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.

1 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 individually 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 al1977 and Sax, 1992)

Parameter measured* (estimated) (mg/kg bw)	Value (mg/kg bw)	Date of original source	Reference
LD_{50}‡	0.7–2.1	1970	Atzert, 1971, ref 1,2
(MLD actually)			(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	1986	Arena, 1986
	0.15 g for 70 kg person calculated as 2.1 mg/kg bw		
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 (LD_{50}), 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 LD_{50} in humans as 2–5 mg/kg bw. As the basis for the oral LD_{50} 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 LD_{50} 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 'LD_{100}' 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 LD_{50} 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

LD_{50} 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 (LD_{50}) 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 LD_{50} 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.

AOEL = (0.05 mg/kg bw/day)/(10*10*3) = 0.000166 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.)

1 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

2 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/carcinogenity 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:

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