Lord Howe Island Rodent Eradication Project

EPBC Public Environment Report December 2016

Appendix K - Human Health Package

K.1 Toxikos Human Health Risk Assessment Report
K.2 SA Health Letter Eradication Plan with Brodifacoum
K.3 NSW Health Letter Eradication Plan with Brodifacoum
K.4 Toxikos Response to SA Health Comments
K.5 Pacific Environment Response re: Toxikos Report
Human Health Risk Assessment on the use of Brodifacoum for the Lord Howe Island Rodent Eradication Plan

Prepared by: Roger Drew, PhD, DABT
Toxikos Pty Ltd.

Prepared for: Lord Howe Island Board

Toxikos document TR010610-RF2
15th September 2010

Roger Drew, PhD, DABT
Toxicologist and Health Risk Assessor
Disclaimer
This report was prepared by Toxikos Pty Ltd as an account of work for the Lord Howe Island Board (the 'Client'). The material in it reflects Toxikos’ best judgement in the light of the information available to it at the time of preparation. However, as Toxikos cannot control the conditions under which this report may be used, Toxikos will not be responsible for damages of any nature resulting from use of or reliance upon this report. Toxikos’ responsibility for the information herein is subject to the terms of engagement with the client.

Copyright and any other Intellectual Property associated with this report belongs to Toxikos Pty Ltd and may not be reproduced in any form without the written consent of Toxikos. The Client is granted an exclusive licence for the use of the report for the purposes described in the report.

About Toxikos Pty Ltd

Toxikos Pty Ltd is a consulting company formed on December 1st 2000 to provide clients with independent excellence in toxicology and health based risk assessment. Its charter is to assist industry and government make science based decisions regarding potential effects and management of environmental and occupational chemicals. For over twelve years, prior to and since the establishment of Toxikos, staff have provided toxicology and health risk assessment advice to clients in a wide range of industries and government in Australia, New Zealand and South Africa.

About the author: Dr Roger Drew is one of the Directors and Principal consultants of Toxikos Pty Ltd. He has primary degrees in biochemistry and pharmacology and postgraduate degrees in toxicology. Postdoctoral training was undertaken at the National Institutes of Health, National Cancer Institute in the USA and he spent twelve years teaching medical students and conducting toxicological research at Flinders University of South Australia. He was corporate Toxicologist to ICI/Orica Pty Ltd for twelve years before creating Toxikos Pty Ltd. Dr Drew is the only consultant toxicologist in Australia certified by the American Board of Toxicology.

Dr Drew has been a toxicology consultant to Australian Federal and State Authorities; a member of several standing expert committees of the National Health & Medical Research Council of Australia and the National Occupational Health and Safety Commission of Australia. He has been a member of many expert task groups of the World Health Organization for the International Programme on Chemical Safety.

Dr Drew is Adjunct Associate Professor in the Department of Epidemiology and Preventive Medicine, Monash University and teaches various aspects of toxicology to undergraduate and postgraduate students at local Universities. He is a member of several professional toxicology societies and is a recognised national and international expert in toxicology and risk assessment. He is currently on the editorial board of the international scientific journal "Regulatory Toxicology and Pharmacology".
Executive Summary

The Board of Lord Howe Island (LHI) is intending to eradicate mice and rats on the Lord Howe group of islands using brodifacoum in a rodent baiting program. A draft eradication plan has been released for public comment (LHI 2009). The bait chosen for the eradication programme is Pestoff®20R and has been extensively used in New Zealand for similar purposes. The bait contains brodifacoum at 0.002% and also a water soluble emerald green dye which makes it less attractive to birds. The dye will also colour moist tissues such as the tongue and mouth. It is intended to spread large size baits (10 mm in diameter) from helicopters in areas outside the settlement and outside defined buffer zones. There will be a 30 m buffer between the edge of aerial baiting and dwellings, and other sensitive areas such as stock holding locations. Smaller bait (5.5 mm diameter) will be hand broadcast in the settlement, around dwellings, and public space. On average a large pellet will contain 40 micrograms (µg) of brodifacoum and the smaller pellet 10 µg.

Toxikos has been requested to undertake a human health risk assessment for the eradication campaign as proposed in the draft plan.

The effects of brodifacoum:
Brodifacoum is an anticoagulant that indirectly inhibits blood coagulation by inhibiting the regeneration of Vitamin K after it has catalysed the synthesis of vitamin K dependent clotting factors. When the existing clotting factors are used up by the body more cannot be made because there is insufficient Vitamin K. Hence frozen plasma (which contains clotting factors) and Vitamin K (which allows more to be made) are efficient antidotes to the effects of brodifacoum.

In humans the toxic signs are bleeding from the gums, nosebleeds, small red or purple spots on the skin caused by capillary haemorrhage, predilection to bruising after usually inconsequential bumps, blood in the urine and faeces (tarry stools). These effects occur before the onset of life threatening internal bleeding. There are no other toxic effects. The toxicity of brodifacoum is easily treated with the antidotes. However, since brodifacoum stays in the liver for a long time oral treatment with Vitamin K may need to continue over a few to several months depending on the severity of poisoning. If a large amount is suspected to have been ingested then within a few hours, a slurry of charcoal and laxative may be given to decrease absorption from the gut. Death is very rare in situations of incidental ingestion (e.g. in children mistaking rodent bait as candy), and even when brodifacoum rodent bait is intentionally eaten for suicide death is
uncommon if treatment is provided within a reasonable time frame. The onset of clinical signs of poisoning may be delayed several days after exposure to an effective single large dose or after a few weeks of repeated ingestion of small doses.

The severity of poisoning is monitored by a simple test which measures how quickly blood coagulates. The test is called the prothrombin coagulation time (PT). An increase in PT occurs before any signs of toxicity (i.e. before effects associated with increased bleeding occur). Thus PT is a precursor event before the onset of toxicity. A certain amount of brodifacoum in the body is required to increase PT and across a number of species the threshold dose of brodifacoum to affect PT is about the same. There are no major differences between mammalian non-ruminant species regarding their toxicological sensitivity to acute doses of brodifacoum. The no observed effect level (NOEL) is the dose of brodifacoum that does not cause an increase in PT; i.e. this is the dose that has no effect on the body.

No observed effect levels (NOELs):
Because brodifacoum can accumulate in the liver with continuous daily doses, the NOEL is different for different periods of exposure. For an acute single dose the NOEL is 0.15 milligram per kilogram body weight (shortened to 0.15 mg/kg), for 42 days of daily exposure the NOEL is 0.005 mg/kg/d, and for 90 days exposure it is 0.001 mg/kg/d. The acceptable daily intake (ADI) over an entire lifetime is 0.0000005 mg/kg/d.

Because the LHI rodent eradication programme is finite and noting bait completely disintegrates with 100 days, the appropriate NOEL for judging the importance of human exposure to brodifacoum is either the 42 or 90 day NOEL. For many of the assumed exposure pathways the 42 day value is appropriate. The ADI is inappropriate because this is a guideline intended for situations where exposure could be for every day of a person’s lifetime of 70 years.

Potential exposure pathways:
This health risk assessment for human exposure to brodifacoum rodent bait is specific for the Lord Howe Island group and takes into account the particular bait intended to be used, the method of application, the longevity of the bait in the terrestrial and aquatic environments, and management practices to be undertaken to minimise human exposure to the broadcasted bait.

A number of possible theoretical exposure pathways have been considered (Figure 3.1). These include:
- Direct ingestion of rodent bait.
- Inhalation of dust containing brodifacoum
- Ingestion of soil contaminated by brodifacoum from bait.
- Dermal exposure to bait and contaminated soil.
- Ingestion of water (ground water and tank water) that may become contaminated by bait.
- Consumption of:
  - vegetables and fruit,
  - poultry produce,
  - fish that may have ingested bait inadvertently distributed to shore waters,
  - meat and dairy produce,
  - goat produce,
  - wild ducks.

Many of these exposure pathways will not occur due to pre-emptive management practices that are to be put in place during and after the proposed eradication campaign (e.g. removal of poultry and cattle from the Island, and isolating cows and goats from exposure to rodent bait). Consumption of wild ducks is said not to occur on the Island.

An important consideration in estimating exposure to brodifacoum by direct ingestion of bait pellets, or indirectly via potentially contaminated water, soil, and seafood is the stability of the pelletised form of the bait in the environment. The bait completely disintegrates into a few particles of grain within 100 days of being broadcast. It only remains as an entity that can be picked up by children or birds for about 15 – 21 days. Hence with two broadcast campaigns approximately two weeks apart, solid bait may be on the ground in such a ‘pick-up-able’ form for about 4 – 5 weeks. In water, bait pellets are reported to disintegrate within 15 minutes, sooner if there is wave action.

**Direct ingestion of rodent bait:**

The most important way that a young child may be exposed to rodent bait during the proposed eradication campaign is by picking the bait up and eating it. Pestoff®20R rodent bait contains a water soluble green dye that will colour the tongue and mouth and thus assist to alert parents.

Even though brodifacoum is acutely very toxic to a range of species including humans, the amount of bait needed to be ingested by a child at one time to cause health effects is quite large. Small bait pellets (5.5mm diameter) are intended to be hand distributed in the settlement and around dwellings. These are therefore the ones most likely to be picked up by a child. The number of pellets required to be ingested to reach the acute NOEL (0.15 mg/kg) for
prolongation of prothrombin time is approximately 200 which weigh about 100 g. This amount of bait is put into perspective by considering commercial rat bait Talon®, which has two-and-a-half times the amount of brodifacoum, is sold in 150 g packets containing six prepacked pellet trays of 25 g each.

Assuming there will be two bait campaigns about two weeks apart, the time that bait will be in a physical form able to be picked up by a child is 4 - 5 weeks. It will require ingestion of 6 -7 small pellets every day by a small child over this period to acquire a dose equivalent to the 42 day NOEL. This is unlikely to occur.

It is a fact that unless it is consumed with the intention self harm (e.g. suicide attempt) it is unusual for a person to suffer toxic effects (anticoagulant symptoms) from incidental ingestion of brodifacoum rodent bait. The parents of children who have accidently eaten rat bait understandably seek medical advice; however the majority of children do not require medical intervention. Even with intentional ingestion with the aim of suicide most people do not die. This is because there are several days between ingestion and the appearance of toxic effects which allows time to objectively gauge the severity of poisoning with the PT test, and if need be administer the antidotes which are very efficient.

It is also theoretically possible that Island residents could be exposed to bait dust in the air during, or soon after broadcast by helicopters. A reasonable maximum estimate of the amount of brodifacoum that might be inhaled during this time is 5 million times less than the dose that does not affect the body.

*Indirect exposure pathways:*
Brodifacoum, because of its physical chemical properties, is unable to contaminant groundwater. It doesn’t leach from soil. Similarly it does not contaminate vegetables and fruit because it is not transported from water or soil into the plant. The surface of the plant could become contaminated if the bait was physically broadcast onto the plant. While this should not occur (as bait is to be hand broadcast in the settlement area), if it does, bait particles can be easily washed off during food preparation.

Contamination of soil, fish and seafood, and tank water are hypothetical but nonetheless plausible pathways through which LHI residents may become exposed to brodifacoum. Even though it is very unlikely such exposure will occur, possible intake of brodifacoum by a 2 year old child has been estimated for these pathways. This is the population sector most at risk from exposure to chemicals in the environment. It is emphasised there is uncertainty associated with
accurately calculating brodifacoum intakes. Consequently conservative ‘high end’ estimations
have been undertaken so any error is more likely to be on the side of over-estimation rather
than under-estimation.

The high end estimation of brodifacoum dose by these exposure routes is less than the 42 day
and 90 day NOELs. For some of the indirect exposure routes the dose is many orders of
magnitude lower.

Overall, it is concluded there is negligible risk for human health from these exposure pathways.
This includes infants and young children\(^1\) who are the most vulnerable group.

It is unlikely fish will have much opportunity to eat bait that might fall into the ocean, it is also
unlikely humans will catch such fish in numbers where it may become a health issue. In New
Zealand there has been a very large accidental spill of Pestoff\(^{20R}\) into the sea, even so
brodifacoum was not measureable in fish flesh.

Contamination of tank water may occur if aerial broadcasting of bait accidently spreads pellets
onto roofs. The draft eradication plan has management contingency for this event. Less obvious
ways that brodifacoum might get onto roofs is by birds eating bait and depositing droppings on
roofs and gutters, or birds picking bait up and discarding it onto roofs. While these events
appear plausible they are intuitively unlikely to place significant amounts of brodifacoum onto
the roof, this is confirmed by the exposure calculations.

Ingestion of brodifacoum contaminated soil is a very minor pathway. It is unlikely all soil
incidentally ingested (mostly by hand to mouth transfer) will be contaminated soil. Soil residue
data from New Zealand when incorporated into the intake calculations results in negligible
doses of brodifacoum. Furthermore brodifacoum is tightly bound to organic carbon in soil which
significantly lowers the amount that may be absorbed into the body. Indeed swallowing a slurry
of charcoal is a treatment option for large amounts of brodifacoum that have been ingested up
to about 4 hours earlier.

Health risk from current practice
Relative to the health risk associated with current household practice of controlling rodents on
LHI, the Pestoff\(^{20R}\) pellets present the same hazard and potential health risk as Ratsak. But

\(^{1}\) In this report an infant is considered to be a child who is not yet walking, a young child is less than 6 years of age.
Calculation of potential exposures to children have followed Australian practice and assumed the child is 2 years old
(enHealth 2004).
because they are bigger the health risk associated with ingestion of a large number of pellets of Pestoff®20R is greater than for the same number of Talon® pellets. However, this is put in context when it is considered such incidental ingestion poses negligible risk to the health of infants or young children. Generally for the same weight of bait ingested, Pestoff®20R presents a lower risk because it has a lower concentration of brodifacoum than products sold on the domestic market. This is however balanced by the absence of a taste deterrent which is in some, but not all commercial products. It is noted that with the current use of rodent bait there is an ongoing risk of inadvertent ingestion of rodent bait. This long term risk will be removed if rodents are eradicated from the Island.

Conclusions:
Although brodifacoum is an acutely toxic substance that has the potential to cause toxicity and possibly death through internal bleeding, the human health risk to Lord Howe Islanders during the proposed eradication campaign is very low.

The most important exposure pathway is direct ingestion of bait pellets picked up off the ground or from bait stations. The draft LHI rodent eradication plan indicates there will be an education campaign targeting children and parents of the dangers associated with eating the bait. Nonetheless parents will need to be especially watchful of their young children during the 4 -5 weeks bait will be on the ground and in a form able to be picked up. This vigilance is similar to that currently required with the ongoing use of rodenticides in the settlement area.

Even though exposure is unlikely, indirect exposure pathways are primarily managed during the eradication programme by removing or isolating human food sources that may theoretically become contaminated (e.g. poultry, beef meat and dairy produce). Other human foods (e.g. seafood) are unlikely to be affected.

Tank water may be impacted if bait is strewn over roofs during aerial broadcasting. There are management contingencies to mitigate this. Theoretically tank water may also become contaminated with brodifacoum if birds transport pellets onto roofs or after eating pellets leave their droppings on roofs. Both these scenarios are regarded as improbable but if they do occur are very unlikely to affect tank water to the extent it is unsafe to drink.

Exposure to brodifacoum by indirect pathways (i.e. not direct ingestion of rodent bait) is negligible in comparison to the NOELs and human health effects are very unlikely.
The health risks due to brodifacoum via Pestoff®20R are the same as current practise using commercially available rat bait. However for the same number of pellets ingested, the risk may be higher depending on the constituents and pellet size of the commercial product. Generally for the same weight of bait ingested, Pestoff®20R presents a lower risk because it has a lower concentration of brodifacoum. This is balanced by the absence of a taste deterrent which is in some, but not all commercial products. Notwithstanding the different relative risks associated with different rodent bait products, the likelihood of health effects occurring in infants and young children from incidental ingestion of bait is negligible.

The eradication campaign, if successful in removing rats and mice from LHI, will result in a smaller (zero) ongoing risk of exposure to rodent poisons.

**Recommendations:**

All mitigation measures as outlined in the *Draft Lord Howe Island Rodent Eradication Plan* should be implemented to minimise risks posed by use of rodent bait during the programme.

As a precautionary measure it would be prudent to advise Islanders not to consume the livers of fish that have been caught within 200m of the shore line until 6 months after the last bait broadcast.

Although there is a negligible health risk from drinking tank water during the eradication campaign, for peace of Islander’s mind, consideration could be given to a programme of strategic testing of tank water.

It would be prudent to advise those individuals involved with the control of non-native duck populations that they should not consume duck during the eradication programme, and not the liver for perhaps a year after the program has ceased.
Contents

Executive Summary .......................................................................................................................................................... 3

Contents ........................................................................................................................................................................... 10

1. Introduction .............................................................................................................................................................. 11
  1.1 Bait use ................................................................................................................................................................. 11
  1.2 Issue identification and scope ............................................................................................................................... 12

2. Hazard identification ................................................................................................................................................... 13
  2.2 Properties, toxicology and health effects of brodifacoum ...................................................................................... 13
    2.2.1 Physical and chemical properties .................................................................................................................. 13
    2.2.2 Toxicology ....................................................................................................................................................... 14
    2.2.3 Human signs and symptoms ............................................................................................................................ 18
  2.3 Properties of the rodent bait .................................................................................................................................... 20
    2.3.1 Description .................................................................................................................................................... 20
    2.3.2 Physical stability of bait ................................................................................................................................. 20
  2.4 Summary of important data for HRA ..................................................................................................................... 25

3. Exposure and risk ......................................................................................................................................................... 27
  3.1 Potential exposure pathways .................................................................................................................................. 27
    3.1.1 Direct ingestion of bait (Pathways A1 & A2) .................................................................................................. 29
    3.1.2 Ingestion of soil (Pathway A3) ...................................................................................................................... 31
    3.1.3 Dermal exposure (Pathway A4) .................................................................................................................... 32
    3.1.4 Ingestion of water (Pathways B1 & B2) ........................................................................................................ 33
    3.1.5 Consumption of fish (Pathway C) .................................................................................................................. 37
    3.1.6 Consumption of vegetables (Pathways D1 & D2) .......................................................................................... 41
    3.1.7 Exposure via poultry (pathway E) ................................................................................................................ 41
    3.1.8 Meat and dairy products (Pathway E) .......................................................................................................... 42
    3.1.9 Goat produce (Pathway G) .......................................................................................................................... 43
    3.1.10 Consumption of wild ducks (Pathway H) ................................................................................................. 43
    3.1.11 Dust inhalation during aerial baiting (Pathway I) ....................................................................................... 44

4. Existing risk from commercial rodent bait ................................................................................................................. 47
  4.1 Bait constituents ....................................................................................................................................................... 47
  4.2 Bait stations ............................................................................................................................................................. 49
  4.3 Conclusions ............................................................................................................................................................. 49

5. General discussion and conclusions ............................................................................................................................ 50

6. Recommendations ........................................................................................................................................................ 55

References ....................................................................................................................................................................... 56

Appendix 1: Design of bait stations ................................................................................................................................ 60
1. Introduction

The Board of Lord Howe Island (LHI) is intending to eradicate mice and rats on LHI using the rodenticide brodifacoum. A draft eradication plan has been released for public comment (LHI 2009). The draft plan considers many of the benefits and risks which primarily focus on issues associated with:

- operational practicalities to ensure success of the operation,
- impact to wildlife that might result from inadvertently broad casting bait to ecological sensitive locations and
- reinfestation of the island.

Toxikos has been requested to undertake a human health risk assessment for the eradication campaign as proposed in the draft plan.

1.1 Bait use

The following is a compilation of information from the draft eradication plan (LHI 2009) that is useful for understanding how the rodent bait will be distributed and therefore also the possible human exposure pathways. The latter are discussed in detail in Section 3. The reader should consult the plan for more detail and contextual information regarding the aims and management issues associated with the rodent eradication program.

After consideration of a number of rodenticides it was decided by the LHI Board to use a commercial product registered in New Zealand for control of rodents and possums. This product (Pestoff® 20R) contains 0.002% brodifacoum (20 mg brodifacoum/kg bait) and a water soluble bright emerald, water soluble green dye. It is proposed to use 10 mm diameter size baits for aerial application (e.g. to areas outside the settlement and outside identified buffer areas on the island) and 5.5 mm baits for all hand-baiting operations (e.g. hand broad casting within the settlement and around other dwellings, for indoor and under house bait stations/trays for targeting mice).

On average, each 5.5 mm bait pellet weighs approximately 500 mg, and each 10 mm pellet about 2 grams. Each pellet respectively contains 0.01 mg and 0.04 mg of brodifacoum. In the settlement area, 5.5 mm baits will be hand-broadcast at a nominal density of at least one bait every half square metre. However, bait distribution will not always be so uniform for example the density of baits in garden beds will be greater than that on lawns.
The aerial broadcast aims for about one bait per two square metres. For aerial application it is currently planned to have a 30m buffer zone around dwellings, containment areas for livestock and other sensitive areas. Within the buffer zones specialised equipment will be used or the bait will be spread by hand.

All hand spread bait will be in the open, not under buildings or elsewhere where it is not subject to weathering. Trials on LHI found that the Pestoff® 20R bait pellets disintegrated completely after approximately 100 days (further information on the stability of the bait in the field is in Section 2.3.2). It is intended that bait be re-broadcast about 14 days after the first campaign to ensure its availability in a palatable form to rodents that may have missed the first bait campaign (e.g. those that emerge from the nest).

Where broadcasting bait cannot be undertaken, bait stations will be used (See Appendix 1). It is planned to use open trays similar to those provided with commercial rat bait for roof cavities and ceiling/under floor spaces. These are approximately the size of match boxes and will hold about 25 – 50 g of bait. Bait will be removed 100 days after rats or mice are no longer detected.

1.2 Issue identification and scope

As seen in Section 2, brodifacoum is a potent poison to many mammalian species. Because its effects are delayed by up to several days there is potential for ongoing exposure without realising a potentially harmful dose has occurred.

Many residents have expressed apprehension about aerial broadcasting of bait and problems with non-target species and secondary kills occurring. With respect to human health, the primary concern is that the bait will be widely broadcast in the settlement and around dwellings with consequent exposure and potential poisoning of children. This health risk assessment (HRA) only deals with public health risks and theoretical pathways for human exposure to brodifacoum during the eradication campaign.

The HRA does not consider occupational risk to personnel implementing the program as there will be detailed health and safety operating procedures for these people. Nor does the HRA address ecological and non-target species concerns raised during the public comment period.
2. Hazard identification

2.2 Properties, toxicology and health effects of brodifacoum

The following information has been obtained from a variety of organisations, particularly the World Health Organization (IPCS 1995, WHO 1995), the Handbook of Pesticide Toxicology (Pelfrene 1991), Encyclopedia of Toxicology (Spiller 2005), European Commission reports (EC 2005a, 2005b, 2005c and 2005d) and Department of Conservation, New Zealand (Fisher and Fairweather 2008). The information in these reviews has been supplemented by scientific articles where indicated.

2.2.1 Physical and chemical properties

Chemical structure:

![Chemical structure diagram]

Chemical name: 3 –{(4’-Brom biphenyl-4-yl)-1,2,4-terahydro-1-naphthyl]-4-hydroxy-2H-chromene-2-one.

CAS Number: 56073-10-0 (formerly 66052-95-7).

Molecular formula: C_{31}H_{23}BrO_{3}

Molecular weight: 523.4

Water solubility: Often described as insoluble, very low solubility, or practically insoluble.

At 20°C: 0.0038 mg/L at pH 5.2
0.24 mg/L at pH 7.4
10 mg/L at pH 9

pK_a: Dissociation constant in water = 4.5 (calculated).

K_{OC}^2: 50,000

^2 K_{OC} = Organic carbon partition coefficient. A measure of the tendency for organic substances to be adsorbed by soil or sediment, expressed as:

\[ K_{OC} = \frac{\text{mass adsorbed substance}}{\text{mass organic carbon}} \] 

\[ \text{mass concentration of absorbed substance} \]

The K_{OC} is substance-specific and is largely independent of soil properties. The higher the value of K_{OC} the stronger the binding to organic carbon in soil, the more organic carbon the greater the mass of substance that can be bound.
Brodifacoum binds rapidly and strongly to soil particles with very slow desorption and no leaching (IPCS 1995). This property is used in one of the optional treatments; if a toxic dose is suspected to have been ingested, then within 4 hours oral administration of activated charcoal and a cathartic may be given. The charcoal strongly binds the brodifacoum to significantly decrease absorption from the gut and the cathartic hastens the passage of the charcoal-brodifacoum complex through the gut.

Vapour pressure: $< 1 \times 10^{-9}$ kPa at $20^\circ$C.
This, with the low Henry’s law constant, indicates very little propensity to vaporise into air.

Henry’s Law Constant: $< 2.18 \times 10^{-3}$ Pa m$^3$ mol$^{-1}$ at pH 7, and $< 5.23 \times 10^{-5}$ Pa m$^3$ mol$^{-1}$ at pH 9.

Log $K_{ow}$ $^3$:

8.5 (This an extreme value outside the range that can be determined experimentally, therefore it is a calculated value). This value indicates brodifacoum has a tendency to distribute into fatty tissue (e.g. liver and adipose).

2.2.2 Toxicology

**Mode of action and basis for antidote:**

- Brodifacoum is an anticoagulant that indirectly inhibits blood coagulation. It has this effect by slowing down the biosynthesis of vitamin K-dependent clotting factors, i.e. factors II (prothrombin), VII, IX and X. An essential step in their biosynthesis is the Vitamin K dependent carboxylation of glutamate residues, during this process Vitamin K is converted to its epoxide but is normally regenerated by the action of an enzyme called Vitamin K epoxide reductase so more clotting factor can be made. Brodifacoum and warfarin both inhibit Vitamin K epoxide reductase and hence the regeneration of Vitamin K, however brodifacoum is a stronger and longer lasting inhibitor. Inhibition of Vitamin K epoxide reductase is a key event in the toxicity of brodifacoum.

Under normal physiological conditions there is constant turnover of these clotting factors. As they become catabolised replacement factors are made in the liver. Hence inhibiting the regeneration of Vitamin K means new clotting factors are not made and there is a gradual decrease over several days in circulating levels in blood. This leads to internal haemorrhaging and if uncorrected, death. In humans, low levels of clotting factors also occur in Vitamin K deficiency.

Administration of plasma (which contains clotting factors) and Vitamin K$_1$ (which allows synthesis of new clotting factor) efficiently reverse the anti-coagulating effects of brodifacoum. However because brodifacoum is poorly metabolised and eliminated from the body (see below), in symptomatic poisoned patients oral Vitamin K$_1$ therapy is required for several weeks, or months depending on the severity of poisoning.

$^3 K_{ow} =$ octanol-water partition coefficient. Ratio of the solubility of a chemical in octanol divided by its solubility in water. This a measure of lipophilicity (fat solubility) used in the assessment of both the uptake and physiological distribution of organic chemicals into organisms and prediction of their environmental fate.
The serum circulating half life ($t_{1/2}$) of Vitamin K dependent clotting factors\(^4\) in humans is:
- Factor II: 48 – 72 hrs,
- Factor VII: 1.5 – 6 hrs,
- Factor IX: 17 – 24 hrs,
- Factor X: 24 – 48 hrs.

With regard to the toxic outcome, insufficiency of clotting factor II (prothrombin) is the most important. Measurement of prothrombin clotting time (PT) is simple and a good method for determining and monitoring the severity of poisoning. A prolongation of PT occurs before signs and symptoms of bleeding tendency appear.

The fact that it takes time for circulating clotting factors to decline to levels that lead to bleeding explains why the onset of toxicity is delayed for up to several days after ingestion of a toxic dose. Thus in cases of human poisoning where a large amount of brodifacoum bait is suspected to have been consumed, PT may need to be measured over several days or weeks. It also means rodents can continue to eat bait even though they most likely consumed more than a lethal dose in the first feeding.\(^5\)

Absorption, distribution and elimination:
- Brodifacoum is readily absorbed into the body from the gastrointestinal tract and lungs, but much less so through the skin. For example in rats the dermal dose required for lethality is about 200 times higher than if it is ingested:
  - Oral LD\(_{50}\) = 0.27 mg/kg
  - Dermal LD\(_{50}\) = 50 mg/kg

  The European Commission estimate intestinal absorption of brodifacoum in the rat to be 64% at 10 mg/kg and >75% at 0.25 mg/kg. Dermal absorption is estimated to be 1.87% (EC 2005 a, c).

- In rats and rabbits dosed with brodifacoum the substance can be found in liver and a number of other tissues. The concentration in liver is approximately 20 times greater than in plasma. It is the primary organ for accumulation and storage of unchanged brodifacoum.

  10 days following a single oral dose to the rat of 0.25 mg/kg, 74.6% of the dose was retained in the tissues. The proportion of the retained dose was highest in the liver (22.8 %), followed by the pancreas (2.3 %), and then the kidney (0.8 %), heart (0.1%) and spleen (0.2 %). The remainder of the dose (approximately 50 %) was present in the carcass and skin (EC 2005c).

  Liver, pancreas and kidney contain vitamin K-epoxide reductase and brodifacoum has high binding affinity for this protein.


\(^{5}\) EC (2005b) comment that a wild rat may ingest as many as 80 LD\(_{50}\) doses in 6-7 days if feeding only on bait and as many as 40 LD\(_{50}\) doses if offered a choice of bait or untreated food. Since severe symptoms or death occur only after several days from brodifacoum consumption, rats and mice will behave normally (feeding and behaviour) during this time, allowing toxicant to build-up in the organism.
In dogs elimination from the liver is slow and biphasic (Pelfrene 1991):
  o Initial phase: \( t_{1/2} = 2 – 8 \) days.
  o Slow terminal phase: \( t_{1/2} = 130 \) days.

In rats elimination from the liver is also biphasic at high doses (EC 2005c).
  o Initial phase: \( t_{1/2} = 4 \) days.
  o Slow terminal phase: \( t_{1/2} = 128 \) days.
  o At lower doses not associated with PT prolongation, \( t_{1/2} = 282 – 350 \) days.

In mice at 0.5 LD50 liver \( t_{1/2} = 15.8 \) days (Vandenbroucke et al. 2008).

- Metabolism is slow and metabolites have not been well characterised due to the acute toxicity in mammals. However, by analogy with other coumarins (i.e. the group of anticoagulant poisons that include brodifacoum and warfarin), metabolites are likely to be various hydroxylated brodifacoums and will be inactive as anticoagulants.

- In poisoned patients (primarily suicide attempts) with clinical symptoms of toxicity, plasma \( t_{1/2} = 15 – 56 \) days (Weitzel al. 1990, Hollinger and Pastoor 1993, IPCS 1995, Spahr et al. 2007, Olmos and Lopez 2007).

Thus it can take 2 – 5 months for brodifacoum to be removed from the body after poisoning.

Plasma \( t_{1/2} \) in other species:
  o Rat: >156 days (Pelfrene 1991).
  o Mice: 91.7 days for a 0.5 LD50 dose (Vandenbroucke et al. 2008).
  o Chickens: 1.1 days (Fisher 2009).

- The majority of brodifacoum is eliminated in faeces.
  Concentration in rat faeces can be approximately 2 – 12 \( \mu \)g/g dry weight (ppm) (Fisher 2009).
  This makes rodent droppings a potential source of brodifacoum exposure to humans.

Toxic Effects:

- Warfarin has been used for decades for treatment of thromboembolic disease and, when serum levels are stabilised within the therapeutic range, therapy has been relatively free of untoward effects or signs of toxicity.

- Brodifacoum is not mutagenic or genotoxic \textit{in vitro} or \textit{in vivo}, not embryotoxic or teratogenic \(^6\), nor a skin sensitiser.

---

\(^6\) Brodifacoum did not induce developmental effects in two adequate prenatal toxicity studies in the rat and rabbit, respectively. In particular, in the rat studies maternal hemorrhages were observed at dose levels > 0.01 mg/kg (NOEL 0.001 mg/kg) whereas no effects on conceptuses were detected up to the top dose level of 0.02 mg/kg bw. In the rabbit study, the top dose of 0.005 mg/kg caused a high proportion of maternal deaths, whereas no significant effects on litters were observed (EC 2005b).
Brodifacoum is highly acutely toxic to a number of mammals. In rats death occurs after 3 - 7 days.

Single dose LD$_{50}$ (mg/kg) (from Pelfrene 1991 unless otherwise indicated):
- Rat 0.27 [rat LD$_{50}$ range reported by Fisher (2009) = 0.17 – 0.9].
  [0.47 reported in confidential propriety test by EC 2005b].
  [0.42 (M) & 0.56 (F) reported by US EPA 1998].
- Mouse 0.4
- Guinea pig 0.28
- Rabbit 0.3
- Dog 0.25 – 1.0
  0.25 – 3.56 (Eason and Ogilvie 2009).
- Cat 0.25 – 25 (Eason and Ogilvie 2009).
- Possum 0.17 (Eason and Ogilvie 2009).
- Sheep 5 – 25 (Eason and Ogilvie 2009).
- Feral pigs 0.52 (O'Brien and Lukins 1990).
  0.1 (Eason and Ogilvie 2009).

In rats, single oral doses of 0.1 – 0.33 mg/kg resulted in a steep dose response for effects on plasma prothrombin complex measured within 24 hours of administration (Pelfrene 1991, details of the study were not provided).
- 0.1 mg/kg had no effect,
- 0.2 mg/kg reduced activity to 7% of normal values, and
- 0.33 mg/kg to 4% of normal.

The European Commission had access to propriety data conducted to GLP when assessing operator risks associated with handling brodifacoum (EC 2005a, c).

In the EC (2005a) evaluation of toxicological data, the no observed effect level (NOEL) from a single dose (i.e. acute) study was judged to be 0.15 mg/kg. Rats were given a single non-toxic dose of brodifacoum (0.02 or 0.15 mg/kg) whilst a further group received a dose at 0.35 mg/kg. Blood was taken at regular intervals to measure prothrombin time (PT). At 0.02 and 0.15 mg/kg, clotting times were unaffected throughout the study but were significantly increased at 0.35 mg/kg.

Above a certain dose the effect is maximal and further changes in clotting factors and coagulation time are minimal in relation to the increase in dose. However with larger doses the inhibition of vitamin K epoxide reductase and hence also clotting factor synthesis lasts longer, which necessitates longer administration of the antidote.

Given the relative consistency of the LD$_{50}$ between non-ruminant mammal species it would be reasonable to assume similar sensitivity for humans (i.e. on average a lethal dose would be expected to be about 0.25 – 0.5 mg/kg).

IPCS (1995) estimated the average fatal dose for a human adult (60 kg) to be about 15 mg brodifacoum per person (i.e. 0.25 mg/kg). This is equivalent to:
- 300 g of 0.005% bait (e.g. Talon® or Ratsak)
- 750 g of 0.002% bait (e.g. Pestoff®20R)

In Australia brodifacoum rodent bait is sold under a variety of trade names, for example Talon® and Ratsak both at 0.005% brodifacoum. Additional information on commercial baits is in Section 4.
In a 42 day feeding study in rats a diet concentration of 0.1 ppm (0.005 mg brodifacoum/kg bw/d) did not cause any adverse effects (Pelfrene 1991).

In Beagle dogs given oral brodifacoum (0.0001, 0.0003, 0.001, 0.003 or 0.01 mg/kg bw/d) for 42 days the NOEL for blood coagulation effects was 0.003 mg/kg/d (EC 2005c, d).

In a 90 day rat study using feed concentrations of 0.2 and 0.8 ppm brodifacoum (corresponding to doses of 0.001 and 0.004 mg/kg bw/d) summarised by EC (2005a, c) the NOEL for PT was 0.001 mg/kg/d. Haematology measurements were made at 45 and 90 days. There were no effects on prothrombin time after 45 days but significant increases after 90 days but only at the highest dose tested (0.004 mg/kg/d). The NOEL was set at the next lowest dose, 0.001 mg/kg/d.

The current Australian acceptable daily intake (ADI) is 0.0000005 mg/kg body weight; i.e. 0.0005 μg/kg bw. This was originally set in 1990. The NOEL recorded against this ADI is 0.001 mg/kg. Further information on the ADI derivation is not available but it appears a safety factor of 2000 may have been applied to the NOEL.

It is important to note the ADI is the daily intake of a chemical which, during a lifetime, appears to be without appreciable risk. ‘Without appreciable risk’ is taken to mean that adverse effects will not result even after a lifetime of daily exposure to the ADI (enHealth 2004). This is not an appropriate guideline value for judging the importance of human exposure to substances that are acutely toxic and where exposure is limited as is the situation with the proposed rodent eradication programme for LHI.

The allowable maximum residue limit (MRL) in Australia for brodifacoum is 0.00002 mg/kg for cereal grains and 0.00005 mg/kg for edible offal and meat. These have been set ‘at or about’ the analytical limit of detection (FSANZ 2010).

For any food in New Zealand the MRL is 0.001 mg/kg, also described as set ‘at or about’ the analytical limit of detection (NZFSA 2010).

Brodifacoum in meat, including liver, is not destroyed during baking at 180°C for 20 minutes (O’Connor et al. 2001).

Brodifacoum is non-toxic to plants. This is to be expected since it has low water solubility and is tightly bound to soil it is not taken up by plants (WHO 1995).

2.2.3 Human signs and symptoms

If toxic amounts of brodifacoum have been ingested blood coagulation will be impaired with the following common symptoms usually becoming apparent prior to life threatening internal bleeding. Death is rare in situations of incidental ingestion (e.g. in children mistaking rodent bait as candy). Even when brodifacoum bait is intentionally eaten for suicide attempts fatality is uncommon if treatment is provided within a reasonable time frame. The onset of clinical signs of poisoning may be delayed several days after exposure to a single large dose or after a few
weeks of repeated ingestion of small doses (World Health Organisation (IPCS 1995, WHO 1995). The early signs of toxicity are:

- Gum bleeding.
- Epistaxis (nosebleed).
- Petechial rash (small red or purple spots on the skin caused by minor haemorrhage).
- Ecchymosis (subcutaneous hematoma, a small bruise) which may be spontaneous or in response to minor bumps.
- Hematoma (large bruise), especially of the articulating joints.
- Haematuria (blood in urine).
- Melenae (blood in faeces which makes them black and tarry).

Even though there is only a small difference between a dose of technical brodifacoum (i.e. unformulated brodifacoum) that has no effect on prothrombin time (PT) and that which causes a prolongation of PT, symptomatic poisoning in children caused by incidental ingestion of rodent bait is rare. This is primarily attributed to the low concentrations of brodifacoum in the bait (0.002% or 0.005%). Nevertheless serious symptoms have been described in children who have ingested a large amount of bait in a short time or lower amounts over a longer period. This can occur in children with compulsive behaviour. For example Travis et al. (1993) reported on a 36 month old girl with a history of pica (habitual ingestion of soil). The child was admitted to hospital with excessive bruising that occurred over a week and a day of bleeding from the nose and mouth. On admission the PT was greater than 50 seconds (normal is around 10 – 15 seconds) and the child was treated with intravenous Vitamin K, plasma and packed red blood cells. Bleeding stopped shortly after administration of plasma and PT returned to normal after approximately a week, readmissions to hospital occurred over the next few weeks due to failure of the mother to administer oral Vitamin K as directed. Although serum brodifacoum steadily declined it was measureable for approximately 4 months and Vitamin K therapy was continued until after it was not detected.

Most incidental ingestions of rat bait by children do not cause clinical symptoms and do not require intervention, although medical attention is often provided (US EPA 1998). However it is a feature of poisoning by brodifacoum, that should symptoms develop which is often several days after ingestion of sufficient brodifacoum, Vitamin K treatment is usually required for an extended period.
In adults, most cases of brodifacoum poisoning have occurred as the result of causing intentional harm. Many of these involve consumption of 1 – 8 boxes of rat bait approx 43 gm each at 0.005% active ingredient, i.e. approximately 2 – 18 mg brodifacoum per person, or 30 – 250 μg/kg for a 70 kg person (Kruse and Carlson 1991, Ross et al. 1992, Bruno et al. 2000, Spahr et al. 2007).

Notwithstanding the above, there is a wide variation in susceptibility to brodifacoum among individuals. People suffering from liver disease, or who are taking prescription anticoagulants or other medication that may affect blood clotting (e.g. some non-steroidal anti-inflammatory drugs) are more susceptible to brodifacoum poisoning.

2.3 Properties of the rodent bait

2.3.1 Description

The bait intended to be used in the LHI rodent eradication program is Pestoff® Rodent Bait 20R. It is a pellet containing 0.002% brodifacoum formulated with cereal, sugars, waxes and binders. The pellets are dyed emerald green with water soluble food grade dyes to make them less attractive to birds. The pellets are of two sizes:

- Small, 5.5 mm diameter for hand broadcasting and indoor bait stations, each pellet weighs approximately 500 mg and contains 0.01 mg brodifacoum.
- Large, 10 mm diameter for aerial broadcasting, each pellet weighs approximately 2,000 mg and contains 0.04 mg brodifacoum.

The dye is water soluble and will colour skin if pellets are handled when wet or with wet hands, or colour the mouth and tongue if pellets are eaten. This is evident from observations in trials of Pestoff® on LHI. The beaks and mouths of non target species that consumed baits were coloured (LHI 2009).

Should young children accidently eat Pestoff® pellets it is highly likely parents will notice lips, tongue or mucous membranes are coloured green.

2.3.2 Physical stability of bait

*Stability on land:*

The bait is cereal based and designed to break down following absorption of soil moisture, or after rain. Baits will break down by swelling, cracking, then crumbling, depending on the
temperature and humidity. Mould and fungi can appear rapidly as breakdown proceeds. Once this has happened baits are less likely to be eaten by non-target species (Brown et al. 2006).

Craddock (2004) undertook field stability trials of Pestoff® in New Zealand (Tāwharanui Regional Park, North of Auckland) to determine the time for the pellets to completely disintegrate and how much brodifacoum was left in the soil. Twenty 10 mm diameter pellets (approximately 10 - 50 g) were laid on the ground under wire cages in eight different vegetation types and monitored for 5 months. The descriptions of various stages of bait decay are depicted in Figure 2.1. These descriptions have been incorporated into the New Zealand Code of Practice for aerial and hand broadcast application of Pestoff® Rodent Bait 20R (NZFSA 2006).

In the Craddock (2004) bait stability trial, pellets very quickly started to degrade after being placed on the ground but the rate of decay decreased over time (Figure 2.2). Most pellets had become soft and degraded from condition 1 to condition 2 within 48 hours of placement. After 8 days, most pellets were beginning to lose shape and had reached condition 3 or higher (i.e. mushy pellet or pile of mush). After these degradation stages pellets showed a high degree of variation in breakdown. Pellets frequently varied by up to 4 condition index scores within a single site (i.e. a site could typically have pellets scoring condition indexes 3, 4, 5 and 6 on the same monitoring date).

In pasture the majority of pellets took 80 days to completely degrade, all were degraded in 110 days. The times were slightly, but not significantly different for baits laid in other types of vegetation.

Investigations on the environmental longevity of Pestoff® Rodent Bait 20R have also been undertaken on Lord Howe Island. It was found in these trials that the bait completely disintegrated within 100 days (LHI 2009). These results are similar to those reported by Craddock (2004).

In summary: Pestoff®20R pellets rapidly, in less than 8 days, become soft and covered in mould thereby losing attractiveness to be picked up by young children. With further degradation the bait reasonably quickly loses its physical form such that after about 2 - 3 weeks a pellet becomes quite difficult to be picked up whole from the ground.
Condition 1: Fresh Pellets/Pellets not discernable from fresh bait.

Condition 2: Soft pellets. <50% of pellet matrix is or has been soft or moist. Bait is still recognisable as a distinct cylindrical pellet, however cylinder may have lost its smooth sides. <50% of bait may have mould. Bait has lost little or no volume.

Condition 3: Mushy Pellet. >50% of bait matrix is or has been soft or moist. <50% of pellet has lost its distinct cylindrical shape. >50% of bait may have mould. Bait may have lost some volume.

Condition 4: Pile of Mush. 100% of bait matrix is or has been soft or moist. Pellet has lost distinct cylindrical shape and resembles a pile of mush with some of the grain particles in the bait matrix showing distinct separation from the main pile. >50% of bait may have mould. Bait has lost some volume.

Condition 5: Disintegrating Pile of Mush: 100% of bait matrix is or has been soft or moist. Pellet has completely lost distinct cylindrical shape and resembles a pile of mush with >50% of the grain particles in the bait matrix showing distinct separation from each other and the main pile. >50% of bait may have mould. Bait has definitely lost a significant amount of volume.

Condition 6: Bait Gone: Bait is gone or is recognisable as only a few separated particles of grain or wax flakes.

Figure 2.1: Description of various stages of bait decay
Soil residue concentrations

After aerial application of Talon® 20P (0.002% brodifacoum) over an island off New Zealand brodifacoum was not detected in soil when randomly sampled 2, 12, 34 or 210 days post application at a detection limit of 0.02 µg/g soil (Ogilvie et al. 1997). Similarly after application of Talon® 20P to a different island, Morgan and Wright (1996) found no brodifacoum in soil when sampled 1 month after aerial sowing.

In the Craddock (2004) trial, brodifacoum concentration in soil immediately beneath the pellets and after they had completely broken down was very low (0.05 ± 0.02 µg/g soil, mean ± SE,

Figure 2.2: Breakdown curves for Pest-Off bait pellets at four sites at Tāwharanui Regional Park in New Zealand.

The Y-axis represents the various stages of pellet decomposition as depicted in Figure 3.1. After approximately 15 – 21 days the degradation has passed stage 4 and is not in a form that can easily be picked up by children or potentially transported by birds.
n = 16). The soil sample was a 4 cm diameter plug taken to a depth of 4 cm, analytical detection limit was 0.02 µg/g. Figure 2.3 shows the average concentration of brodifacoum over time.

![Figure 2.3: Average brodifacoum concentration (µg/g) in soil samples over time at two pasture sites at Tāwharanui Regional Park. Least Detectable Level (0.02 µg/g) is also shown.](image)

WHO (1995) describe laboratory investigations of soil binding and leaching using $^{14}$C-brodifacoum for different soil types. Binding to soil was rapid and strong, desorption was very slow and no detectable levels of radioactivity were found in leachate.

WHO (1995) concluded binding to soil particles was quick, with very slow desorption and no leaching properties.

**Bait stability in water:**
Rat eradication on an island off New Zealand was conducted in 1996 with Talon® 7-20 pollard baits (cereal-based pellets containing 0.002% brodifacoum manufactured by Animal Control Products Ltd, the same manufacturer of Pestoff® 20R). Prior to the program being undertaken, 12 mm pellet bait formulated without brodifacoum was distributed into the sea (30 m offshore...
and 10 m depth) and monitored by a diver. This experiment was done because it was considered aerial distribution of bait near the shoreline may result in some of it being dropped into the sea. The bait pellets disintegrated within 15 minutes. Under wave action it was rationalised it would be unlikely for bait to remain intact for more than a few minutes (Empson and Miskelly 1999).

As the result of a road transport accident a very large spill of Pestoff® occurred into the sea off the coast of New Zealand. The spill was approximately 18 tonnes packaged in 25 kg double walled paper bags with polyethylene liner, released bait was observed to quickly soften and disintegrate. At the seabed where the spill occurred particles of bait had set into a layer >100 mm which had the consistency of thick porridge. It took about a week for these congealed areas to be dissipated by wave action so kibbled grain material was no longer visible (Primus et al. 2005). Monitoring of the local fauna was undertaken for 21 months (see also Section 3.1.5).

After aerial baiting islands with Talon® 20P (0.002% brodifacoum) brodifacoum was not detected in water from streams sampled up to 1 month after application (Morgan and Wright 1996, Ogilvie et al. 1997).

2.4 Summary of important data for HRA
From the above data and discussion on the toxicology and health effects of brodifacoum there are a number of pieces of information that are important for understanding human exposure and health risks that may be associated with the LHI rodent eradication programme.

*Physical and chemical properties of brodifacoum:*  
1. Binds strongly to soil.  
2. Does not leach out of soil.  
3. Does not evaporate and contaminate air.  
4. Has very low water solubility (~0.2 mg/L).  
5. Is fat soluble.

*Toxicology and health effects:*  
1. Brodifacoum is readily absorbed through the gut, but much less so through skin.  
2. Brodifacoum has the tendency to distribute to fatty tissue.  
3. The majority of brodifacoum is excreted in faeces.  
4. Brodifacoum binds strongly to vitamin K epoxide reductase and therefore has very long half life \( t_{1/2} \) in those tissues with high levels of this protein, especially the liver were \( t_{1/2} \) can be 3 – 4 months.
5. The anticoagulant effect requires depletion of existing Vitamin K dependent clotting factors, therefore onset of toxic symptoms is delayed.

6. Prolonged prothrombin clotting time (PT) is a precursor indicator to toxicity (bleeding).

7. PT is an efficient monitoring method for severity of poisoning.

8. Vitamin K and plasma are effective treatments.

9. Most people, including infants and young children, with incidental ingestion don't require treatment.

10. Symptomatic poisoning, e.g. from suicide attempts, may require treatment with Vitamin K for several months until PT returns to normal.

11. The only toxic effects are associated with anticoagulant activity.

12. Highly toxic to mammals, LD\textsubscript{50} = 0.2 – 0.5 mg/kg bw across a number of species, death is within 7 days of ingesting a fatal dose.

13. No observed effect level (NOEL) for affecting PT (the precursor to toxicity):
   - Rat - acute single oral dose, 0.15 mg/kg bw.
   - Rat - 42 day feeding study, 0.005 mg/kg bw.
   - Rat – 90 day feeding study, 0.001 mg/kg bw.

14. The Australian acceptable daily intake (ADI) over a lifetime is 0.0000005 mg/kg bw.
   (Note this is not suitable as a guideline for the LHI risk assessment because it is for an assumed lifetime exposure).

**Bait properties and application:**

1. Pestoff\textsuperscript{®} 20R pellets do not contain a taste deterrent.

2. The pellets have a water soluble green dye that will colour lips, tongue and mouth.

3. After 2 -3 weeks on the ground pellets have lost their physical form and are difficult to pick up, after 100 days they are completely disintegrated.

4. Soil residues of brodifacoum have not been detected in field trials, but in an outdoor experiment 0.05 µg brodifacoum/g soil was measured in soil immediately under pellets.

5. In water individual bait pellets disintegrate within 15 minutes.

6. In Pestoff\textsuperscript{®} 20R bait there is:
   - 10 µg brodifacoum in an individual 5.5 mm diameter pellet, each pellet weights approximately 500 mg, and
   - 40 µg brodifacoum in a 10 mm pellet which weighs about 2 g.

7. Target coverage of Pestoff\textsuperscript{®} 20R is:
   - One 5.5 mm pellet per 0.5 m\textsuperscript{2} near dwellings, or
   - One 10 mm bait per 2 m\textsuperscript{2} away from dwellings.
3. Exposure and risk
There are a number of ways which residents on the island may be potentially exposed to brodifacoum as a result of the proposed rat eradication program. Because the dose of brodifacoum associated with all pathways cannot be reasonably quantitated the exposures and risk for these are discussed qualitatively. For other exposure pathways conservative assumptions have been made to estimate 'high end' intakes of brodifacoum. Judgement has been made on whether a particular exposure pathway, in the circumstances of Pestoff® use on LHI, may be significant and possibly allow enough brodifacoum to be absorbed to cause effects in children or adults. This was done by comparing the estimated intakes with no effect levels (NOELs) for prolongation of PT.

3.1 Potential exposure pathways

Figure 3.1 depicts the theoretical exposure pathways. Some of these have been included because during the commentary period of the draft eradication plan LHI residents expressed concern regarding possible exposure.

The exposure pathways are divided into three groups;

- The first and by far the most important is that associated with direct ingestion of bait, either by being picked up from the ground or from bait stations within or around dwellings.
- The second exposure pathway considered is via water consumption.
- The third set of exposures are those connected to possible contamination of human food.

The specific details and risks for each of these exposure pathways are discussed in detail below.
Potential human exposure pathways

<table>
<thead>
<tr>
<th>Route</th>
<th>Media</th>
<th>Description</th>
<th>Likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>Ingest</td>
<td>Picked up from soil surface</td>
<td>Possible a</td>
</tr>
<tr>
<td>A2</td>
<td>Ingest</td>
<td>From bait station in, under or around house</td>
<td>Possible a</td>
</tr>
<tr>
<td>A3</td>
<td>Soil</td>
<td>Contaminated soil under where bait lay</td>
<td>Very low b</td>
</tr>
<tr>
<td>A4</td>
<td>Dermal</td>
<td>Soil Contaminated soil under where bait lay</td>
<td>Very low b</td>
</tr>
<tr>
<td>A5</td>
<td>Inhal</td>
<td>From broadcast bait or indoor bait stations</td>
<td>Incomplete c</td>
</tr>
<tr>
<td>B1</td>
<td>Ingest</td>
<td>Percolation into groundwater</td>
<td>Incomplete d</td>
</tr>
<tr>
<td>B2</td>
<td>Ingest</td>
<td>Bird faeces or bait dropped onto roof, washed into tank water</td>
<td>Low e</td>
</tr>
<tr>
<td>C</td>
<td>Ingest</td>
<td>Fish Bait dropped or flushed into ocean/lagoon and eaten by fish</td>
<td>Very low f, g</td>
</tr>
<tr>
<td>D1</td>
<td>Garden</td>
<td>Taken up from soil</td>
<td>Incomplete d, g</td>
</tr>
<tr>
<td>D2</td>
<td>Garden</td>
<td>Dropped onto plants</td>
<td>Low g</td>
</tr>
<tr>
<td>E</td>
<td>Ingest</td>
<td>Chicken Chicken eats bait &amp; transferred to flesh and eggs</td>
<td>Incomplete h</td>
</tr>
<tr>
<td>F</td>
<td>Meat &amp; dairy</td>
<td>Cattle/cows eat bait, brodifacoum transferred to flesh &amp; milk</td>
<td>Incomplete h</td>
</tr>
<tr>
<td>G</td>
<td>Meat &amp; dairy</td>
<td>Goats eat bait and brodifacoum transferred to flesh and milk</td>
<td>Incomplete h</td>
</tr>
<tr>
<td>H</td>
<td>Ingest</td>
<td>Wild ducks eat bait and are shot</td>
<td>Incomplete h</td>
</tr>
<tr>
<td>I</td>
<td>Inhal</td>
<td>Dust Fine dust from aerial dispersion</td>
<td>Very low k</td>
</tr>
</tbody>
</table>

a The most risky exposure to rodent bait is direct ingestion of bait picked up from the ground or from indoor bait stations and eaten. Due to behaviour patterns young children are most at risk.
b The probability of consuming soil from the exact spot under a bait pellet is low, the dose would be very low and furthermore brodifacoum binds strongly to soil and absorption into the body is significantly impaired. Dermal absorption of brodifacoum is low even without being adhered to soil.
c Brodifacoum is a solid and does not volatilise.
d Brodifacoum binds strongly to soil and does not leach.
e Birds may eat bait, brodifacoum is excreted in faeces which may be deposited on the roof. Birds may pick up bait pellet and drop onto roof. The amount of brodifacoum washed off the roof will be very small, it is also poorly soluble in water so will be bound to tank sludge. It is unlikely aerial broadcasting will drop bait on roofs (if this is a possibility the management plan has a contingency action).
f It is unlikely large amounts of bait will be dropped into the ocean. Bait rapidly disintegrates, the dose to fish should be low, the likelihood of catching a fish that has consumed bait is low, most brodifacoum is in fish liver which is not consumed by humans.
g Not taken up by vegetables from soil. If dropped onto plants washing vegetable during preparation will remove bait.
h Chickens and cattle will be removed from the Island. Dairy cows are to be isolated from bait. Some goats will remain but these are pets not used for consumption or milk/cheese making.
i There is no duck hunting on LHI.
j Fine dust particles dispersed during aerial bait broadcasting are inhaled. Exposure is very low.

Figure 3.1: Summary of potential exposure pathways to brodifacoum.
3.1.1 Direct ingestion of bait (Pathways A1 & A2)

It is intended that small 5.5 mm bait be hand broadcast around gardens and public areas in the settlement. It is therefore possible that a young child may pick bait up and suck, chew or swallow it.

The green dye in the bait pellet will colour the mouth and tongue green alerting parents that the child has put rodent bait into its mouth.

All the considerations below are for a healthy 'normal' child or adult; it should be remembered that persons who have anaemia, liver disorder, a blood clotting disorder, or are taking medication that affects blood clotting could be more sensitive to the toxic effects of brodifacoum. In these individuals prothrombin clotting time may not need to be changed as much as in a 'normal' person for bleeding symptoms to occur. Calculations have not been undertaken for such sensitive persons because relevant quantitative dose response data was not located.

Unless specifically stated otherwise, calculations in this and other sections of this report have been performed for the small 5.5 mm Pestoff® 20R bait because this is the size that young children are most likely to encounter. The larger 10 mm diameter bait has four times the amount of brodifacoum (0.04 mg/pellet) so the calculations below need to be adjusted accordingly.

Risk associated with single ingestion of bait:

The acute dose of brodifacoum (B) in the rat that does not cause prolongation of prothrombin clotting time (i.e. the NOEL) is 0.15 mg/kg bw (Section 2.4). The available evidence in Section 2.2.2 indicates no major difference between mammalian non-ruminant species regarding their toxicological sensitivity to acute doses of brodifacoum. Hence it is reasonable to assume a 2 yr old child will be as sensitive as the rat. The default body weight of a 2 year old child is 13.2 kg (enHealth 2004) and there is 0.01 mg brodifacoum/pellet (0.01 mg B/pellet).

The number of pellets that need to be ingested by a 2 yr old to reach the NOEL is:

\[
\frac{(0.15 \text{ mg B/kg bw} \times 13.2 \text{ kg bw})}{(0.01 \text{ mg B/pellet})} = 200 \text{ pellets}
\]

At a nominal distribution of 1 pellet/0.5m² a young child would have to gather up all the pellets from approximately 100 m².
Since each pellet weighs approximately 0.5 g, therefore the weight of bait needed to be ingested by a 2 yr old for the NOEL is:

\[ 200 \text{ pellets} \times 0.5 \text{ g} = 100 \text{ g} \]

This amount of bait is put into perspective by considering commercial Talon® is sold in 150 g packets containing six prepacked pellet trays of 25 g each. The indoor and under floor open tray bait stations for Pestoff® 20R are proposed to be about the same size, but these will contain only 40% of the brodifacoum that would be found in an equivalent weight of Talon® bait.

**Risk associated with low but multiple ingestion of bait:**
The LHI plan indicates the bait will be broadcast twice, approximately 14 days apart to ensure all rodents on the islands encounter the bait. Given it takes 2 -3 weeks for bait to lose its physical form and become difficult to pick up as a pellet (Sections 2.3.2 and 2.4), there is a window of about 4 – 5 weeks during which pellets may be available to be picked up and potentially eaten by a 2 yr old. Thus the appropriate NOEL for this scenario is the 42d rat NOEL for no effect on prothrombin time, i.e. 0.005 B mg/kg bw (Sections 2.2.2 and 2.4).

Following the same logic as above, the number of Pestoff® pellets needed to be eaten per day to ingest an amount equivalent to the 42 day NOEL is:

\[ (0.005 \text{ mg B/kg/d} \times 13.2 \text{ kg}) \div (0.01 \text{ mg B/pellet}) = 6 - 7 \text{ pellets/d}, \]

i.e. about half a desert spoon full per day.

Anticoagulant symptoms in adults arising from incidental poisoning by brodifacoum is rare. There are however many recorded instances where purposeful ingestion for self harm has resulted in significant clinical symptoms of bleeding. Efficient treatment with antidote has meant the vast majority of these cases have not resulted in death.

**Discussion and conclusions:**
It is unlikely that a child will consume at a single time the large amount (about 100 g) of bait required to cause prolongation of prothrombin clotting time. However a much smaller amount (about half a desert spoon of pellet) of Pestoff® 20R per day over 6 weeks is needed for the same effect. While this is unlikely to occur over the 5 week time period when the bait is in a form that could be picked up whole, the small amount of bait involved per day makes it appear feasible.
Notwithstanding the above, the key to ensuring small children are not exposed to the Pestoff® bait is educating children and parents about the bait, and close vigilance by parents during the eradication campaign.

For an adult the World Health Organisation (IPCS1995) considers the lethal dose of brodifacoum to humans to be about 0.25 mg/kg bw, i.e. the same as for a rat. The amount of 0.002% bait required to result in death, assuming treatment is not given, is 750 g. This quantity is put into context by the realisation that a box of commercial Talon (0.005% brodifacoum) contains 150 g of bait.

It is concluded direct incidental ingestion of Pestoff® 20R rodent bait such as may occur if a child mistook the bait for candy is associated with very low, negligible, health risk. This conclusion is based on:

- the large amount of bait that must be consumed at one time in order to affect blood clotting, and
- national, and international, experience that shows the vast majority of such ingestions do not require medical intervention.

3.1.2 Ingestion of soil (Pathway A3)

The inadvertent ingestion of soil is a common and important human exposure pathway to be considered in risk assessments where soil may be contaminated. Young children are particularly prone to ingest soil as they have greater contact during play, have greater hand to mouth activity, and have not developed soil avoidance strategies of older children and adults.

The US EPA *Child-specific exposure factors handbook* (US EPA 2008) recommends a central tendency for outside soil ingestion of 30, 50, 50 mg soil/day for newborns (6–<12 months), 1–5 year olds and 6–20 year olds respectively. These values are recommended for use in Australia when the risk assessment is not considering ingestion of indoor dust (enHealth 2010). Indoor dust is usually considered in situations where outside soil is suspected of being relatively uniformly contaminated such that the contaminant may be tracked indoors by people and pets. In this case the default soil plus house dust ingestion rate of a young child is 0.1 g soil/d (enHealth 2004, 2010). In the scenarios considered for LHI, brodifacoum bait is not uniformly distributed but nominally spread at 1 pellet/0.5m², therefore the default incidental soil ingestion of 100 mg/d for a child used in this assessment is considered to be very conservative.
Soil residues of brodifacoum have not been detected in field trails (e.g. Ogilvie et al. 1997) but in an outdoor experiment an average of 0.05 µg brodifacoum/g soil was measured in soil immediately under pellets after they had broken down (Sections 2.3.2 and 2.4).

On the assumption that all the soil ingested by a young child is exactly from underneath where bait pellets lay, the amount of brodifacoum ingested per day will be:

\[
(0.1 \text{ g soil/d} \times 0.05 \text{ µg B/g soil}) ÷ 13.2 \text{ kg} = 0.0004 \text{ µg B/kg bw/d (or 0.0000004 mg/kg/d)}.
\]

This is significantly less (12,500 times) than the NOEL dose of 0.005 mg B/kg/d.

**Discussion and conclusion:**
A very conservative estimate of the daily dose of brodifacoum (0.0004 µg B/kg bw/d) that might be achieved from soil ingestion is 12,500 times lower than the relevant sub-chronic NOEL for prolongation of prothrombin time (0.005 µg B/kg/d).

Furthermore
- The amount of soil assumed to be ingested is higher than what might occur,
- it is highly unlikely that all incidentally ingested soil will be from beneath where pellets lay, and
- brodifacoum tightly binds to carbon in soil thereby markedly lowering its absorption from the gut. Indeed oral administration of a slurry of activated charcoal is an optional treatment soon after ingestion of large amounts of brodifacoum.

It is concluded there is negligible health risk from incidental consumption of soil that may contain brodifacoum.

**3.1.3 Dermal exposure (Pathway A4)**
Brodifacoum is very poorly adsorbed across the skin (Sections 2.3.2 and 2.4).

If pellets are handled without gloves it is only the brodifacoum on the outside of the pellet that is potentially available to transfer from the pellet to the skin, and thence be subject to absorption through the skin. Thus only a very small fraction of the brodifacoum in a bait pellet is likely to be transferred to the skin, and only a small fraction of that is absorbed.
If soil from beneath distributed bait pellets were contaminated with brodifacoum and each day spread over the entire surface area of the hands of a child (soil adherence 0.5 mg soil/cm$^2$ of skin [enHealth 2004], surface area of the hands of a 2 – 3 yr old child is 0.03 m$^2$ [US EPA 2008]) and the soil contains 0.05 µg brodifacoum/g soil (Sections 2.3.2 and 2.4) the amount of brodifacoum on the skin of the hands is:

$$0.5 \text{ mg soil/cm}^2 \times 0.03 \text{ m}^2 \times 10^4 \text{ (cm}^2/\text{m}^2) \times \text{d}^{-1} \times 0.05 \text{ µg B/g soil} \times 10^{-3} \text{ (g/mg soil)}$$

$$= 0.0075 \text{ µg B/d}$$

If 1.8% of this is absorbed through the skin (Section 2.2.2) of a 2 yr old child (weight 13.2 kg) the dose of brodifacoum is:

$$(0.0075 \text{ µg B/d} \times 0.018) \div 13.2 \text{ kg} = 0.00001 \text{ µg B/kg bw/d.}$$

**Discussion and conclusion:**

The above calculations are conservative and significantly overestimate the amount of brodifacoum that might be absorbed through the skin if contaminated soil was smeared over the hands of a 2 year child. Nevertheless the dose (0.00001 µg brodifacoum/kg bw/d) is 500,000x less than the sub-chronic NOEL for prolongation of prothrombin time (0.005 mg B/kg/d).

The calculated dose is conservative because:

- Not all the soil on hands will be from beneath where pellets lay.
- Not all the surface of the hands (both sides) will be covered in soil.
- This will not happen each day.
- Brodifacoum is tightly bound to soil which significantly decreases the already low absorption through skin.

It is concluded the dermal absorption of brodifacoum through the skin is negligible and not a pathway of importance for residents of LHI during the eradication campaign.

### 3.1.4 Ingestion of water (Pathways B1 & B2)

Theoretically residents of LHI may become exposed to brodifacoum if ground water used for drinking becomes contaminated, or if brodifacoum from rodent bait contaminates the roof of buildings from which drinking water is collected.
Pathway B1 – contamination of ground water:
Brodifacoum binding to soil is rapid and strong, desorption is very slow and leaching from the soil is negligible (IPCS 1995). WHO (1995) consider the use of brodifacoum rodenticide is unlikely to be a source of water contamination.

Groundwater therefore will not become contaminated with brodifacoum during the rodent eradication campaign. It is noted however that ground water on LHI is not suitable for human consumption (EWS 2000).

Pathway B2 – contamination of tank water:

a. Accidentally dropped onto roofs when broadcasting: The most obvious way that tank water may become contaminated with brodifacoum rat bait is if it is accidently dropped onto roofs during aerial broadcasting. The LHI draft rodent eradication plan indicates a 30m buffer zone is to be applied when aerial broadcasting bait near dwellings and containment areas. Assuming this buffer zone is able to be practically maintained then bait should not find its way onto roofs. The draft plan also acknowledges that if it is anticipated bait may drift onto roofs, or if it accidently occurs, then the water collection system will be disengaged and remedial works undertaken.

b. Brodifacoum in bird droppings: A potential pathway for brodifacoum to find its way into tank water is if a bird eats rodent bait and excretes the ingested brodifacoum in its faeces onto a roof. Birds have a cloaca, which means there is a common opening for faecal and urinary waste. A bird dropping contains three components urine, solid urate and the faeces. In trials at LHI it was found that most birds did not eat the bright green bait, the beaks or mouths of those that did were coloured green. Should birds eat the bait, the water soluble dye will colour the watery portion of bird droppings a distinct green. It should be noted however that this is not the only way bird droppings may be coloured green; many birds usually have dark green or blackish green droppings. Green faeces may also indicate infection or liver disease.

Fisher (2009) gave a non-lethal single gavage dose of brodifacoum (0.5 mg/kg) to chickens and measured brodifacoum in their faeces at 1, 4, 7 and 14 days after dosing. This dose is roughly equivalent to a 1.5 kg chicken in a very short time eating about 40 g of 0.002% bait (i.e. about 75 of the small Pestoff pellets) and is much higher than anticipated a wild bird will eat. The highest concentration of brodifacoum in droppings was on day 1 (0.17 µg B/g wet weight dropping) and was not detectable 7 days after administration (Section 3.1.7). It is very difficult to know how much brodifacoum, if any,
may be deposited onto a roof by bird droppings; intuitively it would be expected to be very little. A rough, conservative quantitation of human exposure to brodifacoum introduced into tank water by bird droppings is below.

Small birds with a high metabolism rate defecate more frequently than larger birds which have lower metabolism rates. For example budgerigars defecate approximately once every 30 minutes but magpies and Macaws about once per hour (Harrison and Ritchie 1994; Fowler [date unknown]).

Assuming:
- a bird dropping will be deposited onto a roof once per hour during daylight hours (i.e. 12 hours)
- for 25 days (see footnote to Section c below),
- each dropping weighs about a gram, and
- all droppings have brodifacoum content the same as a chicken 1 day after dosing with 0.5 mg/kg (see above), and
- all brodifacoum in droppings is washed into a half full small rain water tank (10,000L capacity).

The concentration of brodifacoum in the water may be:

\[
\frac{1 \text{ poo/hr} \times 12 \text{ hr/d} \times 25 \text{ d} \times 0.17 \text{ } \mu g \text{ B/g poo} \times 1 \text{ g/poo}}{5,000 \text{ L}} = 0.01 \text{ } \mu g \text{ B/L}
\]

Thus an upper end estimate of brodifacoum intake for a 2 year old child weighing 13.2 kg who drinks 1L per day (US EPA 2008) in this theoretical exposure scenario is:

\[
(0.01 \text{ } \mu g/L \times 1 \text{ L/d}) \div 13.2 \text{ kg} = 0.0008 \text{ } \mu g/kg/d.
\]

This speculative dose to a 2 year old child is substantially lower than the sub-chronic NOEL for prolongation of prothrombin time (0.005 mg B/kg/d) by 6,250 times. The dose estimation is speculative and conservative because:
- From trials on LHI it is not anticipated birds will eat such large quantities of bait as was given to chickens in the Fisher (2009) experiment.
- It is unknown how often birds may defecate onto a roof. Nevertheless the assumptions of 1 poo/hr for 12hr/d and 25 d are likely conservative.
- It is also unknown how much the bird droppings may weigh.
Overall it is considered human exposure to brodifacoum in tank water by this route is unlikely to occur, but if it does it will be very low. However it is acknowledged there is uncertainty regarding the dose calculations but the large difference between the calculated dose and the NOEL indicates negligible risk to human health.

c. *Pellet transport by birds:* Another potential way for rodent bait to get onto roofs is for a bird to pick the bait up and subsequently discard it on the roof or into the gutter. This is anticipated to be a rare event. However if is assumed one hundred 10mm pellets (i.e. approximately 200 gm) were dropped onto the roof by birds during the eradication campaign (i.e. about four every day, ten every 2 -3 days⁷) and the roof collected water into a small tank (say 10,000L), then the amount of brodifacoum potentially washed into the water tank is 4,000 µg. Even though the water solubility of brodifacoum is low (0.24 mg/L, Section 2.2.1) all the brodifacoum in the pellets washed into the tank could theoretically be dissolved in the tank water. This would give a concentration of 0.8 µg/L if the tank was half full (4,000 µg ÷ 5,000 L = 0.8 µg/L). The 95th percentile water intake for a 2 – 3 year old is approximately 1 L/d (US EPA 2008). Thus an upper end estimate of brodifacoum intake for a 2 year old child weighing 13.2 kg in this theoretical exposure scenario is:

\[
(0.8 \text{ µg/L} \times 1 \text{ L/d}) \div 13.2 \text{ kg} = 0.06 \text{ µg/kg/d (i.e. 0.00006 mg/kg/d).}
\]

This dose is lower than the sub-chronic NOEL for prolongation of prothrombin time (0.005 mg B/kg/d). However there is much uncertainty associated with the calculation of the dose:

- It is not anticipated that birds will lift pellets off the ground and transport them to roofs, it is nonetheless a possibility.
- The amount of pellets assumed to be dropped onto a roof is most likely an over estimate but to what extent is unknown.
- It has been assumed all the brodifacoum in the pellets is dissolved in the tank water, in reality most will remain bound to pellet constituents and partition into sludge at the bottom of the tank.
- The average size of rain water tanks on LHI is 25,000L, a much smaller tank assumed to be half full has been used in the dose calculations.

---

⁷ From Figure 3.2 bait will remain in a form for birds to pick up for about 10 days, if two applications of bait are made about 14 days apart the 10 mm pellets will be able to be lifted by birds for approximately 25 days. Thus the assumed number of pellets (100) dropped on the roof is equivalent to four every day (i.e. ~ ten every 2 -3 days).
The above scenario is regarded as being quite unlikely and the dose calculations for brodifacoum intake by contaminated tank water to be conservative ‘high end’ estimates. Nonetheless they are lower than the NOEL for affecting blood coagulation.

**Discussion, conclusions and recommendation:**
Discussion of each of the transport pathways of brodifacoum into potable water (i.e. into ground water, accidental pellet broadcast onto roofs, bird transporting bait onto roofs, and bird droppings onto roofs) are discussed in the individual sections above.

Although there is uncertainty associated with brodifacoum dose estimations to a 2 year old child, the doses have been calculated to be conservative and overall this exposure pathway (i.e. by drinking water) is very unlikely to be a health threat to residents on LHI.

Although there are negligible health risks from drinking tank water during the eradication campaign, for peace of Islander’s mind, consideration could be given to a programme of strategic testing of tank water.

### 3.1.5 Consumption of fish (Pathway C)
Many comments provided to the LHI board on the proposed rodent eradication plan expressed concern regarding the potential impact on certain fish populations, particularly in the lagoon, should aerially dispersed bait be deposited onto marine water. While this section contains information relevant to the concern expressed by LHI residents the impact on the marine ecology is not specifically evaluated or discussed, the focus is on potential exposure to humans should fish that have been exposed to rodent bait be eaten by people. The assessment has been undertaken by consideration of the stability of rodent bait in marine water, the likelihood that fish or shellfish will consume bait, the likelihood that a fish that has consumed bait will the caught and eaten, how much fish will be eaten, and assumptions regarding the amount of brodifacoum in edible portions of fish.

*Consumption of rodent bait by fish and shellfish*
Empson and Miskelly (1999) report on fish feeding trails with Talon® 7-20 pollard baits (12 mm pellets) containing 0.002% brodifacoum, this bait is similar to Pestoff® 20R and made by the same manufacturer. Non-toxic bait dropped into the sea rapidly disintegrated and three species
of fish were observed by divers to feed on the suspended particles. In contrast, in aquarium feeding trials using bait containing brodifacoum with acclimatised marine fish not fed for the previous 24 hours, it was observed the fish were not particularly interested in the bait. They did however eat mussel flesh immediately after the trial. Nonetheless six fish were observed to eat the bait but only one died, two others not observed to eat bait also died of symptoms of brodifacoum poisoning. Although liver concentrations of brodifacoum were measured in this study they unfortunately are not reported by Empson and Miskelly (1999).

This study shows that not all fish presented with the opportunity to consume disintegrating rodent bait will do so.

WHO (1995) consider that because of its very low water solubility brodifacoum in bait formulations is unlikely to be available to fish unless the bait is misused.

Cole and Singleton (1996) investigated the impact on fish at Kapiti Island (off the coast of the North Island of New Zealand) after two aerial applications approximately 4 weeks apart of brodifacoum rodent bait. The monitoring sites, close to steep terrain, were chosen on the likelihood that bait could have found its way into the sea. No evidence was found that the application of bait to the island had resulted in a decline of fish density populations.

Risk to humans
From the above, and if the bait was to find its way into the marine environment, it appears feasible humans could catch and consume marine fish that had eaten non-lethal amounts of particles from Pestoff® 20R.

The likelihood of human exposure, and risk, to brodifacoum via consumption of fish is a combination of the following:

- The probability that significant amounts of bait will find its way into the marine environment.

According to the LHI draft plan, while it is possible small quantities of bait may end up in the sea it is considered unlikely there will be large amounts. Such an outcome is an expensive waste. The plan stipulates aerial baiting will be carefully undertaken and controlled on foreshore areas. Wash-off from land into the sea, or into surface water bodies, is unlikely because brodifacoum is poorly water soluble and binds tightly to soil. The NZ Department of Conservation states “Even when baits were sown directly into streams during pest eradication operations, brodifacoum residues have not been recorded in water” (Fisher and Fairweather 2008). If soil particles with adsorbed
brodifacoum are washed into the sea the brodifacoum will have considerably reduced absorption from the gastrointestinal tract (see Section 2.2.1).

- **The probability that fish will consume the bait.**
  If it is assumed that if Pestoff® 20R is accidently dropped into the marine environment it will most likely be at the water’s edge. In shallow water fish of suitable size for human consumption are unlikely to encounter the bait. It is however feasible that in deeper water (e.g. off cliffs) such fish may come across the disintegrating bait and some may eat it; however the availability of particulates from rodent bait to be eaten would only be for a short time before they were dispersed.

- **The probability that a fish which has consumed brodifacoum bait will be caught by an angler.**
  This is possible but unlikely given the small numbers of fish liable to be exposed and the short time bait will be available to fish.

- **The probability that caught fish contains high amounts of brodifacoum in edible portions.**
  The fact the fish is alive to be caught indicates it has either not consumed Pestoff® bait or only small amounts thereof. Consequently there will be no, or only very little brodifacoum in the animal. Of the brodifacoum present, the majority will be in the liver which is not normally consumed by humans. Being fat soluble brodifacoum may also be present in the skin which is also not normally eaten by people. In fatty fish there may be low amounts of brodifacoum in edible flesh.

Fish, shellfish and other animals were monitored in the immediate area around a very large spill of Pestoff®, approximately 18 tonnes, into the ocean off the coast of New Zealand (Primus et al. 2005). A butterfish sampled 9 days after the spill had liver brodifacoum residues of 0.04 ppm, 0.02 ppm was in the gut but muscle was below detection limits (<0.02 ppm [<0.02 µg/g] muscle). Residues in other fish sampled (a scorpion fish, two herrings, and an unknown species) collected 14 – 16 days after the spill were all less than detection limit. Thirteen crayfish and one crab sampled at the point source 8 – 14 days after the spill had unmeasurable residues, < 0.02 ppm (tissues not specified).

Primus et al. (2005) also reported on brodifacoum concentrations in mussels after the accidental spill of Pestoff® into the sea. The greatest exposure was observed within 100 m of the spill, there was only minor exposure 100 – 300 m from the epicentre of the
spill. Brodifacoum concentrations in mussels in the vicinity of the spill peaked at 0.41 ppm and averaged just above the detection limit of 0.001 ppm by day 29. However the average of five mussel samples collected at 353 days was 0.002 ppm indicating a slow depuration rate from the organism. The concentrations of brodifacoum occurred in mussels as a result of their filter feeding after a huge spill of rodent bait which caused a cloudy plume over approximately 100 m² for 24 hours. Individual pellets dropped into the sea from aerial broadcasting will not cause such concentrations of particulate bound brodifacoum in the water body. The disintegration of individual pellets will be rapidly dispersed as discussed in Section 2.3.2.

- The probability that high amounts of fish will be consumed by an individual.

The average seafood consumption rate for a 2-3 year old male child reported by Australian Bureau of Statistics (ABS 1999) is 6.9 g/d and the 95th percentile 11 g/d. These consumption rates are for total ‘fish and seafood products and dishes’ and include fin fish (excluding canned), crustacean and molluscs (excluding canned), packed (canned and bottled) fish and seafood, fish and seafood products, and mixed dishes with fish and seafood as the major component. In estimating the amount of brodifacoum exposure by a 2 year old child for this risk assessment it has been assumed the ‘total’ seafood consumption at the 95th percentile is all fish, and that 10% of this may contain brodifacoum.

In screening risk assessments it is a common conservative practice to assume the concentrations of chemical in environmental media may be present at half the analytical detection limit when the actual amount cannot be quantitated by the analysis. Thus the assumed conservative concentration of brodifacoum in edible portions of fish is 50% of 0.02 µg/g fish, i.e. 0.01 µg/g. It should be noted that the analytical detection limit in Primus et al. (2005) for mussels was an order of magnitude less than for fish.

The daily dose of brodifacoum from high end consumption of fish is potentially estimated to be:

\[(11 \text{ g fish/d/child} \times 0.1 \times 0.01 \text{ µg B/g fish}) + (13.2 \text{ kg bw}) = 0.0008 \text{ µg B/kg bw}\]

This is considerably less (by 6,250 times) than the sub-chronic NOEL for prolongation of prothrombin time (0.005 mg B/kg/d). However there is much uncertainty associated
with the calculation of the dose, nonetheless it is considered to be a ‘high end’ estimate.

**Conclusions:**
In considering the above probabilities and the chance they will act in unison, it is concluded the risk to human health from this exposure route is negligible.

Nevertheless for Islanders’ peace of mind it may be appropriate and precautionary to advise them not to consume the livers of fish.

### 3.1.6 Consumption of vegetables (Pathways D1 & D2)

Because brodifacoum is poorly soluble in water and tightly bound to soil WHO (1995) concluded it is not taken up from soil by plants.

There is a possibility that while being hand broadcast in gardens the rodent bait may land on a vegetable plant. If distribution of bait is carefully performed this should be a very infrequent occurrence. Nevertheless if it does occur vigilant washing of vegetables before consumption will remove particles of bait. Due to the physicochemical properties of brodifacoum the chemical will not transfer from the bait matrix onto the surface of the plant.

Exposure to brodifacoum from eating home grown vegetables and fruit is negligible.

### 3.1.7 Exposure via poultry (pathway E)

This exposure pathway is incomplete because all poultry are to be removed from LHI during the rodent eradication campaign. They will not be reintroduced until after all the distributed bait has fully degraded. Contextual information regarding the distribution and elimination of brodifacoum in chickens is provided below.

Fisher (2009) gave a non-lethal single gavage dose of brodifacoum (0.5 mg/kg) to chickens and measured brodifacoum tissue concentrations at 1, 4, 7 and 14 days after dosing. During this time there were no ‘in life’ signs of poisoning or evidence of internal bleeding during tissue sampling. The weight of the chickens was ~ 1.25 – 2 kg and did not change during the study.
The liver had approximately 10 – 20 times higher concentration of brodifacoum than muscle (Table 3.1). The liver levels were relatively constant and an elimination half life from this tissue could not be determined. Although plasma concentrations approached those of liver at day 1 they declined to less than detection limit by day 7.

The administered dose (0.5 mg/kg) is equivalent to about 25 g Pestoff® bait per kg body weight (approximately 60 – 100 pellets of the 5.5 mm size bait per chicken).

Table 3.1: Distribution of brodifacoum in chicken

<table>
<thead>
<tr>
<th>Day</th>
<th>Plasma</th>
<th>Liver</th>
<th>Breast muscle</th>
<th>Abdom fat</th>
<th>Ovary</th>
<th>Faeces</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.22</td>
<td>0.66</td>
<td>0.06</td>
<td>0.06</td>
<td>0.13</td>
<td>0.17</td>
</tr>
<tr>
<td>4</td>
<td>0.12</td>
<td>0.65</td>
<td>0.06</td>
<td>0.06</td>
<td>0.13</td>
<td>0.17</td>
</tr>
<tr>
<td>7</td>
<td>- b</td>
<td>0.71</td>
<td>0.015</td>
<td>0.015</td>
<td>0.02</td>
<td>- b</td>
</tr>
<tr>
<td>14</td>
<td>- b</td>
<td>0.62</td>
<td>0.016</td>
<td>0.016</td>
<td>0.005</td>
<td>- b</td>
</tr>
</tbody>
</table>

| Half life (t½) (days) | 1.1 d | c | 5.3 d | 2.8 d | 3.2 d | c |

a Data is adapted from Fisher (2009). Units are µg brodifacoum/g wet weight.
b Concentrations less than detection limit (< 0.001 or 0.005 µg/g depending on tissue).
c Half life could not be calculated.

Fisher (2009) also describes a study by Lund (1981) in which four laying hens were fed brodifacoum bait and the eggs fed to a single laboratory rat over 10 days. The four hens died within 10 – 12 days after an average intake of 10.5 mg/kg brodifacoum. After consuming 218 g of eggs the rat showed no sign of toxicity and according to Fisher (2009) it was stated in Lund (1981) that “. . .eggs laid during an anticoagulant feeding period contain no toxic residues representing a risk to the consumer”.

3.1.8 Meat and dairy products (Pathway E)

Cattle are to be removed from LHI during the eradication campaign and dairy cows will be quarantined from exposure to bait. Therefore the human brodifacoum exposure pathway via meat and dairy products will not occur.

O’Connor et al. (2001) 8 have used sheep as a model to investigate possible contamination of cow’s milk after ingestion of brodifacoum. Lactating ewes were given a low and high dose of brodifacoum. Blood and milk were collected at 2, 4, 8, 16, 24 and 32 days. Although the doses

---

8 This study is reported in a non-peer reviewed journal.
are not provided the high dose is described as equivalent to a 60 kg sheep eating 3 kg of brodifacoum bait (i.e. about 8 boxes of 150g Talon® bait as sold in hardware stores). The low dose was described as being akin to levels recorded in wildlife around bait lines. Significant concentrations of brodifacoum were found in the blood at 2 and 4 days after the high dose, but at this dose only one milk sample was above the detection limit of 0.01µg/mL. No brodifacoum was detected in milk beyond 4 days. The authors concluded human poisoning through milk was very unlikely.

The study by O’Connor et al. (2001), and the fact that care will be taken to isolate LHI dairy cows from exposure to bait makes human exposure to brodifacoum by consumption of milk very low or incomplete.

3.1.9 Goat produce (Pathway G)

It is anticipated that brodifacoum uptake and distribution in goats will be similar to that in sheep (see Section 3.1.8) and therefore it is possible that if they ate large amounts of rodent bait, some brodifacoum could be in meat and milk. In the draft eradication plan goats on LHI are not intended to be removed but will be kept in isolated areas away from the broadcast rodent bait. These animals are kept as pets and not used for meat, milk or cheese making hence no exposure to brodifacoum will occur.

3.1.10 Consumption of wild ducks (Pathway H)

In the draft LHI rodent eradication plan it is noted that in trials conducted on the Island hybrid mallard/black ducks did eat the baits. Since it may be anticipated the uptake and distribution of brodifacoum may be similar as in chickens (Section 3.1.7) it raises the possibility a recreational duck hunter eating wild birds may be exposed to brodifacoum, especially if the liver was consumed.

Toxikos is advised ducks are occasionally shot by designated licensed fire arm owners on the island as part of a control programme to remove mallards and mallard/pacific black duck hybrids that are non-native. Pacific black ducks are protected and are not shot. There is no hunting on the island that would result in duck consumption as would be the case on the mainland.

---

9 Personal communication with Dr Ian Wilkinson, NSW Department of Environment, Climate Change and Water.
It would therefore seem that exposure to brodifacoum by consumption of wild duck is not a significant exposure pathway. Nevertheless it would be prudent to advise those individuals involved with the control of non-native duck populations that they should not consume duck during the eradication programme, and not the liver for perhaps a year after the program has ceased. The time of a year is precautionary because it is unknown how long brodifacoum may remain in the liver of ducks.

3.1.11 Dust inhalation during aerial baiting (Pathway I)

The hypothetical inhalation exposure scenario for LHI residents to fine dust dispersed during the proposed eradication program when the bait is aerially broadcast is summarised in Figure 3.2.

**Figure 3.2: Hypothetical inhalation exposure to dust during aerial broadcasting of rodent bait.**

The total amount of bait dispersed in two campaigns approximately 14 days apart is 12 and 8 kg/ha. It has been assumed the bait is dropped from a 50 m height along an 80m swath. The amount of inhalable fine particulates in rodent bait dispersed from buckets beneath helicopters has been calculated from data obtained in New Zealand.

In calculating the exposure of a person to brodifacoum it has also been assumed there is no wind or breeze to remove inhalable particulates away from the air space in which they were scattered, that the particulates stay in the air for 8 hours, that a child may be in the impacted air for 8 hours, and all the brodifacoum on dust breathed in will be absorbed into the body.
**Exposure assumptions and calculations:**

- The bait is to be spread at a total rate of 12 kg/ha (i.e. 12 kg/10,000m²) in the first campaign and 8 kg/ha in the second campaign.

- Pellets are released at approximately 50m in a swath 80m wide. Over an area 80m x 40m the amount of bait dispersed is:
  \[(12 \text{ kg/10,000m}^2) \times (80 \text{m} \times 40 \text{m}) = 3.84 \text{kg} \text{ (say 4kg bait)}.\]

- Torr and Agnew (2007) found approximately 130 - 150 g fine material (<2mm size) in a 25 kg bag of bait as delivered. They also determined the amount of fines produced by mechanical abrasion during aerial dispersion from a number of different style hoppers to be approximately 50 – 330g per bag. The maximum amount of fine particles (<2mm [<2000 µm]) in the supplied bait and potentially generated by dispersion machinery is therefore approximately 500 g per 25 kg of bait \(^{10}\) (i.e. approximately 2% of the total bait).

- The particle size that may be inhaled (i.e. drawn into the mouth and nose during breathing) is 100 µm. Large particles (>10µm) in the inhalable fraction are caught in mucous and subject to expectoration or swallowing. Particles ≤ 10 µm may reach the bronchi where they will be caught in mucous and transported to the throat and swallowed, the very fine particles (≤4 µm) may reach the deep lungs and be phagocytised by macrophages and transported up the ciliary ladder to be swallowed (CEN 1993, ACGIH 2008). Chemicals in, or on particulates of about 100 µm size that are inhaled are potentially absorbed into the body after the particles are swallowed, or after the chemical dissociates from the particle and absorption occurs across the lungs. Particles larger than 100 µm are not inhaled.

The amount of inhalable particles in the < 2mm fine material measured by Torr and Agnew (2007) is unknown. A conservative assumption would be 25% may be inhalable, if so up to 0.5% (25% of 2%) of the pellet bait could be potentially dispersed as inhalable particulates (i.e. up to 125 g per 25 kg bag bait).

This means in the 4 kg of bait dispersed into the hypothetical air volume described above there will be:

\[^{10}\text{Maximum amount of fines } < 2\text{mm is 150 g as delivered in bags plus 330 g produced during dispersion } = 480 \text{ g (rounded up to 500 g).}\]
4 kg x (0.5/100) = 0.02 kg (i.e. 20 g of inhalable particulates).

- Assuming the inhalable particles are dispersed in a volume of air 80m x 40m x 50m = 160,000 m³, and there is no wind or breeze to move them away from this theoretical air volume, and they stay suspended, then the concentration of inhalable particulate in air may be:

  \[ 20 \text{ g} + 160,000 \text{ m}^3 = 0.000125 \text{ g/m}^3 \text{ (i.e. 0.125 } \mu \text{g/m}^3) \]

- The amount of brodifacoum in the bait is 0.002%, hence the concentration of brodifacoum in the air could be:

  \[ 0.125 \mu \text{g/m}^3 \times \left( \frac{0.002}{100} \right) = 0.0000025 \mu \text{g brodifacoum/m}^3 \]

  \[ (0.0000025 \mu \text{g B/m}^3) \]

  The occupational exposure limit applied to protect workers from the effects of brodifacoum during manufacture of rodent bait is 2 µg/m³ (Syngenta 2006). Thus the maximum estimate of brodifacoum in inhalable particulates in air during aerial broadcasting is about eight hundred thousand times (800,000x) lower than the concentration used to protect workers.

  This assumes there is no wind that diluted and dispersed the particulates outside of the theoretical air volume in which they have been scattered.

- A 2 -3 year old child breathes 9.5m³/d (US EPA 2008) and weighs 13.2 kg (enHealth 2004). If it is assumed inhalable particulates remained suspended for 8 hours, a child spends 8 hours outside in the impacted air, and 100% of the brodifacoum on the particulates are absorbed into the body (bioavailability = 1). Then in these very unlikely circumstances the dose of brodifacoum to a 2 -3 year old child will be:

  \[ [0.0000025 \mu \text{g B/m}^3 \times 9.5 \text{m}^3/d \times (8 \text{hr}/24\text{hr}) \times 1] \div 13.2 \text{ kg} = 0.0000006 \mu \text{g B/kg bw/d} \]

  This is significantly less, in fact 250,000,000 (250 million) times less than the NOEL (150 µg/kg bw) for acute effects (single exposure) on PT time.

- The above calculations are for the first baiting programme of 12 kg/ha, a second programme will be undertaken at 8 kg/ha. Following the same steps as above, the dose to a 2 – 3 year old child from inhalation of particulates for the second programme would be 0.0000004 µg B/kg bw/d.
The total dose during the eradication campaign for this inhalation exposure pathway is;

\[ 0.0000006 \text{ µg B/kg bw/d} + 0.0000004 \text{ µg B/kg bw/d} = 0.000001 \text{ µg B/kg bw/d} \]

This is 5,000,000 (5 million) times less than the 42 day NOEL for prolongation of PT (5 µg B/kg bw).

**Conclusion**

Although fine dust may be released during aerial bait broadcasting, the amount is very small. The maximum dose of brodifacoum to a small child that could occur by inhaling this dust is negligible when compared to the doses that do not have any affect on the body. The dose to a child is about 250 million times less than a single dose of brodifacoum that has no effect, and five million times less than the dose which if taken daily over 42 days has no effect. LHI residents are only likely to be exposed by inhalation twice during the proposed eradication campaign.

The risk to human health from this inhalation exposure pathway is negligible.

**4. Existing risk from commercial rodent bait**

**4.1 Bait constituents**

Rodent control on LHI currently consists of baiting with warfarin and commercially available brodifacoum baits (0.005%). As with the proposed use of Pestoff® in the eradication program the human health risks are primarily associated with direct ingestion of bait with the intention of causing self harm. With warfarin the risk is considerably lower than with brodifacoum baits because it is more rapidly cleared from the body and not as strong an inhibitor of vitamin K epoxide reductase (WHO 1995, IPCS 1995).

Since commercial rodent bait sold in Australia has a brodifacoum concentration of 0.005% as compared to 0.002% for Pestoff® there is greater health risk from consumption of commercial bait than there is from an equal weight of Pestoff®20R.
Table 4.1 summarises some of the salient properties of commercial rat bait with those of Pestoff®20R. The greater health risk associated with the higher concentration of brodifacoum in commercial baits is dependent upon the commercial brodifacoum bait used by LHI residents. Some commercial bait (e.g. Talon® and Ratsak) contain bittering agents that act as taste deterrents to incidental ingestion of bait. These are incorporated into the bait on the premise children will quickly spit the bait out of their mouths. Pestoff®20R and some commercial bait (e.g. Bromakil 11) do not contain taste deterrents and so can be envisaged as presenting a greater risk for incidental ingestion.

The average weight of a small Pestoff®20R pellet is greater than that of both Talon® and Ratsak (see Table 4.1). In the case of Ratsak the amount of brodifacoum per pellet is the same as for the small Pestoff® pellet, while for Talon® there is less brodifacoum compared to Pestoff®20R. Therefore on a per pellet consumption, most likely for incidental ingestion of bait, the health risk associated with Pestoff®20R is the same as Ratsak, but greater than for Talon®.

However, any differences in relative health risk associated with incidental ingestion of small numbers of pellets from different products should be viewed in the context of the negligible health risk posed by such ingestion (see section 3.1.1).

Table 4.1: Comparison of commercial brodifacoum rodent bait with Pestoff®20R

<table>
<thead>
<tr>
<th>Product</th>
<th>Taste deterrent</th>
<th>Conc&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Package</th>
<th>Pellet</th>
<th>Diam (mm)</th>
<th>Weight (mg)</th>
<th>Brodifacoum (µg/pellet)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Talon</td>
<td>✓</td>
<td>0.005%</td>
<td>150 g (6 x 25 g prepacked open trays)</td>
<td>~ 4.5</td>
<td>~ 130 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>~ 6.5</td>
<td></td>
</tr>
<tr>
<td>Ratsak</td>
<td>✓</td>
<td>0.005%</td>
<td>200 g (4 x 50 g prepacked open trays)</td>
<td>~ 5</td>
<td>~ 220 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>~ 11</td>
<td></td>
</tr>
<tr>
<td>Bromakil &lt;sup&gt;b&lt;/sup&gt;</td>
<td>✗</td>
<td>0.005%</td>
<td>200 g (bulk, to be dispensed into open trays)</td>
<td>~ 4.5</td>
<td>~ 200 &lt;sup&gt;a&lt;/sup&gt;</td>
<td>~ 10</td>
<td></td>
</tr>
<tr>
<td>Pestoff®20R</td>
<td>✗</td>
<td>0.002%</td>
<td>Bulk, to be dispensed into open trays</td>
<td>~ 5.5</td>
<td>~ 500</td>
<td>~ 10</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>~ 10</td>
<td>2,000</td>
<td>~ 40</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> Average pellet weight determined by Toxikos by weighing ~ 50 pellets from product bought in a hardware store.

<sup>b</sup> Does not contain brodifacoum but another second generation anticoagulant, bromadiolone.

---

11 Note Bromakil does not contain brodifacoum but another second generation anticoagulant, bromadiolone, at 0.05%.
4.2 Bait stations
Within houses (e.g. roof spaces, under floors and other areas inaccessible to children) open trays, similar to those supplied with commercial bait holding approximately 25 gm of small pellets are intended to be used. These will present the same opportunity for exposure as current practice with commercial baits. The health risks for the duration of the eradication campaign, subject to the considerations in Section 4.1, will also be the same.

Outside of dwellings, T- or J- shaped bait stations purpose made from plastic storm water pipe are currently used (Appendix 1), and these or similar are intended to also be used in the eradication campaign. Again subject to the varying constituents in the commercial baits, the exposure opportunity and health risk for adults and children when using Pestoff®20R will be the same as is the current practice.

A major difference between the health risks associated with the proposed eradication campaign and what is currently practiced is the length of time bait will be used. If the eradication campaign is successful then there will not be a need for continuous rodent control by residents or commercial operations on the island. The long term exposure and health risks are therefore markedly less than if the eradication programme did not proceed and an ongoing need to continue using rat poison remained.

4.3 Conclusions

The relative opportunity for exposure to brodifacoum in bait stations via Pestoff®20R is the same as current practise using commercially available rat bait.

However, for the same number of pellets ingested the health risk may be higher depending on the constituents and pellet size of the commercial product.

Generally for the same weight of bait ingested Pestoff®20R presents a lower risk because it has a lower concentration of brodifacoum than products sold on the domestic market. This is however balanced by the absence of a taste deterrent which is in some, but not all commercial products.
The eradication campaign, if successful in removing rats and mice from LHI, will result in a smaller (zero) ongoing risk of exposure to rodent poisons.

5. General discussion and conclusions

This health risk assessment for human exposure to brodifacoum rodent bait is specific for the Lord Howe Island group and takes into account the bait intended to be used, the method of application, the longevity of the bait in the terrestrial and aquatic environments, and management practices to be undertaken to minimise human exposure to the broadcast bait.

A number of possible theoretical exposure pathways have been considered (Figure 3.1). These include:

- Direct ingestion of rodent bait.
- Inhalation of dust from bait during aerial broadcasting.
- Ingestion of soil contaminated by brodifacoum from bait.
- Dermal exposure to bait and contaminated soil.
- Ingestion of water (ground water and tank water) that may become contaminated by bait.
- Consumption of:
  - vegetables and fruit,
  - poultry produce,
  - fish that have ingested bait inadvertently distributed to shore waters,
  - meat and dairy produce,
  - goat produce,
  - wild ducks.

Many of these exposure pathways will not occur due to pre-emptive management practices that are to be put in place during and after the proposed eradication campaign (e.g. removal of poultry and cattle from the Island, isolating cows and goats from exposure to rodent bait). Consumption of wild ducks is said not to occur on the Island.

Brodifacoum, because of its physical chemical properties, is unable to contaminate groundwater because it doesn’t leach from soil. Similarly it does not contaminate vegetables and fruit because it is not transported from water or soil into the plant. In this instance the bait would
have to be physically broadcast onto the plant; this should not occur but if it does bait particles can be easily washed off during food preparation.

An important consideration in estimating exposure to brodifacoum by direct ingestion of bait pellets, or indirectly via potentially contaminated water, soil, and seafood is the stability of the pelletised form of the bait in the environment. The bait completely disintegrates into a few particles of grain within 100 days of being broadcast. It only remains as an entity that can be picked up by children or birds for about 15 – 21 days. Hence with two broadcast campaigns approximately two weeks apart, solid bait may be on the ground in such a form for 4 – 5 weeks. In water bait pellets are reported to disintegrate within 15 minutes, sooner if there is wave action.

Contamination of soil, fish and seafood, and tank water are hypothetical but nonetheless plausible pathways through which LHI residents may become exposed to brodifacoum. Even though it is very unlikely such exposure will occur, conservative (i.e. ‘high end’) intakes of brodifacoum have been estimated for these pathways. Figure 5.1 shows the theoretical intakes by a 2 year old child and compares them to the 42 day (0.005 mg/kg/d) and 90 day (0.001 mg/kg/d) NOEL for prolongation of prothrombin time. Brodifacoum doses for a two year old were estimated because this is the population sector most at risk from exposure to chemicals in the environment; the behaviour of young children brings them into closer contact with soil and because they weigh less than adults potential doses are higher. It is emphasised there is a lot of uncertainty associated with the intake estimations. Consequently conservative ‘high end’ estimations have been undertaken so any error is more likely to be on the side of over-estimation rather than under-estimation of intakes.

The probability of seafood being contaminated by brodifacoum is qualitatively discussed in Section 3.1.5. Overall, it is unlikely fish will have much opportunity to eat bait that might fall into the ocean, it is also unlikely humans will catch such fish in numbers where it may become a health issue. The conservative estimations of intake via seafood was undertaken using data from New Zealand for levels of brodifacoum in fish after a very large spill of Pestoff®20R into the sea. Brodifacoum was not measureable in the flesh of fish so potential exposure to brodifacoum in this risk assessment has been done assuming it may be present at half the analytical detection limit. The estimated intake is predicted to be less than both the 42d and 90d NOEL. Despite the low risk a precautionary recommendation for consideration in regard to fish consumption has been made.
Figure 5.1: Estimated ‘high end’ intake of brodifacoum by a hypothetical 2 year old child for various exposure pathways.

Note the breaks in the y-axis.

The 42 day and 90 day NOEL (0.005 mg/kg/d and 0.001 mg/kg/d respectively) are higher than the estimated doses in the exposure pathways below. The NOEL is the dose that does not cause any effect on prothrombin clotting time, the precursor event that leads to toxicity.

It should be noted there is uncertainty associated with these intake estimates. For example, it is not known whether exposure via these pathways will actually occur, hence the question marks in the figure. They are nonetheless plausible and the brodifacoum intake estimates are calculated to be conservative ‘high end’ estimates.

Ingestion of contaminated soil is very unlikely to occur since it is only that soil immediately beneath the bait pellets that will contain brodifacoum. Since brodifacoum is very tightly bound to soil negligible amounts would be expected to be absorbed into the body.
Contamination of tank water may occur if aerial broadcasting of bait accidentally spreads pellets onto roofs. The draft eradication plan has management contingency for this event. Less obvious ways that brodifacoum might get onto roofs is by birds eating bait and depositing droppings on roofs and gutters (brodifacoum is excreted in droppings), or birds picking bait up and discarding it onto roofs. The likelihood of these events is unknown. They are plausible but intuitively unlikely to place significant amounts of brodifacoum onto the roof.

Ingestion of brodifacoum contaminated soil is also considered to be a very minor pathway. It is unlikely all soil incidentally ingested (mostly by hand mouth transfer) will be contaminated soil. Furthermore brodifacoum is tightly bound to organic carbon in soil which significantly lowers the amount that may be absorbed into the body. Indeed swallowing a slurry of charcoal is a treatment option for large amounts of brodifacoum that have been ingested up to 4 hours earlier.

The high end estimation of brodifacoum dose by these exposure routes is less than the 42 day and 90 day NOELs (Figure 5.1). It is concluded there is negligible risk for human health from these exposure pathways.

The most likely and important way that a young child may be exposed to rodent bait during the proposed eradication campaign is by picking the bait up and eating it. Pestoff®20R rodent bait contains a water soluble green dye that will colour the tongue and mouth and thus assist to alert parents if they are vigilant.

Even though brodifacoum is acutely very toxic to a range of species the amount of bait needed to be ingested by a child at one time to cause health effects is quite large. Small bait pellets (5.5mm diameter) are intended to be hand distributed in the settlement and around dwellings. These are therefore the ones most likely to be picked up by a child. The number of pellets required to be ingested to reach the equivalent brodifacoum intake of the acute NOEL (0.15 mg/kg) for prolongation of prothrombin time is approximately 200 which weigh about 100 g. This amount of bait is put into perspective by considering commercial Talon® is sold in 150 g packets containing six prepacked pellet trays of 25 g each. Weight for weight, Talon® also has more brodifacoum than does Pestoff® 20R.

Assuming there will be two bait campaigns about two weeks apart, the time that bait will be in a physical form able to be picked up by a child is about 4 -5 weeks. It will require ingestion of 6 -7 small pellets per day, each day by a small child over this period to acquire a dose equivalent to the 42 day NOEL. This is unlikely to occur.
It is a fact that unless it is consumed with the intention of self harm (e.g. suicide attempt) it is quite unusual for a person to suffer toxic effects (anticoagulant symptoms) from incidental ingestion of brodifacoum rodent bait. Even with intentional ingestion most people do not die. This is because there are several days between ingestion and the appearance of toxic effects which allows time to assess the severity of poisoning and administer antidotes (plasma and Vitamin K) which are very efficient in reversing the effects. There are no long term consequences associated with recovery of poisoning by brodifacoum.

Relative to the health risk associated with current household practice of controlling rodents on LHI, the small Pestoff®20R pellets present the same hazard and potential health risk as most commercially available bait. This risk is very low (Section 3.1.1). Compared to Talon®, which has a taste deterrent and less brodifacoum per pellet (Table 4.1), the health risk associated with ingestion of a large number of Pestoff®20R pellets is greater. It is noted however that currently there is an ongoing risk of inadvertent ingestion of rodent bait associated with continuation of the current practice. This long term risk will be removed if rodents are eradicated from the Island. It is also noted health effects from incidental ingestion of any of the rodent baits, including Pestoff® 20R, is very low.

**Conclusions:**
Although brodifacoum is an acutely toxic substance that has the potential to cause toxicity and possibly death through internal bleeding, the human health risk to Lord Howe Islanders during the proposed eradication campaign is very low, indeed negligible. The most important exposure pathway is direct ingestion of bait picked up off the ground or from bait stations. The draft LHI rodent eradication plan indicates there will be an education campaign targeting children and parents to inform them of the dangers associated with eating the bait. Nonetheless parents will need to be especially watchful of their infant and young children during the 4 -5 weeks bait will be on the ground and able to be picked up. It is noted that with current rodent control practice residents also need to be vigilant, with removal of rodents from LHI the ongoing risk of bait ingestion, albeit low, and vigilance will also be removed.

Even though exposure is unlikely, indirect exposure pathways are managed primarily by removing or isolating human food sources that may become contaminated (e.g. poultry, beef meat and dairy produce). Other human foods (e.g. seafood, vegetables and fruit) are unlikely to be affected.
Tank water may become impacted if bait is strewn over roofs during aerial broadcasting. There are management contingencies to mitigate this if required. Theoretically tank water may also become contaminated with brodifacoum if birds transport pellets onto roofs or, after eating pellets, they leave their droppings on roofs. Both these scenarios are regarded as improbable but if they do occur, are very unlikely to affect tank water to the extent it is unsafe to drink.

Exposure to brodifacoum by indirect pathways (i.e. not direct ingestion of rodent bait) is negligible in comparison to the NOELs.

6. Recommendations

All mitigation measures as outlined in the *Draft Lord Howe Island Rodent Eradication Plan* should be implemented to minimise risks posed by use of rodent bait during the programme.

As a precautionary measure it would be prudent to advise Islanders not to consume the livers of fish that have been caught within 200m of the shore line until 6 months after the last bait broadcast.

Although there are negligible health risks from drinking tank water during the eradication campaign, for peace of Islander’s mind, consideration could be given to a programme of strategic testing of tank water.

It would be prudent to advise those individuals involved with the control of non-native duck populations that they should not consume duck during the eradication programme, and not the liver for perhaps a year after the program has ceased.
References

ACGIH (2008). TLVs and BEIs: Threshold limit values for chemical substances and physical agents, biological exposure indices. Appendix C: Particle size-selective sampling criteria for airborne particulate matter American Conference of Governmental Industrial Hygienists, Cincinnati, OH.


Fowler, A. (date unknown). Looking at Bird Poo.

http://www.fourthcrossingwildlife.com/LookingatBirdPoo.pdf

FSANZ (2010). Schedule 1.4.2, maximum Residue Limits, Australia only. Food Standards Australia and New Zealand,


www.avianmedicine.net/ambook.pdf


http://www.inchem.org/documents/hsg/hsg/hsg093.htm


Appendix 1: Design of bait stations

T- and J- shaped bait stations to be deployed when necessary around the settlement and dwellings are depicted below. The stations are made from plastic storm water pipe with cross wires at the entrance.
Dear Dr Wilkinson

Re: The Draft Lord Howe Island Rodent Eradication Plan

You emailed Dr Lewis, while I was on annual leave, the draft Lord Howe Island Rodent Eradication Plan (the Plan) and a toxicology health risk assessment of the plan carried out by Toxikos Consultants (Toxikos), and you asked that the South Australian Department of Health review these documents. This we have done.

The draft plan indicates that there will be an intentional exposure of the environment to brodifacoum by distributing 42,000 kg of edible bait containing 840,000 mg of brodifacoum as a 0.002% pellet (20 mg/kg active ingredient) as PostOff Rodent Bait 20R (Animal Control Products Ltd) at a rate of 20,000 g per hectare (or 2 g bait/m² equating to 4 µg of active ingredient/m²) by hand or mechanical or aerial broadcasting over a total of 2100 ha. These criteria are modified by various factors including a 50% higher rate when applied by air in certain circumstances (pg 27), with at least one large bait every 2 square metres and at least one small bait every half square metre in the ‘settlement area’ (pg 28), and the use of bait trays. Toxikos advises that each bait pellet contains 10 or 40 µg of brodifacoum. A map of the various broadcast methods and likely density would have better illustrated the Plan especially in relation to domestic dwellings, and where children are likely to frequent.

We agree that there is a potential risk for humans being exposed to the chemical. This Toxikos has summarised well. We also agree with the assessment that the most likely route of exposure is direct oral ingestion of the bait by children. Indirect exposure via the poison partitioned into liver of animals etc was rightfully included. The plan includes mitigation strategies to deal with this and other exposure pathways.

As with any risk management prevention of exposure is the best course of action. Within the hierarchy of controls for risk management the Plan considers elimination and concludes that a chemical method is the most appropriate. We make no comment on this. Substitution of the long acting highly lipophilic and therapeutically active brodifacoum with another less toxic, perhaps shorter acting poison, could be considered. Notwithstanding, the risk controls are likely to be similar. The following text assumes fait accompli and hence an engineered solution is required.

In this case, eliminating or reducing the risk that children: (1) are able to gather sufficient baits and (2) have a desire to consume them appears to be the best solution. There are a number of drivers that can increase the likelihood of a child gathering and consuming baits. Of concern is the lack of data on how palatable and acceptable the pellets are to children. The palatability in some cases can be directly proportional to the risk of consumption. The pellets are manufactured from a cereal based flour and coloured green. The binders are unknown, but any binder or other excipient that sweetens the pellet is likely to increase the
probability of consumption, especially repeat consumption. The green colour is unlikely to be a deterrent and indeed it may be an attractant.

Recommendation: Ensure pellets are not likely to be attractive for consumption, especially multiple doses, due their taste or colour.

Of concern is a lack of bittering agent (taste deterrent) irrespective of whether the pellets are palatable. The presence of a taste deterrent should increase the chance of a child spitting out pellets and not ingesting them (European Commission 2009 report p25) or would perhaps limit repeated episodes of ingestion.

Recommendation: Give consideration to rendering the pellets unattractive to consumption by adding a bittering agent.

The number of doses a child may consume is proportional to the child’s gathering ability. The further apart the baits the lower the chance a child of consuming multiple pellets. The report gives no indication on the success of otherwise of the various broadcast methods in uniformly distributing the baits. It is apparent that “lumps” of pellets, where more than one pellet is placed in close proximity to another, will elevate the risk markedly. These data are essential to inform the broadcast methods and ensure that they place the nominated concentration of pellets per unit area of soil.

Recommendation: the broadcast methods are evaluated and appropriately modified to ensure that multiple pellets are not placed within close proximity to each other (this risk is missing from “poor aerial baiting application”) in the risk – mitigation matrix.

The toxicological outcome of brodifacoum is well defined and described by Toxikos. However, there are sensitive subpopulations for which exposure has a higher risk of morbidity. These individuals are most likely easily identifiable which will allow greater precautions to be applied either by care givers or authorities laying the baits.

Recommended: That consideration is given to preparing a specific risk management plan for the highly sensitive subpopulation or at least identifying whether such a sub-population exits. These may include those with coagulopathies (whether genetic, drug induced or some other reason) and those with potential vitamin K deficiencies such as children with cystic fibrosis etc.

There was some concern that the Plan implies that because the chemical is sold as baits for domestic purposes, from which few poisonings are recorded, the risk of exposure on Lord Howe Island from this proposal is low. The deliberate mass distribution of 42,000 kg of bait over a wide area cannot be compared with the use of baits in the domestic situation. Therefore, the risks created by the proposal need to be managed, not ignored. Furthermore, historic use of such baits (pg 80), although it may create familiarity among adults (who may or may not respond appropriately) does not impinge the child – whether or not such baits have been used in the past does not alter the risk to children in any way, for a child does not learn from such events, unless perhaps they are actually involved.

Recommendation: That the information packages do not underestimate the familiarity of the use of brodifacoum containing baits, and that their effectiveness in communicating the essential information is tested before utilising.

The calculation of the risk that exposure may occur cannot be drawn from the fact that the product is sold in various jurisdictions (page 79). The distribution and exposure pathways are too different in this proposal to allow a sensible comparison. However, knowledge that exposure is measurable and can usually be successfully managed, especially if treated early, is comforting. The literature has many case reports on this topic.

In terms of the risk management of the project, prevention of exposure is the key. Whether a 30 m buffer zone around dwellings is suitable (pg 27) needs to be assessed on a case by
case basis. I am not confident that a helicopter will accurately disperse pellets boarded by a 30 m buffer zone, and there is an issue of overlap increasing the density of the pellets. There also is no mention of avoidance of children’s play areas, walkways or road-side verges frequented by children or areas where children play or congregate.

Recommendation: The plan elaborates on means by which land which is frequented or may be frequented by children is not contaminated with baits.

The numeration of the residual risk is problematic. The best data would be from human studies that measure dose against, say, change in prothrombin time. However, these data seem to be absent or too uncertain to be useful (such as data from poisoning cases). Therefore, the numeration of the lowest dose that would cause an effect needs to be extrapolated from animal data. For anticoagulants it is more useful to use the anticoagulant effect rather than death as the endpoint. This is because death is a manifestation of a range of physiological failures and not the primary response to the brodifacoum. Toxikos used the effects on the prothrombin complex, but quoted data from the European Commission 2005 report – a more recent 2009 report exists.

Recommendation: It is suggested that perhaps Toxikos re-examines its recommendations in light of the European Commission 2009 report.

What is interesting is that Toxikos did not apply an “uncertainty factor” but rather used the actual No Effect Level (NOEL) of the rat to derive the dose that may produce an effect. This inherently limits the usefulness of the derived value (page 29 & 30 Toxikos).

The literature indicates that there is a difference in responses (LD50) between sexes of a species, within a species, and between species, and most likely between laboratories. For instance pigs may be more sensitive than rats based on LD50. One then can presume that the underlying physiological response may be somewhat variable as well. Hence there is always some uncertainty as to the actual dose that may cause an effect in a generic animal and furthermore, given the range of values, it is likely the human will respond differently from some animals. These uncertainties are usually accounted for by dividing the lowest observable effect level (LOEL) or NOEL by some factor that ensures the criteria value will fall within a ‘safe’ range for humans. This the European Commission 2009 did in their deliberations.

Toxikos pointed out that the therapeutic index is very small – that is, the difference between the dose that causes an effect and the dose that causes death is small. Therefore other endpoints may be more pertinent (although I would argue the PT is the most fundamental). The European Union "Directive 98/8/EC" for brodifacoum (2009) utilized a different endpoint. This organisation suggested that the effect of brodifacoum found in a study examining whether the chemical caused teratogenic effects was more appropriate. In this study the mothers suffered effects from which the lowest observable effect was found to be 0.001 mg/kg, somewhat lower than the 0.15 (acute) or 0.005 (chronic) mg/kg bw /day used by Toxikos. Although the effect was from pregnant females, who may not behave the same as children, the effect warrants consideration. Using the EU 2009 figure and not applying a safety margin and using the same method as Toxikos (page 29) the maximum number of pellets a child could consume without an effect is less than two pellets based on:

\[
(0.001 \text{ mg/kg bw} \times 13.2 \text{ kg})/0.01 \text{ mg brodifacoum per pellet} = 1.3 \text{ pellets.}
\]

These data indicate there is some uncertainty in calculating a “safe” level for the consumption of these pellets.

Toxikos rightly indicates that a chronic dosing regime may be appropriate (pg 30) hence uses a 42 day no effect level on prothrombin time from a rat study, also without a safely margin, to arrive at a maximum dose of 0.005 mg/kg bw/day or about 6-7 pellets per day.
The assumption the Plan seems to take is that the child is unlikely to dose multiple times. This needs better argument: to my mind it is plausible unless the pellets are extremely hard to forage, or unpalatable, or distasteful (the emerald green colouring may not be a detractive). For instance, the foraging of pellets from a bait tray is a real and measurable risk. Such risks need numeration. Of note is the fact that water solube dyes in some cases can colour the urine – this may be an avenue of surveillance for care-givers.

**Recommendation:** The risk from consuming pellets multiple times is assessed and numerated, if possible, to ensure that mitigation strategies can be built into the plan if needed. And in particular of a child consuming brodifacoum from single or multiple bait trays or due to pellets being poorly spread.

On purely clinical basis, the 2 mg dose that Toxikos derived from acute (NOEL) appears to be somewhat high. Warfarin is purported to be less pharmacologically active than brodifacoum (eg Gill JE, Redfern R, 1983, J Hyg 91(2), 351). To achieve anti-coagulation in a human a "loading" dose is usually given (5-10 mg in an adult or 0.2 μg/kg/day in a child) followed by 2-10 mg/day in an adult or 0.1- 0.4 mg/kg/day for a child (eg Martindale, The Complete Drug Reference, or Australian Therapeutic Guidelines: Cardiovascular 2008). These doses, albeit for warfarin, appear to be very close to the calculated maximum allowable dose for a child with brodifacoum. The mitigating factor is the very long half-life of brodifacoum and the need for chronic dosing.

**Recommendation:** It may be prudent to ensure Toxikos is comfortable with the value they derived, given no safety margin has been allowed for, and that fact that rats may be somewhat different from humans, with pigs perhaps more sensitive (their LD50 was reported to be less than rats in a study) and in light of the EU 2009 report.

The toxicology of the dye in the pellet is not discussed, but was raised with you by phone. I understand that Tokicos has considered its toxicity.

**Recommendation:** The Plan mentions the dye and the out-come of Toxikos's deliberations as to its risk as a toxicant.

In terms of the Plan itself:

The Plan unfortunately simplifies the treatment of an exposure to brodifacoum; treatment can be considered relatively simple provided no sequelae to the exposure occurs. The Plan also makes no assessment on the ability to actually assess and treat paediatric or adult patients. Other factors such as the ability to measure the INR, which is a prerequisite in management of vitamin K antagonist ingestions, need consideration.

**Recommended:** if not already performed, a management plan for the accidental exposure to brodifacoum needs to be considered, especially for the paediatric patient.

The Plan erroneously states that warfarin is less toxic than brodifacoum (pg 12): it is not (as pg 21 indicates). In the illustrated case (pg 12) the controlling factor is dose (as concentration) not toxicity. On page 31 (6.1 Human Health) the Plan incorrectly states that "Brodifacoum at the low concentrations specified for this operation is of low toxicity to humans." This statement is misleading; caregivers reading this may reasonably and incorrectly assume that low levels of vigilance are required when supervising young children during the baiting program; dose matters more. The statement also contradicts the logic of statements that follow on page 31 indicating that parents will need to be 'vigilant'.

The Plan uses the term 'small children': it is presumed that 'young' children is the subject of observation in these cases.

It appears that the Plan does not account of differences in the community in terms of parenting skill nor capacity of parents to adequately prevent children from engaging in behaviours that may increase the risk of ingesting baits; some parents may be sight impaired,
intellectually disabled or infirmed or otherwise unable to provide the necessary level of supervision. Developing a means for providing assistance for such parents needs to be considered.

*Recommended: if not already performed, a management plan for providing assistance to parents with additional needs and challenges to be considered.*

I hope this has been of use. Should you require further discussion please don’t hesitate in calling me (08 8226 7100 or email david.simon@health.sa.gov). I also acknowledge the help of my toxicology section for providing useful and critical advice.

Yours sincerely

[Signature]

Dr David Simon
Director
Scientific Health Branch
Public Health

19/11/2010
9 December 2010

Mr Stephen Wills
Chief Executive Officer
Lord Howe Island Board
PO Box 5 Lord Howe Island NSW 2898

Email: stephen.wills@lhib.nsw.gov.au

Dear Mr Wills

RE: Human Health Risk Assessment on the Use of Brodifacoum for the Lord Howe Island Rodent Eradication Plan

I refer to my letter of 24 November 2009 concerning the South Eastern Sydney Illawarra Public Health Unit’s assessment of the ‘Draft Lord Howe Island Rodent Eradication Program’ and my request for a human health risk assessment to be undertaken of the program by an independent expert in health impacts and for the recognized Health Risk Assessment framework to be used for the assessment. I also refer to a meeting held with the Public Health Unit and the NSW Food Authority to discuss aspects of the proposal as addressed by Dr Ian Wilkinson.

It was understood from the original request that it is the intention to conduct a one off aerial spraying and hand broadcasting of the bait Pest Off20R, which contains brodifacoum. It was also advised that there would be a 30 metre buffer around all dwellings and that hand broadcasting will be undertaken in the residential areas of the Island.

Human Health Risk Assessment

In October 2010 the Public Health Unit was emailed a copy of the report “Human Health Risk Assessment on the use of Brodifacoum for the Lord Howe Island Rodent Eradication Plan’ undertaken by Toxikos Toxicology Consultants and signed off by Dr Roger Drew, Toxicologist and Health Risk Assessor. I am pleased with the report and its inclusions and that a suitable independent assessor has been engaged to undertake the assessment.

In detail all potential exposure pathways, indirect exposure pathways and health risk from current practice have been explored and examined. I would fully support and agree with all of the following recommendations as outlined in the Executive Summary of the report:
• All mitigation measures as outlined in the *Draft Lord Howe Island Rodent Eradication Program* should be implemented to minimize risks posed by use of rodent bait during the program.

• As a precautionary measure it would be prudent to advise Islanders not to consume the livers of fish that have been caught within 200m of the shore line until 6 months after the last bait broadcast.

• Although there is negligible health risk from drinking tank water during the eradication campaign, for peace of mind of the Island residents, consideration could be given to a program of strategic testing of tank water.

• It would be prudent to advise those individuals involved with the control of non-native duck populations that they should not consume duck during the eradication program, and not the liver for perhaps a year after the program has ceased.

• If the program goes ahead, during the operation the Public Health Unit will be available for health advice if required.

I advise that the Public Health Unit is able to provide comment on any intended strategic sampling program for the tank water and would be pleased to provide comment on the health component of the education program for the residents.

Yours sincerely

[Signature]

Professor Mark J Ferson MPH MD FRACP FAFPHM
Director & Medical Officer of Health
Toxikos response to SA Health comments on the Human Health Risk Assessment for Rodent Eradication on LHI

Prepared by: Dr Roger Drew, PhD, DABT
Toxikos Pty Ltd

Prepared for: Dr Ian Wilkinson
c/o Lord Howe Island Board

Toxikos document: TR020311-RF2
16th March 2011

Roger Drew, PhD, DABT
Toxicologist and Health Risk Assessor
1. Risk assessment methodology

SA Health indicates the quantitation of the risks from exposure to brodifacoum is difficult due to imprecise determination of critical doses for adverse effects in humans. Toxikos agrees with this, it is however no different from many other chemicals to which humans are exposed. In these circumstances it is usual to use information for the most sensitive effect observed in experimental animals which have been given defined doses of the chemical. In agreement with the Lord Howe Island (LHI) risk assessment, SA Health notes the anticoagulant effect, rather than death, is the more useful and appropriate end point to use in the risk assessment. This is because anticoagulation is the primary response to brodifacoum, uncontrolled bleeding and subsequent death are consequences of anticoagulation. There are no other effects that occur from exposure or poisoning with brodifacoum. An effective measure of anticoagulation is prolongation of prothrombin time (PT). In the LHI risk assessment Toxikos used experimental doses in rats that have no-effect on PT (i.e. no observed effect levels, NOELs) for comparison with conservative estimations of human exposure on the Island should the rodent eradication plan for LHI proceed.

SA Heath comment Toxikos did not apply uncertainty factors to the NOEL and hence the “usefulness of the derived value” is limited. It is apparent that SA Health have expected, or interpreted the risk assessment to have been undertaken using a toxicity reference value (TRV) that reflects an acceptable or safe dose. This was purposefully not done due to the difficulty in applying a TRV across different exposure pathways, particularly the direct ingestion of pesticide pellets where an estimated reliable exposure dose cannot be calculated for comparison with the TRV (see below for more comments on this exposure pathway). In addition the endpoint of interest used in the risk assessment is a biochemical response rather than a toxicological outcome, such as bleeding, which is usually used in setting a TRV. The biochemical action is however a necessary event for toxicity to occur.

Although it is not explicitly stated in the risk assessment Toxikos utilized the margin of exposure (MOE) method for characterizing risk from exposure to brodifacoum. In this technique an estimation of dose is compared with the appropriate NOEL, i.e. the highest dose that has no effect on the endpoint of interest. It is worth noting Toxikos has not “derived” a value for characterizing the risk. The NOEL used in this method is the unmodified value directly taken from experimental data with no uncertainty (safety) factors applied. This is a well recognized option, recommended by the World Health Organization (WHO 2005, 2008), the International Life Sciences Institute (ILSI 2008) and used by WHO bodies (e.g. JECFA 2005) and Australian authorities (e.g. NICNAS 2007, 2010a, 2010b), for characterizing public health risk from exposure to chemicals.
The larger the MOE the lower is the health risk; the rule of thumb is MOEs>100 are generally regarded as indicative of low health risks. In the risk assessment the calculated MOEs were not specifically described as margins of exposure; they were presented as the number of fold the estimated exposure was less than the NOEL. On reflection Toxikos acknowledges it could have been made more explicit what method of risk characterization was being applied. However there was a desire to limit the extent of technical jargon in the risk assessment. The lack of categorical reference to MOE terminology does not detract from, or compromise the LHI risk assessment.

The table below shows the MOEs calculated in the LHI the risk assessment. It should be noted MOEs were not calculated for direct ingestion of bait because the potential dose is not easily enumerated as it is patently dependent upon the behaviour of the child. This is discussed later in this document.

<table>
<thead>
<tr>
<th>Exposure Scenario</th>
<th>MOE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingestion of potentially contaminated soil</td>
<td>12,500</td>
</tr>
<tr>
<td>Dermal exposure after handling bait</td>
<td>500,000</td>
</tr>
<tr>
<td>Ingestion of tank water contaminated by bird droppings</td>
<td>6,250</td>
</tr>
<tr>
<td>Consumption of fish</td>
<td>6,250</td>
</tr>
<tr>
<td>Dust inhalation</td>
<td>5,000,000</td>
</tr>
</tbody>
</table>

The MOE method for risk characterization is more transparent than comparing exposure estimations with a TRV because the uncertainty factors embedded within a generic TRV, and hidden during risk characterization using the TRV, are not part of the situation specific assessment. While there are broad international guidelines on how to choose the size of the uncertainty factors, in actuality they are markedly influenced by the science policy and regulatory risk assessment framework of an authority, level of concern for the health endpoints, study interpretation, agency expertise, extent and product use patterns in the country, and exposure circumstances. Thus different authorities may develop different TRVs for a substance even though they are using the same study upon to which to base the TRV derivation. The MOE avoids these issues and allows the risk manager to choose the margin of safety to fit the situation circumstances before concern and/or management action is required.
2. The no observed effect level (NOEL)

Toxikos has used three NOELs in characterizing the human risk from ingestion of brodifacoum depending on the length of time it is assumed the pellets may be available for consumption after they have been broadcast on the island. These are:

- 0.15 mg/kg body weight for a single episode of eating bait,
- 0.005 mg/kg/d assuming bait is eaten every day for 42 days, and
- 0.001 mg/kg/d if bait is eaten every day for 90 days.

The NOELs used by Toxikos are consistent across a number of studies. A brief description is below.

Pelfrene (1991) reported a 42 day rat feeding study in which there were no adverse effects at 0.005 mg/kg/d. However the details of the study were not provided. The European Commission (2005a, b, c) describe an unpublished confidential 90 day feed study in rats which included an interim assessment of haematology parameters; the NOEL after 45 days was 0.004 mg/kg/d and at the end of 90 days was 0.001 mg/kg/d. The same description of the study is provided in 2009 (EC 2009) as is in EC (2005a, b). Another proprietary repeat dose study (Hodge et al. 1980), in fact a study designed to investigate developmental effects in the foetus, is described by US EPA (1998). Groups of 10 pregnant rats were administered brodifacoum dissolved in ethanol/water at 0.001, 0.01 or 0.02 mg/kg/d by gavage on days 6 – 15 of gestation (i.e. 10 days exposure); the NOEL for equivocal haemorrhagic effects was judged to be 0.001 mg/kg/d (US EPA 1998). This study is described in more detail below as it the one used by EC (2009) for setting a TRV which SA Health suggested might be used for the LHI risk assessment.

Thus two studies indicate a NOEL of 0.005 (0.004) mg/kg/d) after 42 (45) days of daily exposure. A traditional 90 day feed study gave a NOEL of 0.001 mg/kg/d). Although the 10 day gavage rat developmental study of Hodge et al. (1980) also produced a NOEL of 0.001 mg/kg/d, as discussed below the effect was marginal (US EPA 1998) and may have been affected by the physiological changes that occur in gravid animals.

After reviewing the information from the European Commission (EC 2009) the NOELs used by Toxikos remain the most appropriate for determining the MOE after 45 or 90 days of potential exposure to brodifacoum on LHI.
3. The European Commission assessment (EC 2009)
SA Health have pointed out that Toxikos has partly relied upon an European Commission review of brodifacoum that was conducted in 2005 (EC 2005 a, b, c), they have suggested the evaluation undertaken in 2009 by the Commission (EC 2009) is more appropriate as in the latter a toxicity reference value (TRV) has been derived that perhaps should be used in the risk assessment. As described above the methodology applied by Toxikos did not use TRVs, and we consider the TRV from EC (2009) to be inappropriate for the risk assessment.

With regard to toxicological information and description of studies, the EC (2009) review does not contain any additional information than is in EC (2005). The European Commission (EC 2009) established an “acute” TRV from the rat developmental study of Hodge et al. (1980). SA health acknowledged the effect was from pregnant females who may not behave the same as children but nonetheless suggested the effects warranted consideration. It is well known a number of physiological changes occur during pregnancy that can affect the absorption, metabolism and distribution of drugs. Toxikos’ consideration follows.

EC (2009) does not describe any of the experimental details of the Hodge et al. (1980) study, not even the dose levels used, not the mode of administration, not the evaluation techniques, or findings at each dose level. Reported in EC (2009) is a single sentence in which it is stated maternal haemorrhages at doses >0.01 mg/kg (NOEL 0.001 mg/kg) occurred and that there were no effects on the foetus at any dose.

Note this is a repeat dose study and the dose should be described as mg/kg/d as is convention and in US EPA (1998). For a more comprehensive description of the Hodge et al. (1980) study one must go to US EPA (1998). The dose details are as described in Section 2 above, but it should be appreciated the dosing method was bolus gavage of dissolved brodifacoum directly into the rat forestomach which is different from the mode of administration (dietary) in the rat 90 day study. Quite apart from the animals being pregnant, compared with dietary administration, gavage studies often yield different results for acutely toxic substances due to faster absorption of the bolus dose causing a blood-time curve with a sharper peak. The brodifacoum to be used on LHI is mixed with a cereal base to form pellets and potential exposure from direct ingestion of pellets is more similar to the exposure in the rat feed studies than to a bolus dose in ethanol/water.

SA Health suggests that the European Commission (EC 2009) in setting their TRV have used a “different” end point that is more appropriate than the one used by Toxikos. In fact both have used haematological events that are related; the EC (2009) bleeding and Toxikos prolongation of PT.
The endpoint used for determining the maternal NOEL in the developmental rat study of Hodge et al. (1980) was blood in the uteri observed when the animals were sacrificed at the end of the gestation period (day 21). The incidence was 0.001 mg/kg/d (0%), 0.01 mg/kg/d (1%) and at 0.02 mg/kg/d (30%). At the mid dose the US EPA (1998) considered the effect equivocal, but for conservatism and because the observation was possibly related to brodifacoum administration (and consistent with the mode of action) considered the NOEL was 0.001 mg/kg/d. It should be noted there is a 10x difference between the NOEL (0.001 mg/kg/d) and the next dose (0.01 mg/kg/d) in which the response was equivocal, but just a 2x dose difference between the mid dose and the top dose (0.02 mg/kg/d) in which the effect was unambiguous. The large dose difference between the low and mid dose strongly suggests the ‘true’ NOEL in this study is somewhat higher than the experimental dose of 0.001 mg/kg/d.

EC (2009) applied a composite 300 fold safety factor to the rat maternal NOEL to establish the TRV (10x interspecies, 10x intraspecies differences and 3x for concern for suspected developmental effects). In fact EC (2009) states “no significant effects on litters were observed”, US EPA (1998) states “there were no indications of any dose related developmental effects”. Similarly a rabbit study was negative for developmental effects (EC 2005 b, 2009, US EPA 1998). There is also no indication of adverse effects on the human foetus after exposure to high intake of brodifacoum such as after suicide attempts (e.g. Zurawski and Kelly 1997). It is therefore odd that EC (2009) have used an additional safety factor of 3x for developmental effects when the available data for brodifacoum indicates it does not cause this effect. The perceived concern, contrary to experimental evidence, arises by analogy with warfarin which is known to induce a range of developmental outcomes which are unlikely to be due to its anticoagulant effects as a rodenticide. Warfarin and brodifacoum are different molecules. It should also be noted the brodifacoum concern regarding developmental effects is a provisional decision in EC (2009). It is doubtful whether authorities in the US or Australia would establish an ‘acute’ TRV in this manner. A TRV based on the maternal effects in a rat developmental study would more likely be established with a safety (uncertainty) factor of 100 (see the discussion on MOE above).

SA Health intimates the EC (2009) evaluation is more up to date and therefore greater weight should be given to it rather than the EC (2005) evaluation. While it is certainly more recent it does not invalidate or replace the information in EC (2005). Indeed the EC (2009) document contains far fewer study details than EC (2005) or US EPA (1998). Frustratingly EC (2009) does not even identify the studies from which it cites information. After carefully considering the information in EC (2009), it is Toxikos’ conclusion the EC (2009) evaluation does not improve or overturn the methodology, or alter the outcome of the risk assessment for LHI.
4. Species differences

Based on differences in LD50 values cited in the LHI risk assessment SA Health argues the underlying physiological response between species may be somewhat variable and it is likely humans will respond differently from animals. This is the basis for SA Health to suggest uncertainty factors should have been applied to the NOEL in order that exposures could be compared to a ‘safe’ dose. If the risk assessment had been performed using a “criteria” value Toxikos agrees with SA Health that uncertainty factors applied to the toxicological NOEL should be sufficient to ensure the “criteria value” (TRV) would fall within a safe range for humans. As described above this was not the method used to characterise the risk of brodifacoum exposure at LHI and it is not necessary that it be used.

Toxikos has used doses in the rat that do not prolong PT as the NOELs to calculate margins of safety. The risk manager can decide what MOE should generate concern, i.e. in effect determine a safety margin with which they are comfortable. The underlying question from SA Health is whether the rat is the most sensitive species from which to obtain the NOEL used in the calculations. The literature searches undertaken by Toxikos indicate investigation of brodifacoum induced changes in PT have not been conducted for a wide range of species. However all species have the same effect of death if uncontrolled bleeding occurs. Since this occurs by the same mode of action in all species (i.e. inhibition of coagulation as measured by PT) the LD50 provides a means to judge the relative sensitivity of different species to the anticoagulant effects of brodifacoum.

In the LHI risk assessment information on LD50 was obtained from reviews, the specific study from which the data was reported was not sought. For non-ruminant mammals the single dose LD50’s were:

- Overall in rats from four reviews 0.27 mg/kg.
- In dogs 0.25 – 1.0 (Pelfrene 1991) and 0.25 – 3.56 mg/kg (Eason and Ogilvie 2009).
- In guinea pig, mouse and rabbit 0.28 – 0.4 mg/kg (Pelfrene 1991).
- In pigs O’Brien and Lukins (1990) reported 0.52 mg/kg, but Eason and Ogilvie (2009) gave a value of 0.1 mg/kg.

Thus, apart from the information for pigs reported in Eason and Ogilvie (2009), the lowest LD50 was about the same for rat, dog, guinea pig and rabbit at approximately 0.25 mg/kg/d. It is therefore not unreasonable to assume that humans would also be similarly as sensitive to the effects of
Indeed the World Health Organisation (IPCS 1995) estimated the average fatal dose for an adult (60 kg) to be approximately 15 mg brodifacoum (i.e. 0.25 mg/kg), or 300 g of 0.005% bait. Note in the LHI risk assessment Toxikos has also contextualised direct ingestion of brodifacoum relative to the amount of bait that would need to be consumed.

SA Health considered the 0.1 mg/kg LD$_{50}$ data for pigs from Eason and Ogilvie (2009) indicated this species was more sensitive than others and hence it was likely humans may respond differently from other animals. Toxikos has sought to verify this LD$_{50}$ data for pigs.

- Eason and Ogilvie (2009) cite two references as the source for the low LD$_{50}$ value for pigs, Godfrey (1985) and Eason and Spur (1995). Both these papers are not the original source of the data.
- Thus it would appear that Godfrey (1985) is the primary source of the 0.1 mg/kg LD$_{50}$ for pigs reported by Eason and Ogilvie (2009). However this paper is also not the original source of the data, it nevertheless cites the LD$_{50}$ as 10 mg/kg raising the possibility that perhaps Eason and Spur (1995) have misquoted the value in their review.
- Godfrey (1985) cites four papers as the source of the 10 mg/kg LD$_{50}$ in pigs.
  - Bull (1976), a review that does not mention brodifacoum.
  - Duback (1979), the proceedings of a scientific conference that were not available to Toxikos in the time available for this response.
  - Godfrey (1981a), publication not available but from the title is a study in rabbits.
  - Godfrey (1981b), publication not available but from the title is a study in dogs.

It is Toxikos’ conclusion that the concern regarding demonstrable species differences in response to brodifacoum based on the lethality data for pigs cannot be sustained, and that the assumption by Toxikos that humans are likely to be as equally sensitive as rats is valid, indeed it is same assumption as that made by the World Health Organization.

5. Clinical considerations of anticoagulant therapy

SA Health have suggested “the 2 mg dose Toxikos derived from acute (NOEL) appears somewhat high” and have cited clinical loading doses for children of warfarin are about 0.2 µg/kg/d (this is a typographical error by SA Health and 0.2 mg/kg/d is meant) and maintenance doses are 0.1 – 0.4 mg/kg/d. Toxikos presumes the reference to a 2 mg dose refers to calculations in the risk
assessment pertaining to an acute, single ingestion of rat bait. The acute (single dose NOEL) is 0.15 mg/kg, thus for a 13.2 kg child consumption of 1.98 mg of brodifacoum would equate to the NOEL. This is approximately 200 pellets or about 100 g.

We consider the analogy with warfarin loading doses is not appropriate because it occurs over a number of days and is followed by a lower maintenance dose regime, whereas the scenario in the risk assessment commented upon by SA Health is for a single ingestion. Nevertheless comments are provided below.

Achieving the desired level of anticoagulant therapy in patients with warfarin is not straightforward; there have been many algorithms for warfarin loading and determination of maintenance doses (e.g. Desai and Farrington 2000, Bauman et al. 2006, Heneghan et al. 2010). The loading dose of warfarin to children is 0.2 – 0.5 mg/kg/d for 2 – 4 days (maximum 10 mg/d for any given individual), over this period the loading doses are adjusted to achieve the desired target level of anticoagulation as judged by INR (International Normalised Ratio)\(^1\) measurements for the PT measurement technique being used. Maintenance doses of warfarin, usually 0.1 – 0.4 mg/kg/d, are aimed at keeping the INR within the target range for the condition for which anticoagulant therapy is being undertaken. For such repeat dose exposure the risk assessment for LHI has used a NOEL of 0.005 mg/kg/d to characterise the risk from ingesting brodifacoum rather than the single dose NOEL of 0.15 mg/kg.

The acute, single dose brodifacoum response for prolonged PT in rats is no effect at 0.15 mg/kg/d, 0.2 mg/kg reduced activity to 7% of normal values, and 0.33 mg/kg to 4% of normal (Pelfrene 1991). Given that warfarin loading doses occur over 2 – 4 days and are followed by maintenance doses to achieve the desired level of anticoagulation (note, not bleeding), the brodifacoum dose response in rats is consistent with the clinical anticoagulant objective in humans and the repeat dose NOEL’s of 0.005 mg/kg/d and 0.001 mg/kg/d used in the risk characterisation for LHI.

In making its comments SA Health expressed concern that warfarin is less pharmacologically active than brodifacoum, this was probably why the issue of the warfarin loading dose was raised. With equivalent doses, more brodifacoum is found in the target tissue (the liver) and for longer than with warfarin. This is because brodifacoum is more lipid soluble and its metabolism much slower.

---

\(^1\) Prothrombin time is determined by adding a standardised thromboplastin reagent (phospholipid and tissue factor) to the patient’s citrated whole blood. Citrate removes calcium from the blood to prevent clotting. When excess calcium is added after the reagent the blood begins to clot and the time taken recorded. It is common to relate the patients clotting time to that of a control (i.e. ‘normal clotting’). However the ratio of patient to control is influenced by both the laboratory method and the source of the thromboplastin reagent. To allow cross laboratory and international comparisons the PT results are standardised according to the reactivity of the particular thromboplastin preparation, the results is expressed as the INR.
These are the major reasons why brodifacoum is more effective than warfarin as a rodenticide, although different binding to serum albumin affecting the free fraction of the compounds may also play a role. The suggestion that brodifacoum is more pharmacologically active than warfarin is really a question of whether brodifacoum is a more potent inhibitor (i.e. has a lower inhibition constant, Ki) of vitamin K epoxide reductase (VKOR), however Toxikos has been unable to locate information to address the relative specific activities of brodifacoum and warfarin towards VKOR.

SA Health cites Gill and Redfern (1983) to support greater pharmacological action of brodifacoum compared to warfarin. This is an ad libitum feeding study in Meriones shawi (Shaw's gerbil) that incorporates all the differences in rodenticide metabolism and disposition that contribute to the greater field effectiveness of brodifacoum over warfarin as a rodenticide, it does not address the innate pharmacodynamic properties of the two compounds. In this paper the basic measure of rodenticide effectiveness was the number of feeding days required to cause mortality. We also note the test species is somewhat unusual and that the study was undertaken to find an effective control for gerbil population outbreaks in North West Africa.

Regarding the clinical outcome of single unintentional ingestion of brodifacoum rat bait, Su and Hoffman (2006) describe a compilation of 145 paediatric cases. Prolongation of INR occurred in only 8 (5.2%) and only one was reported to have abnormal prolonged bleeding but this did not require medical intervention. Su and Hoffman (2006) stress the majority of patients (usually children) are entirely asymptomatic and have normal coagulation profile after unintentional exposure. Knowing clinical effects are rare they point out most clinicians endorse supportive care without PT measurements, they however recommend unintentional exposure should be considered a potentially significant exposure and prothrombin time monitored daily for at least 2 days.

The situation regarding multiple exposures is different; Su and Hoffman (2006) indicate clinically significant anticoagulation can occur in children following small repeated ingestions of bait. This is recognised in the risk assessment, and is the reason why, for any exposure other than a single ingestion, the 42 day NOEL of 0.005 mg/kg/d was used to characterise the risk of potential prolongation of PT (note not necessarily cause bleeding). The amount of bait that needs to be ingested daily over this time to meet or exceed the NOEL is relatively small, just 6 -7 pellets. The risk assessment for LHI rodent eradication and SA Health highlight this potential. Furthermore SA Health and the LHI eradication plan both discuss mitigation strategies. Related discussion is in the next section.
6. Direct ingestion of rodent bait

SA Health rightly direct attention to the potential risk associated with multiple ingestion of rodent bait pellets. This is consistent with the deliberations in the LHI risk assessment. Due to the uncertainty in predicting how many pellets a child may pick up and consume per day at no time has Toxikos suggested there is a ‘safe’ number that can be consumed. What the risk assessment attempts to provide to the risk manager is contextual information relative to the dose that needs to be ingested for the NOEL to be exceeded. For a single ingestion episode quite a large number of pellets need to be eaten, if the pellets are eaten on a daily basis a much smaller number of pellets are required to reach and possibly exceed the NOEL for prolonged PT. The LOEL that Toxikos has used for these considerations has been chosen after deliberation of the bait’s environmental degradation and the ability of children to pick it up as a pellet to eat, this is less than 4 – 5 weeks, therefore the 45 day NOEL of 0.005 mg/kg/d was used and not a NOEL of 0.001 mg/kg/d, sourced either from the 90 day rat feed study or the Hodge et al. (1983) gavage developmental study, as suggested by SA Health.

SA Health are concerned that the bait may be attractive to children and that the target distribution may not be achieved, perhaps there will be a greater density of pellets on the ground and a child will more easily be able to gather them. An increased amount of pellets on the ground is contrary to the operational information in the LHI rodent eradication plan that Toxikos has assumed will be able to be met. SA Health has appropriately indicated the risks will increase if what is said to occur in the plan does not occur. Toxikos agrees with this, but in conducting a risk assessment for a proposed activity one has to assume the activity will be carried out as described.

It is simply not possible to achieve the outcome of ridding LHI of rats and mice and at the same time guarantee it will be risk free to residents. The plan has a number of operational mitigation strategies. If the broadcasting of pellets is undertaken as described in the plan Toxikos considers it unlikely, but nonetheless feasible, that a child may ingest pellets on multiple days during the 45 days that pellets may be able to be picked up and swallowed. Therefore the risk assessment indicates the key to ensuring small children are not exposed is educating children and parents about the bait, and close vigilance by parents during the eradication campaign. If the education/communication is not robustly conducted then its ability to mitigate the risk from incidental direct ingestion of bait by young children may be compromised. In this Toxikos and SA Heath are in broad agreement.
Taking into consideration the operational aspects of the LHI eradication plan (assuming these are achieved), the stability of the bait, the fact that the vast majority of cases of accidental ingestion of brodifacoum do not require medical intervention, signs and symptoms of poisoning occur before serious outcome is imminent, and the availability of very effective antidote and treatment, Toxikos has concluded the overall risk of health effects is low and negligible.

In retrospect perhaps a better description of the probability of health effects would be, the likelihood of health effects is low and of serious outcome negligible.

7. Summary response to SA Health recommendations

The following (in italics) are recommendations from the SA Health peer review that pertain to the conduct and outcome of the LHI health risk assessment.

- It is suggested that perhaps Toxikos re-examines its recommendations in the light of the European Commission 2009 report.

Toxikos has read and examined the European Commission 2009 report (EC 2009) in detail. The methodology used by Toxikos for characterising the risk is an approved international and national approach that is more appropriate for the circumstances of exposure at LHI than that undertaken by EC (2009). The margin of exposure (MOE) approach taken by Toxikos is transparent and allows greater appreciation of the risks than comparison with a toxicity reference value (‘safe’ dose) as suggested by SA Health. It is acknowledged it was not made explicit in the risk assessment that a MOE method was being used, the MOE being articulated as the number of times the estimated exposure from different potential exposure routes was less than the no effect level identified from experimental animal studies.

From the EC (2009) evaluation SA Health has raised a number of risk assessment aspects that have been examined by Toxikos. For each of these it has been found the information in the LHI risk assessment is appropriate and the outcomes and recommendations of the risk assessment have not been changed. The EC (2009) report, although more recent than the EC (2005) report referenced in the risk assessment, does not add to, or alter the information in the risk assessment.
The risk from consuming pellets multiple times is assessed and numerated, if possible, to ensure that mitigation strategies can be built into the plan if needed. And in particular of a child consuming brodifacoum from a single or multiple bait trays or due to pellets being poorly spread.

The risk assessment has considered the potential health risks should pellets be consumed multiple times by a child. Assuming pellets may be eaten on a single occasion or consumed every day for 45 days, the risk has been contextualised and enumerated by estimation of the number of pellets required to be consumed to achieve the no effect dose. The actual number of pellets that could be eaten by a child, hopefully none if the information and education strategy of the eradication plan is effective, is not possible to enumerate since it is highly dependent upon the behaviour of the child. The risk assessment indicates only a small number of pellets (about 6 – 7) need to be eaten over multiple days before the no effect level for increasing prothrombin time is exceeded. With respect to targets of ‘on-ground’ bait density or the bait being poorly spread, Toxikos has assumed the operational aspects of the eradication plan are achieved. Thus the risk assessment reflects health risks according to the plan.

It may be prudent to ensure Toxikos is comfortable with the value they derived, given no safety margin has been allowed for, and that fact rats may be somewhat different from humans, with pigs perhaps more sensitive (their LD$_{50}$ was reported to be less than rats in a study) and in the light of the EU 2009 report.

Toxikos has investigated this recommendation in detail. The risk characterisation method used in the risk assessment does not require the use of a safety margin; an appropriate safety margin can be identified by the risk manager by choosing the margin of exposure above which health concern may be raised. Examination of the toxicological information has not identified data to suggest humans may be different from rats with respect to response to brodifacoum, on the contrary the information indicates there are no material differences between non-ruminant mammals. Scrutiny of the pig LD$_{50}$ data has found the suggestion that pigs are more sensitive is not sustainable. As indicated above the EC (2009) report does not alter the information or outcome of the LHI risk assessment. Toxikos is comfortable with the risk assessment and its recommendations, detailed reasoning is found in the technical commentary accompanying this response to the SA Health recommendation.
The plan mentions the dye and the outcome of Toxikos's deliberations as to its risk as a toxicant.

Toxikos has not investigated the toxicology of the dye used in the rodent bait pellets. It is identified as a food approved dye, and *inter alia* it has been assumed if safe for food use its toxicity is negligible, and health effects from the dye after pellet ingestion also negligible.

References

**Pertaining to MOE:**


**Pertaining to LD<sub>50</sub>**


Other references


(http://findarticles.com/p/articles/mi_m0FSZ/is_2_26/ai_n18609982/?tag=content;col1)


REPORT

LORD HOWE ISLAND RODENT ERADICATION PROGRAM – RESPONSE TO LETTER

David Kelly - Lord Howe Island Board

Job No: 20113

5 March 2015
PROJECT TITLE: Lord Howe Island Rodent Eradication Program – Response to Letter

JOB NUMBER: 20113

PREPARED FOR: David Kelly - Lord Howe Island Board

PREPARED BY: Jack Dempsey

APPROVED FOR RELEASE BY: Lyn Denison

DISCLAIMER & COPYRIGHT: This report is subject to the copyright statement located at www.pacific-environment.com Pacific Environment Operations Pty Ltd ABN 86 127 101 642 (trading as Toxiko).

DOCUMENT CONTROL

<table>
<thead>
<tr>
<th>VERSION</th>
<th>DATE</th>
<th>PREPARED BY</th>
<th>REVIEWED BY</th>
</tr>
</thead>
<tbody>
<tr>
<td>V1</td>
<td>5/03/2015</td>
<td>J. Dempsey</td>
<td>L. Denison</td>
</tr>
</tbody>
</table>

BRISBANE:
Level 1, 59A Melbourne Street
South Brisbane Qld 4101
PO Box 3306 South Brisbane Qld 4101
Ph: +61 7 3004 6400
Fax: +61 7 3844 5858

Unit 1, 22 Varley Street
Yeerongpilly, Qld 4105
Ph: +61 7 3004 6460

ADELAIDE:
35 Edward St, Norwood SA, 5067
PO Box 3187, Norwood SA, 5067
Ph: +61 8 8391 4032

SYDNEY:
Suite 1, Level 1
146 Arthur Street
North Sydney NSW 2060
Ph: +61 2 9870 0900
Fax: +61 2 9870 0999

MELBOURNE:
Level 10, 224 Queen Street
Melbourne VIC 3000
Ph: +61 3 9036 2637
Fax: +61 9642 1203

PERTH:
Level 1/Unit 3, 34 Queen Street
Perth WA 6000
Ph: +61 8 9481 4961
## CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Title</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EXECUTIVE SUMMARY</td>
<td>1-3</td>
</tr>
<tr>
<td>2</td>
<td>INTRODUCTION</td>
<td>2-4</td>
</tr>
<tr>
<td>3</td>
<td>RESPONSE</td>
<td>3-4</td>
</tr>
<tr>
<td>3.1</td>
<td>Review of the 2010 Toxikos report</td>
<td>3.1-4</td>
</tr>
<tr>
<td>3.2</td>
<td>Response to issues raised by Mr Ratheburger</td>
<td>3.2-10</td>
</tr>
</tbody>
</table>
1 EXECUTIVE SUMMARY

Pacific Environment – Toxikos has conducted a review of the 2010 Toxikos (Report TR010610-RF2 dated 15 September 2010) and considered the issues raised Mr Rathgeber in his letter to the Lord Howe Island Board. Although some errors were found in the original Toxikos report, they do not affect the overall findings that the proposed rodent eradication plan is appropriate and would not pose a risk to the health of the residents of Lord Howe Island.

Some of the issues raised by Mr Rathgeber, although relevant considerations, are in some cases based on a misunderstanding of the toxicological information and the application of workplace and environmental standards.

The findings of this review are that the proposed rodent eradication plan involving the use of brodicafoum will not pose a risk to the health of the residents of Lord Howe Island. The risk management processes included in the plan will mitigate any possible risks posed by the use of brodicafoum.
INTRODUCTION

The Lord Howe Island Board, has requested Pacific Environment – Toxikos to review the issues raised in a letter by Mr Rathgeber on the proposed use of Brodifacoum for pest eradication on Lord Howe Island. In 2010 Toxikos (Report TR010610-RF2 dated 15 September 2010) conducted a toxicological assessment on the use of brodifacoum for the eradication of rodents on Lord Howe Island and concluded that the proposed plan for the application of brodifacoum on Lord Howe Island would not pose a risk to the local human population. Mr Rathgeber questioned some of the findings of the Toxikos report and raised concerns about the potential health effects that the use of brodifacoum may have on the health of the Lord Howe Island residents. He has asked that the eradication program be put aside.

Pacific Environment – Toxikos has reviewed the original Toxikos report and the issues raised by Mr Rathgeber and the findings are presented in Section 3 of this report. It should be noted that the people that have undertaken this current review were not involved in the preparation of the original Toxikos report and the findings can be considered as independent.

RESPONSE

3.1 Review of the 2010 Toxikos report

Format: The 60 page report presents a conventional screening human health risk assessment which discusses the usual steps of issue identification, hazard identification and dose response leading to hazard characterization, exposure assessment and finally risk characterization. References are provided, all calculations are shown in full and all assumptions are transparently discussed and of a conservative nature. A formal sensitivity analysis is not provided presumably because the calculated Margins of Exposure between likely exposure levels and harmful exposure levels were so large.

Comment - This is an appropriate approach to the brief given to Toxikos.

Issue identification: as stated by Toxikos, the Health Risk Assessment (HRA) only deals with public health risks and theoretical pathways for human exposure to Brodifacoum during the eradication program and does not address OHS issues nor risk to non-target species. Throughout the report the 2-year old child is considered to be the most sensitive receptor.

Comment - This is an appropriate approach to the brief given to Toxikos.

Hazard identification: The Toxikos report presents a summary of the Physical and chemical properties (Sect. 2.2.1), Toxicology (Sect. 2.2.2), and Human signs and symptoms (Sect. 2.2.3). The provided detail is adequate and relevant to the HRA. A search of current international reports and publications did not find any significant new information sources. The European Commission published an updated ‘CLH report - Proposal for Harmonised Classification and Labelling’ for Brodifacoum in 2013 but this does not contain significant new toxicological information.

A review of the toxicological profile of Brodifacoum as reported by Toxikos did not find any errors or omissions. Toxicokinetic studies indicate that Brodifacoum has almost complete oral absorption (range >75-100%) and is widely distributed, bioaccumulating mainly in the liver with lower concentrations in the kidney. Elimination from the liver is biphasic, with half-life in the range of 282-350 days. The excretion after oral administration is very slow (11–14% in 10 days), occurring via the

urine and the bile, both as polar metabolites (glucuronide) and parent compound. The metabolism of Brodifacoum is limited and the toxicologically relevant chemical species is the parent compound.

The Toxikos report identified the high acute toxicity of Brodifacoum with oral LD$_{50}$ in rats ranging from 0.17-0.9 mg/kg bw); slightly lower acute toxicity levels are reported for the inhalational (3.05 mg/kg bw, 4h) and dermal routes (3.16 – 7.48 mg/kg bw). Brodifacoum is not a skin or eye irritant. Brodifacoum showed no skin sensitizing potential in a LLNA study in mice, but did cause skin sensitization in guinea pig indicating that Brodifacoum has potential for skin sensitization and thus fulfils the EU criteria for classification as a skin sensitizer. The mode of action of Brodifacoum is unequivocally identified as impairment of the clotting cascade and increased prevalence of haemorrhage leading to death. Repeated dose oral studies show that in the rat and in the dog, the clinical signs, haematological and post mortem data were consistent with this mode of action and there are no indications of other secondary toxicities. Reports of human intoxication by Brodifacoum show toxic responses consistent with the animal studies. The dermal absorption value quoted in the Toxikos report (1.87%) requires a minor change as the recent EC report recommends a value of 5% for pellet/grain bait formulations.

Comment - The toxicological information provided in the Toxikos report is appropriate

**Dose response:** The Toxikos report identifies the following endpoints from the animal studies.

- **No Observed Effect Level (NOEL) for affecting prothrombin clotting time (PT)**
  - Rat – acute single oral dose, 0.15 mg/kg bw
  - Rat – 42 day feeding study, 0.005 mg/kg bw
  - Rat – 90 day feeding study, 0.001 mg/kg bw

- **Australian acceptable daily intake (ADI)** 0.0000005 mg/kg bw

Comment - These values are appropriate and supported by the available studies

**General comment on the risk assessment approach**

Although the approach taken by Toxikos is supportable and understandable in the absence of exposure information, a more conservative approach is recommended using Acceptable Exposure Levels (AELs) rather than NOELs to compare to the crude estimates of exposure. In brief, quantitative risk assessment normally relies on firstly identifying a critical effect for a threshold-based toxicant and secondly having reliable exposure data. Risk characterization then involves comparing the estimated/measured exposure to a derived Acceptable Exposure Level (AEL). The term AEL resembles the AOEL (Acceptable Operator Exposure Level) used in OHS risk assessments. The omission of the term operator underlines that the AEL is the reference value for the human body.

---

b ibid  
c ibid  
d Toxikos report, pg 15  
population as a whole. This is an analogous approach to deriving a Margin of Exposure (MOE) or Margin of Safety (MOS).

In brief, systemic AELs should be derived for acute, medium-term, and long-term exposure via all routes applicable, based on the systemic toxicity of the active substance using appropriate Assessment Factors (AFs). To derive an AEL, the selected NOEL is divided by the AFs to give the AEL. For Brodifacoum, the chosen endpoint is PT which is a threshold response, there are no complicating secondary toxic effects and there are available animal studies of different durations supported by human poisoning cases. The normal AF is 100 (10 fold for human variability, 10-fold for animal to human extrapolation). The literature suggests that humans are less sensitive than rats to Brodifacoum and the mode of action in both species is identical. The estimated average fatal dose for a 60 kg bw human male is 15 mg which using allometric scaling (¾ power) is equivalent to a dose to a rat of 1 mg/kg; as this is ca. 4 times the rat LD50 it appears that humans are indeed less sensitive to the acute toxicity of Brodifacoum and hence it is considered reasonable to remove the 10-fold AF for animal-human extrapolation. The retention of the 10-fold AF for human variability is a conservative approach allowing for the potential increased sensitivity of a young child when compared to an adult. The derived AEL is thus the NOEL/10. Using the NOELS listed above, the AELs for use in risk assessment are shown below.

<table>
<thead>
<tr>
<th>Study</th>
<th>NOEL mg/kg bw</th>
<th>AEL mg/kg bw</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat acute single oral dose</td>
<td>0.15</td>
<td>0.015</td>
</tr>
<tr>
<td>Rat 42 day feeding study</td>
<td>0.005</td>
<td>0.0005</td>
</tr>
<tr>
<td>Rat 90 day feeding study</td>
<td>0.001</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Exposure assessment: The Toxikos report presents a thorough and relevant discussion of the properties and fate of the applied bait in the environment. Section 2.3 ‘Properties of the rodent bait’ describes the physical properties of the intended bait formulation and its stability in soil and water; these are important considerations for the human exposure scenarios described and modelled in the report. In brief, Brodifacoum binds strongly to soil and doesn’t leach, it does not volatilise, it has very low water solubility and is fat soluble. These properties determine the relevance of the exposure scenarios discussed in Sect. 3 ‘Exposure and Risk’ in the Toxikos report.

Sect.3.1.1 Direct ingestion of bait is considered the most likely and important pathway. Toxikos identifies that a 2 year old child would have to consume 200 pellets all at once to reach the rat (and assumed human) acute toxicity NOEL of 0.15 mg/kg bw. If the child consumes smaller quantities each day for the possible 4-5 weeks the pellets are available, then to achieve the rat 42 day NOEL of 0.005 mg/kg bw, the child would have to consume 6-7 pellets per day. A recalculation using the AEL changes these estimates to 20 pellets/day for the single acute exposure and <1 pellet per day, every day, for the repeated exposure. These are conservative calculations and give a 10-fold safety margin when compared to the NOELs. As noted by Toxikos, while intoxication seems unlikely, the presence of an indicator dye in the bait which will stain lips and mouth, in conjunction with an education campaign and parental supervision will minimise risk from the direct ingestion of bait.

1 “Brodifacoum (HSG 93, 1995)”, Inchem.org
Notably, human studies have demonstrated the complete efficacy of antidote treatment (Vit K) for cases of human intoxication by Brodifacoum.

Sect. 3.1.2 Ingestion of soil (Pathway A3). Toxikos uses conservative assumptions of soil ingestion and soil concentration and estimates that a child might ingest 0.0000004 mg/kg bw/d of Brodifacoum. This is insignificant when compared to the 42-day AEL of 0.0005 mg/kg bw/d.

Sect. 3.1.3 Dermal exposure (Pathway A4). Toxikos uses conservative assumptions of soil contamination of the hands of a child and estimates that a child might absorb 0.00001 µg/kg bw/d. Applying the recommended 5% dermal absorption factor from the EC instead of 1.8%, the calculation yields 0.00003 µg/kg bw/d which is insignificant compared to the 42-day AEL of 0.5 µg/kg bw/d.

Sect. 3.1.4 Ingestion of water (Pathways B1 & B2). Using a conservative set of assumptions about bird defecation, dropping size and Brodifacoum concentration, Toxikos estimates that a child might ingest through drinking tank water 0.0008 µg/kg bw/d of Brodifacoum which is insignificant compared to the 42-day AEL of 0.5 µg/kg bw/d.

In a separate calculation for pellets dropped on roofs by birds, Toxikos calculates a child might absorb 0.06 µg/kg bw/d of Brodifacoum which is about 12% of the 42-day AEL of 0.5 µg/kg bw/d. As Toxikos states, this scenario is highly unlikely and of little concern to the risk manager.

Sect. 3.1.5 Consumption of fish (Pathway C). After a review of the available studies on fish consumption of Brodifacoum baits in the marine environment, Toxikos discusses the possible scenarios whereby humans could catch and eat fish that had eaten non-lethal amounts of particles from Pestoff 20R under the following headings:

- the probability that significant amounts of bait will find its way into the marine environment
- the probability that fish will consume the bait
- the probability that a fish which has consumed Brodifacoum bait will be caught by an angler
- the probability that caught fish contains high amounts of Brodifacoum in edible portions
- the probability that high amounts of fish will be consumed by an individual

All the assumptions in the analysis are conservative and appear reasonable. The estimated daily dose of Brodifacoum from high end consumption of fish is potentially estimated to be 0.0008 µg/kg bw/d which is insignificant compared to the 42-day AEL of 0.5 µg/kg bw/d.

Sect. 3.1.6 Consumption of vegetables (Pathways D1 & D2). Uptake into plants is considered to be negligible.

Sect. 3.1.7 Exposure via poultry (Pathway E). As noted in the report, this exposure pathway is incomplete.

Sect. 3.1.8 Meat and dairy products (E). As noted in the report, this exposure pathway is incomplete.

Sect. 3.1.9 Goat produce (Pathway G). As noted in the report, this exposure pathway is incomplete.

Sect. 3.1.10 Consumption of wild ducks (Pathway H). As noted in the report, this exposure pathway is incomplete.
Sect. 3.1.11 Dust inhalation during aerial baiting (Pathway I). This is a potentially important pathway for human exposure as inhaled Brodifacoum is assumed to be 100% absorbed. A series of assumptions based on trial applications is presented to allow for calculation of exposure. e.g. bait is dropped from 50 m height along an 80 m swathe (at the rate of 12 kg/hectare. Dust generation during loading and dispersion is estimated at 500 g per 25 kg of bait. A reasonable assumption is made that up to 25% of the dust may be inhalable yielding 125 g of inhalable dust per 25 kg of bait. The 4 kg of bait released over a 40 m length will thus yield 20 g of inhalable particles. The 2 year old receptor is then assumed to be in the impacted zone for 8 hours, breathing suspended particulates which remain suspended for the entire exposure time; these are very conservative assumptions. Toxikos then calculates the concentration in air as:

\[
\frac{20 \text{ g}}{160,000 \text{ m}^3} = 0.000125 \text{ g/m}^3, \text{ not } 0.125 \text{ g/m}^3 \text{ as reported by Toxikos.}
\]

Pellets contain 20 µg Brodifacoum/g of pellets hence 125 µg/m³ of pellet dust contains 0.0025 µg Brodifacoum/m³.

Comment – a 1000 fold error occurs in the Toxikos calculations.

Toxikos quotes an occupational exposure limit for Brodifacoum as 2 µg/m³ (8 h TWA) (Syngenta 2006 MSDS). No alternative occupational exposure limits were found. The estimated exposure (0.0025 µg Brodifacoum/m³) is thus 800 times less than the only published OHS limit of 2 µg/m³.

Using the assumptions in the Toxikos report and the correct value for Brodifacoum concentration in air, the estimated exposure to a 2-3 year old child would be 0.0006 µg Brodifacoum/kg bw/d. This is 25000 times less than the acute AEL of 0.015 mg/kg bw.

Comment: Toxikos concludes that the risk to human health from the inhalation pathway is insignificant, and despite the 1000-fold error in one of the Toxikos calculations the conclusion is considered correct.

Conclusion: The Toxikos report is a comprehensive scoping human health risk assessment for the proposed Lord Howe Island rodent eradication plan. The basic methodology is sound although this reviewer would prefer exposure estimates to be compared to AELs rather than NOELs. There is little available information to update this assessment other than a revision of the dermal absorption factor. The analysis of the toxicology data otherwise remains sound and well utilised. The exposure scenarios used are complete and the assumptions used in the exposure calculations are uniformly conservative. The only significant pathway of potential human exposure during the application of Brodifacoum is the oral pathway through ingestion of pellets, as identified by the Toxikos report. The risk management procedures proposed for the program, especially the education program for parents, will mitigate this risk. The conclusions of the Toxikos report are sound and the recommendations should remain unchanged.
Recent publication

Bryce M. Masuda, Penny Fisher, Brent Beaven Ecotoxicology and Environmental Safety Volume 113, March 2015, Pages 1–8

The second-generation anticoagulant rodenticide brodifacoum is an effective tool for the eradication of invasive rodents from islands and fenced sanctuaries, for biodiversity restoration. However, broadcast application of brodifacoum bait on islands may expose non-target wildlife in coastal marine environments to brodifacoum, with subsequent secondary exposure risk for humans if such marine wildlife is harvested for consumption. We report a case study of monitoring selected marine species following aerial application of brodifacoum bait in August 2011 to eradicate Norway rats (Rattus norvegicus) from Ulva Island, New Zealand. Residual concentrations of brodifacoum were detected in 3 of 10 species of coastal fish or shellfish sampled 43–176 d after bait application commenced. Residual brodifacoum concentrations were found in liver, but not muscle tissue, of 2 of 24 samples of blue cod (0.026 and 0.092 µg/g; Parapercis colias) captured live then euthanized for tissue sampling. Residual brodifacoum concentrations were also found in whole-body samples of 4 of 24 mussels (range=0.001–0.022 µg/g, n=4; Mytilus edulis) and 4 of 24 limpets (range=0.001–0.016 µg/g, n=4; Cellana ornata). Measured residue concentrations in all three species were assessed as unlikely to have eventually caused mortality of the sampled individuals. We also conducted a literature review and determined that in eleven previous accounts of residue examination of coastal marine species following aerial applications of brodifacoum bait, including our results from Ulva Island, the overall rate of residue detection was 5.6% for marine invertebrates (11 of 196 samples tested) and 3.1% for fish (2 of 65 samples tested). Furthermore, our results from Ulva Island are the first known detection of brodifacoum residue in fish liver following an aerial application of brodifacoum bait. Although our findings confirm the potential for coastal marine wildlife to be exposed to brodifacoum following island rodent eradications using aerial bait application, the risk of mortality to exposed individual fish or shellfish appears very low. There is also a very low risk of adverse effects on humans that consume fish or shellfish containing residual concentrations in the ranges reported here. Furthermore, any brodifacoum residues that occur in marine wildlife decline to below detectable concentrations over a period of weeks. Thus potential human exposure to brodifacoum through consumption of marine wildlife containing residual brodifacoum could be minimized by defining ‘no take’ periods for harvest following bait application and regular monitoring to confirm the absence of detectable residues in relevant marine wildlife.
3.2 Response to issues raised by Mr Ratheburger

In your last email you provided a copy letter from former chairman Alistair Henchman which advised that the dust levels from Pestoff20R were 0.6%, countering my stating that the dust levels were of the level of 2% going up to 5% after exiting the aerial distributing arm on the helicopter.

I said I would go back into my ‘bunker’ to check this as I had recalled a verbal statement that it was indeed of the level of 5%, and went to look for any written record…….alas I found none, but I did find the overheads Dr Wilkinson had shown where the level of dust sampled from trials in NZ was 1.8%, with a ‘rider’ to say most were 0.8%….a very strange ‘rider’, but never mentioned the 0.6% suggested by Mr Henchman.

Anyway in the absence of evidence I will concede the figures of Dr Wilkinson, although there has been a lot of water-under-the-bridge since, yes?

In the course of my going through my hardcopy and computer files looking for the information I came across my Letter-to-the-Editor, No.6 dated 28/8/2008, not sure what Signal edition it was published in, in which I state that the level of dust would exceed the permissible levels for industrial dusts by many-fold, like 43.2 times. Wilkinson in his overheads had shown, we have hard copy, the standard for toxic dusts as 0.0005mg/litre which translates into 0.5mg/m3 for a 4 hour exposure, yet he stated that the fallout of dust particles over Lord Howe Island would be 216g/ha or 21.6 mg/m3, which is 43.2 times the safe limit. Wilkinson talks about the level of brodifacoum in the dust, well toxic dust is toxic dust and the authorities do not adjust, without specific knowledge, the criteria between one toxic dust and another for reasons of simplicity, not knowing the relative toxic intensities of the toxins included in the dust particles. For example we know that the same mass of warfarin and brodifacoum enclosed in the same sized dust particles will have extraordinarily different levels of toxicity…..for brodifacoum is at least 200 times more toxic than warfarin. See further clarification below.

I also looked into the Toxikos Report and analysed the data in Section 4., Existing risk from commercial rodent bait. It is on page 47. Interestingly it states in the first para. ‘With warfarin the risk is considerably lower than with brodifacoum baits because it is more rapidly cleared from the body…….’…..This is one of the points we have been making about brodifacoum and its potential adverse impact on the human body, is the residual time it remains in the body, first thought to be 9 months and now 24 months, and likely for considerably longer as scientific detecting equipment is capable of detecting smaller and smaller levels of contamination.

Comment: In humans, the half-life of Brodifacoum in plasma is about a month while in liver it is about a year. Nanogram quantities detected by improved analytic techniques are not relevant to the toxicologically significant concentrations.

Anyway back to the ‘figures’ in the Toxikos Report, and Section 3.1.11. Dust inhalation during aerial baiting. It starts on page 44. It discusses, as the title states the ingestion of dust particles in a given ‘corridor’ along which the helicopter might traverse, releasing 12kg per ha(10,000m2) in the first campaign and 8kg per ha in the second campaign, and in the sample swath 4kg of bait would be dropped.

The amount of dust in the sample according to Torr and Agnew in 2007, as the Toxikos Report says, found there was 130-150 g of fine material in a 25kg bag of bait as delivered. Using abrasive tests etc., they determined that the amount of fines produced from different designed distribution hoppers would range from 50g to 330g per bag, and the maximum amount of fines in the supplied
bait and potentially generated by dispersion machinery would approximate 500g per 25kg of bait, that is 2%.

The amount of inhalable particles as determined by the scientists, Torr and Agnew is admitted by Toxikos as unknown ??, but then in the absence of data, Toxikos assumed that 25% may be inhalable, ie 25% of the 2%, or 125gm of the 25kg bag.

Therefore of the 4kg of bait dropped in the ‘corridor’, there would be 20g of inhalable material(dust)……..or given the speculation above, it could be 40g or even 60g, but we’ll go with 20g.

Now the above inhalable material would be contained in the corridor ‘volume’ of 80m x 40m x50m or 160,000m³, and Toxikos determined by deduction, 20g divided by 160,000m³ would be 0.000125g/m³…which they erroneously further translate as 0.125mcg/m³(mcg = microgram, ie., a millionth of a gram). The translation more correctly should have been either 0.125mg/m³(mg = milligram, ie., a thousandth of a gram) or 125mcg/m³. Yes, indeed, it all can be very confusing.

Comment: this observation is correct, there is a 1000-fold error in the calculations. However this has importance only for the calculation of inhalational exposure. The margin of exposure is sufficiently large that reducing it by a 1000-fold does not change the conclusion that this exposure pathway is insignificant.

Toxikos goes on to then determine the actual amount of brodifacoum in the dust, as being 0.0000025mcgB/m³, the ‘B’ meaning brodifacoum…..but in fact being ‘out’ by a factor of one thousand, the level is 0.0025mcgB/m³, an acceptable exposure according to Toxikos, BUT in accordance with the regulations of dust measurement it is the dust particle itself that is measured, not the amount of toxin within, as mentioned above. See further clarification below.

Toxikos relate the occupational standard limit of exposure to protect workers from the effects of brodifacoum during manufacture of the rodent bait as 2mcg/m³, giving a reference to Syngenta 2006, indeed the manufacturers of Talon, so it is its own standard.

Therefore by more correct analysis of the ‘accepted’ earlier assumptions, the amount of exposure in the corridor would be 125mcg/m³ of dust containing brodifacoum and with the manufacturer of Talon’s self-imposed regulation as 2mcg/m³, it is 60 times greater, and this correlates to my work in the Letter-to-the-Editor on 28.8.’08, which spoke of us residents being exposed to 43.2 times above the permissible limit for toxic dust exposure levels, working off data provided by Dr Wilkinson. I quote again from my above ‘letter’, ‘Dr Wilkinson produced data on Toxic Dusts and expressed that the acceptable safe limit was 0.5mg/m³. The toxic dust fallout he projected for Pestoff 20R would be 216gm/hectare(in a 10cm thick band) and this would then, from our maths, translate into a dust density of 21.6mg/m³, which is 43.2 times greater than this safe limit.

Dr Wilkinson was talking, as the standard states in terms of toxic dusts, that is, of the dust (containing brodifacoum) in Pestoff20R bait.. Now, as indeed Toxikos did, he went on to discount the dust level relative to the amount of actual brodifacoum contained, however that is not the way to apply the regulation.

Indeed the following extract from the Australian workplace ‘Guidance on the Interpretation of Workplace Exposure Standards for Airborne Contaminants’, see the link below, clarifies the issue on page 19 under INHALABLE DUST; ‘Inhalable dusts that are toxic have an exposure standard based upon the substance of concern. Where the toxic component of the dust is measured, this is satisfactory as long as the exposure standard for dusts not otherwise classified is not exceeded.’ In
other words the discounting of the dust hazard to the level of brodifacoum contained in the dust is WRONG.

Comment: The above interpretation of the Workplace Exposure Standards is misguided. It is the contaminant level in the dust that drives the risk management not the concept of ‘toxic dust’.

Safe Work Australia Guidance on the Interpretation of Workplace Exposure Standards for Airborne Contaminants recommends that “Where no specific exposure standard has been assigned and the substance is both of inherently low toxicity and free from toxic impurities, exposure to dusts should be maintained below 10 mg/m³, measured as inhalable dust (8 hour TWA).” There are workplace exposure standards (WESs) for the various components of dust, such as respirable crystalline silica, and dusts and fumes containing toxins, such as lead.

This 10 mg/m³ is the upper limit for ‘Dust, not otherwise specified’. Where there is a contaminant such as crystalline silica or lead or Brodifacoum, then a WES can be developed for that contaminant and this value drives the monitoring and risk management as long as the total dust level does not exceed 10 mg/m³.

The text below from SWA (pg 26) clearly indicates that the concentration of the toxic substance is the driving factor for the risk assessment.

‘Where no specific exposure standard has been assigned and the substance is both of inherently low toxicity and free from toxic impurities, exposure to dusts should be maintained below 10 mg/m³, measured as inhalable dust (8-hour TWA). However, the exposure standard for dusts not otherwise classified should not be applied where the particulate material contains other substances which may be toxic or cause physiological impairment at lower concentrations. In these circumstances, the exposure standard for the more toxic substance should be applied. For example, where a dust contains asbestos or crystalline silica, like quartz, cristobalite or tridymite, exposure to these materials should not exceed the appropriate value for these substances.’

e.g. with respect to the eradication plan, the total dust level from the helicopter pellet drop is expected to be 0.125 mg/m³ - this is well below the 10 mg/m³ general standard. The calculated concentration of Brodifacoum in the dust is 0.0025 µg/m³ and this is well below the adopted WES of 2 µg/m³.

As said, I have accepted Toxikos’ assumptions of the amount of ‘fines’ contained in the distributed bait, for I have no other information to go by, but given even that, rather than its incorrect analysis giving ‘clearance’ to the air conditions above us during the ‘drops’, a correction of its mathematics shows our exposure to be 60 times the occupational health regulations, and then not to mention


ibid
that the workers in the manufacturing plant would likely have breathing regulators and full body coverage during manufacturing and packaging of the pesticide, Pestoff20R.

As said earlier, I had not made a specific hand note of the 5% dust level of which I had ‘heard’, so I have accepted Toxikos’s figures of 2%, but then at that level of 2%, the exposure of us residents under the corridor would be 60 times the maximum occupational health levels, which would suggest any wind-shear would be quite detrimental to our health only 40m away and certainly all the birds under and around the drop zones. . . . . just from inhalation, and not including additional fallout on birds feathers, our hair and skin, crops, grass etc.

And as I acknowledged to your concern in my recent email, where I said, ‘I appreciate your acknowledgement of the high toxicity of brodifacoum-based products, in your concern for inhaling dust within less than 1 meter of the open packet of Talon . . . . , but hardly would handling a packet of Talon compare to the much greater exposure from Pestoff20R dust floating down on us from aerial baiting.’

For all the ‘clearance’ Toxikos gave to the eradication programme, albeit a very limited study in our opinion, from the Toxikos Report, page 9, the Recommendations state, we quote;

‘Recommendations:

- All mitigation measures as outlined in the draft Lord Howe Island Rodent Eradication Plan should be implemented to minimise risks posed by use of rodent bait during the programme.

- As a precautionary measure it would be prudent to advise islanders not to consume the livers of fish that have been caught within 200m of the shoreline until 6 months after the last bait broadcast.

- Although there is negligible health risk from drinking tank water during the eradication campaign, for peace of islander’s mind, consideration could be given to a programme of strategic testing of tank water.

- It would be prudent to advise those individuals involved with the control of non-native duck populations that they should not consume duck during the eradication programme, and not the liver for perhaps a year after the programme has ceased.’

These words seem to convey a lot of unassuredness on the part of Toxikos. I have always contended that their brief should have included micro-studies of the human reproductive organs, endocrinological studies, and specific studies on the likely impact on the brains of the very young, of such a powerful toxin as brodifacoum.

Comment: No effect has been demonstrated with technical brodifacoum in long term carcinogenicity tests. Studies in rats and rabbits have demonstrated no fetotoxic, embryotoxic or teratogenic effects. Further, the Australian dust regulators web site, http://www.safeworkaustralia.gov.au/sites/SWA/about/Publications/Documents/680/Guidance_Interpretation_Workplace_Exposure_Standards_Airborne_Contaminants%20.pdf, on page 11, section 4.2

\[1\] World Health Organization/International Programme on Chemical Safety; Poisons Information Monographs 77 Brodifacoum pp.1-22 (1990)\]
Skin Absorption, refers to the greater implications of toxins which are absorbed into the skin, as distinct from inhalation. We all know that brodifacoum whilst it slowly dissolves in water, is readily dissolved in our body oils and fats, therefore our skin, yet neither Wilkinson nor Toxikos examined the implications of absorption in their respective studies.....a potentially tragic oversight.

Comment: The dermal absorption of Brodifacoum has been considered in the HRA. Toxikos suggests 1.8% while the very conservative value of 5% for the pellet formulation has been used in the current review of the HRA. The dermal pathway leads to insignificant systemic absorption irrespective of which value is used.

Hank, it’s just simply NOT WORTH THE RISK on our INHABITED island.

Rob Rathgeber.
