidase enzyme, in the respiratory chain of the mitochondrion (in each cell). This is essential for the use of oxygen in all cells in the body to generate energy.

From an acute toxicity point of view the central nervous system and the heart are expected to be the most rapidly effected organs, due to their high energy demand.

Symptoms of cyanide toxicity include: convulsions, reduced respiration rate, dyspnea (difficult or laboured breathing), general or partial paralysis, coma, death. (Kaye 1970; Arena 1986).

A key symptom of cyanide poisoning is that even the venous blood is bright red (rather than dull and bluish) because it is fully oxygenated. This is because the cells throughout the body are unable to use the oxygen of

cellular respiration, so the oxygen concentration in the tissues is elevated and the blood is fully oxygenated. Although cyanide does bind to haemoglobin to produce cyanhaemoglobin this is relatively slow and is not related to the mechanism of toxicity (Arena, 1986). (The reaction of cyanide with methemoglobin (oxidised haemoglobin) is much faster and is used as a detoxification mechanism. (See M7.3.3.)

M7.3.3 Antidotes

The most important distinction between cyanide and 1080 is that there are a number of well proven antidotes available for treatment of cyanide poisoning and these are known to be very effective, particularly if the victim (whether human or animal) is able to receive medical or veterinary assistance.

The antidotes are particularly effective, because the human body has the ability to metabolise small amount of cyanide and does so all the time. The body react free cyanide (which the body receives naturally in some plants in small concentrations) with sulphur to generate thiocyanate.

The available antidotes to cyanide poisoning take advantage of these natural detoxifying mechanisms. Sodium thiosulfate, administered intravenously, provides sulfur to enhance the sulfur transferase-mediated transformation of cyanide to thiocyanate. Other substances are often used to enable the body to inactivate the cyanide temporarily so that it can gradually be detoxified. Amyl nitrite, sodium nitrite and dimethyl aminophenol (DMAP) are used to increase the amount of methemoglobin in the blood by oxidising haemoglobin. The methaemoglobin binds with cyanide to form non-toxic cyanomethemoglobin. The body has enzymes which both detoxify the cyanide and others which reduce metahaemoglobin. (Healthy individuals have more haemoglobin in their body than they need, so this does not risk their oxygen-carrying capacity, unless an excessive amount of haemoglobin is oxidised. Other antidotes include cobalt compounds which are used to form stable, non-toxic cyanide complexes. If treated with these antidotes in time, the body will be able to deal with a large quantity of cyanide by gradual detoxification.

The detoxification of cyanide in the body is an essential process, as human consume cyanide-containing materials in small quantities, mostly from plants. For example, amygdalin (a cyanogenic glycoside) which is present in various staple crops in some parts of the world, particularly, cassava beans and the kernels of pip fruits (bitter almonds, apricots, peaches).

M7.3.4 Speed of action of cyanide

In comparison to 1080, cyanide acts much more rapidly than 1080. This is important point of major difference between the two poisons. In the case of 1080, there is a latency period (1/2–6 hours or so) before serious toxicity occurs, even after a fatal dose has been received.

From a health risk perspective this difference is neither totally a disadvantage, nor totally an advantage.

The Agency considers that the speed at which cyanide acts increases the public health risk to members of the general public from the unlikely accidental poisoning with cyanide bait. If a toxic dose of cyanide has been taken, it is likely that the delay before the person could receive expert emergency assistance would be too long, so that if a fatal dose had been received they would probably not be saved. (Some first aid treatments, such as inducing vomiting may be of assistance).

In respect to occupational exposures, however, although it acts quickly, cyanide provides some advantages, even in remote locations. After the initial first aid field antidotes are available which can be given (even self administered in the case of a person working alone). Although these field antidotes suitable for non-medical use are not as effective as emergency medical intervention, it is likely that they would enable the survival of at least some potentially fatally poisoned individuals.

No field antidotes are available for 1080. As discussed in Appendix B17, some symptomatic medical treatments can enhance the chance of survival, even after a potentially fatal 1080 poisoning.

M7.3.5 Generation of hydrogen cyanide

Cyanide salts present in baits reaction with acid create an additional, highly hazardous gas, hydrogen cyanide. Even without the presence of a strong acid, a small release of hydrogen cyanide occurs from the salts due to equilibrium under damp conditions.

Hydrogen cyanide significantly increase the risk of cyanide as it is so rapidly absorbed into the body, and if produce in significant quantities would represent a risk to people who are down wind of the source. The Agency considers this is a potential high issue for transportation of cyanide containing materials, as an accident involving a vehicle carrying acids is a remote possibility.

M7.3.6 Comparison of health risk to the general public and workers from cyanide and 1080

Antidotes

This is discussed under acute toxicity above. The availability of antidotes is of significance for the reduction of occupational acute risks but is not useful for public risks, as the public will not have antidotes with them, and in the event of poisoning they will not have time to get assistance.

Reproductive and developmental toxicity

For cyanide salts the reproductive and developmental toxicity classification is 6.8B. This indicates that the severity of the effects or

degree to which it is likely to be relevant to human exposures is considered less than for 1080.

The nature of the effect is important. For sodium cyanide, the data which gave rise to this classification were studies of sperm motility and vaginal cytology in rats and mice, which were exposed to 1, 30, 100 and 300 ppm of sodium cyanide in the diet.

The exposure caused slight reduction in cauda epididymal weight in all groups of exposed male rats and in male mice exposed to 300 ppm. In male rats, the number of spermatid heads per testis in the 300 ppm group was less than the number in the controls, and sperm motility in all exposed groups was marginally lower than in the controls.

The Agency notes that these effects are relatively marginal compared to the absence of sperm seen in rat studies for 1080.

In female animals, sodium cyanide produced no adverse effects on oestrous cyclicity in female mice, but at higher concentrations (100 and 300 ppm), sodium cyanide caused a significant increase in the amount of time spent by female rats in proestrus and di-oestrus relative to oestrus and met-oestrus.

The Agency notes that there is evidence of disruption of the female reproductive system which has not been demonstrated for 1080 (apart from in developmental studies).

The Agency concludes that classification of cyanide salts as 6.8B is appropriate, but these effects are minor compared to those of 1080.

Target organ effects

The 6.9A target organ toxicity applied to cyanide has not been extensively reviewed.

The Agency notes that a 6.9A classification is appropriate for cyanide salts on the basis of the known acute target organ systemic toxicity based on human data, anyway, so no detailed review of the animal test data was carried out.

In relation to low level sub-chronic or chronic exposures to cyanide, it is important to take into account the fact that humans are known to tolerate small regular exposures to cyanide in the diet without apparent adverse effect.

For this reason the Agency considers the longer term effects of cyanide are unlikely to be of health significance for exposure of either workers or the general public.

M7.4 Summary of human risk assessment for 'without 1080' scenario

The Agency concludes that for cyanide the acute health hazard to the public from cyanide baits is substantially higher than for 1080 baits due to the higher toxicity level and the speed of action of the poison.

The fact that cyanide is laid by ground-based operations, is likely to result in greater control on the placement of baits (than for aerial applications of 1080) and reduce the likelihood that members of the public will encounter baits.

The acute and chronic health risks to workers from cyanide are considered lower than for 1080. In the case of the acute risks, the availability of proven effective antidotes is of relevance for worker exposures, but not members of the public.

