Genetically induced chronic low-level methaemoglobinaemia in humans can be treated with oral methylene blue daily. Also, vitamin C can occasionally reduce cyanosis associated with chronic methaemoglobinaemia but has no role in treatment of acute acquired methaemoglobinaemia.

### Can sodium nitrite cause sub-lethal effects?

Sodium nitrite, like any other poison, has the potential to cause sub-lethal effects if exposure occurs above certain levels.

Researchers and workers in the pest control industry are the only people likely to be exposed to sodium nitrite levels of potential risk. The broader community is protected from exposure at those levels due to strict controls on the use and handling of sodium nitrite. Safety standards are in place to prevent worker exposure and sub-lethal effects.

Ingestion of sub-lethal doses of sodium nitrite could over time result in genetic defects or adverse effects to organs (blood system). Nevertheless there is a low risk in terms of sub-lethal effects in workers.

To test this mice and rats have been dosed with nitrite. None of 21 studies in mice and rats concerning the possible carcinogenicity of nitrite indicated any carcinogenic effect. Studies with mice given nitrite (up to 1 g/L) in drinking water gave no evidence for teratogenic effects on their foetuses.

Exposure even to workers involved in the pest control industry is far more likely to occur from naturally occurring nitrite in the environment or nitrite in food than it is from baits, provided safety precautions are followed.

### What is the risk to livestock?

Sodium nitrite at the high doses used in baits in bait stations could be toxic to livestock, so farm stock must be kept out of areas where poisons are used for pest control until the risk of poisoning has passed.

Cattle with a larger body weight, e.g. 200 kg, would need to ingest a greater quantity, e.g. 150 to 200 g bait.

Sub-lethal doses of sodium nitrite are eliminated from the tissue of animals that survive accidental exposure within one to two days.

### What is the risk to dogs?

Dogs are vulnerable to sodium nitrite in baits and must be kept out of areas were sodium nitrite baits are being used. If this is not possible, dogs should be kept under control and muzzled until signage states the area is safe.

Small dogs (3 to 4 kg) could conceivably ingest a toxic dose of sodium nitrite from 1.8 g of the bait (sodium nitrite at 100 g/kg), 30-40 kg weight dogs would need to ingest 18 g of bait.

They are may be exposed by scavenging possums that have been killed by sodium nitrite.

It can take up to six months for possum carcasses to degrade, and even longer in cold or dry conditions. However the secondary poisoning risk to dogs from sodium nitrite is much less than that from other toxins. In a moist acidic stomach, nitrite is broken down to nitrogen oxides, including nitric oxide.

### What is the risk to deer or feral pigs when undertaking possum control?

Large amounts of bait in the order to 200 to 300 gm will be needed to kill deer or feral pigs. It is possible that deer or feral pigs could be killed if one animal ate all the bait in a bait station intended for possums but if bait stations are placed well above ground this risk will be reduced.

### What is the risk to birds?

The risk to birds is being evaluated and compared with other toxins as part of the research process.

For sodium nitrite early research indicates that a similar or slightly greater amount of paste bait, when compared to 1080, could be lethal to a 1kg bird. However sodium nitrite bait has to be eaten quickly to cause death in birds due to its lower toxicity, hence the risk should be lower. The bait is coloured green as a deterrent to birds and used in a matrix that is already used commercially in other bait products.

Risk to birds such as hawks and weka scavenging carcasses should be low given the rapid elimination of sodium nitrite by excretion in the target species and further breakdown in carcasses following death, and also because a large bolus dose is needed to induce toxicity.

What is the risk to other species?

Invertebrates are unlikely to be affected. Further research on all non-target species including reptiles is being planned.

### **USEFUL CONTACTS**

Who to contact for more information?

- For information about the control of bovine TB, contact the Animal Health Board: phone 0800 4824 636 (or 0800 4 TB INFO)
- The National Possum Control Agencies (NPCA) can also help with information: phone (04) 499 7559 or email npca@xtra.co.nz
- Connovation Ltd can be contacted at 09 215 4345

CONNOVATION

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# Answers to commonly asked questions on sodium nitrite

### THE POSSUM PROBLEM AND SODIUM NITRITE

Possums adversely affect the farming economy and threaten the survival of many of our endangered plant and animal species. New Zealand needs the most effective possum control programmes possible.

This short publication provides answers to commonly-asked questions about sodium nitrite in the context of it being developed as a poison for possum control.

It is intended to assist those wanting to assess for themselves the benefits and risks associated with the potential use of sodium nitrite for possum control in New Zealand.

### THE POSSUM PROBLEM

### Why are possums such a problem in New Zealand?

Possums are eating the canopy of native forests, causing them to collapse. They preferentially feed on some of the tall canopy species such as tawa, rata, kohekohe, kamahi, and totara. Possums also threaten particular plant species and present a threat to bird life by destroying their habitat and food sources, and preying on eggs and chicks of native birds like the kiwi, kokako and kereru.

Possums are also the main source of bovine tuberculosis (TB) in cattle and deer herds and threaten our meat export industry. Even though other pest animals such as ferrets and wild deer can also spread TB, possums are the main self-sustaining reservoir of the disease in the wild. Bovine TB is a major threat to our economy because New Zealand could be prevented from exporting beef, venison and dairy products to some prime markets.

Possum control is being carried out throughout New Zealand using a range of trapping and poisoning techniques. In common with related work on traps, the strongest focuses for current toxin research are animal welfare; cost –effectiveness; and safety, with one aim being to increase the humaneness of control tools used to kill unwanted introduced animal pests. The Animal Health Board in Wellington has supported researchers at Connovation Ltd and Lincoln University to explore the potential of sodium nitrite for possum control and Auckland Regional Council has supported its development for feral pig control. Feral pigs have been recently linked to the spread of Kauri die-back disease.

### **ABOUT SODIUM NITRITE**

#### What is sodium nitrite?

Sodium nitrite is a compound that has been developed for killing introduced mammalian pests. The risks and benefits of sodium nitrite use for control of introduced mammals were reviewed by the NZ Environmental Protection Authority (EPA) and the ACVM group in MPI in 2010/11.

Following a public hearing in 2013 the EPA approved sodium nitrite for use in bait for the control of possum and feral pigs. Full registration by the ACVM group in MPI is anticipated early in 2014.

Research to examine the potential of sodium nitrite as an additional tool for possum control and feral pigs control included laboratory, pen and field trials to validate its safety and effectiveness, and define its niche in the pest control toolbox.

Sodium nitrite is an inorganic compound with the chemical formula NaNO2. It is a white to slightly yellowish crystalline powder that is very soluble in water.

It is also found at low concentrations in most vegetables. Spinach and lettuce can have some of the highest concentrations but all vegetables will contain some levels of sodium nitrite. It has been explored in human and veterinary medicines as a vasodilator, reducing blood pressure, and is also used as an antidote for cyanide poisoning.

Its major use is as a preservative in meats and fish, and will be found on the ingredients list of preserved meats such as salami. As a food additive, it prevents growth of Clostridium botulinum, the bacterium which causes botulism.

While it prevents the growth of bacteria, it can be toxic in high amounts to animals, including humans. An adult would need to eat a teaspoonful of sodium nitrite powder to cause death.

### How does sodium nitrite work?

Toxic doses of sodium nitrite cause excessive methaemoglobinaemia which prevents the red cells in the blood carrying oxygen to tissues. Once ingested, at a toxic correct dose, affected possums quickly become lethargic and unconscious before death.

Sodium nitrite has been developed in New Zealand on the platform of para-aminopropiophenone (PAPP) which has the same mode of action and the same antidote as sodium nitrite. PAPP is registered for stoats and feral cats and is not toxic to possums; hence the complementary development of a bait containing sodium nitrite.

# Questions & Answers on Sodium Nitrite

December 2013

### What is methaemoglobinaemia?

Methaemoglobinaemia is a disorder characterized by the presence of a higher than normal level of methaemoglobin in the blood. It is a form of haemoglobin in red blood cells that has a decreased affinity for oxygen. When methaemoglobin concentration is elevated in red blood cells, tissue hypoxia (lack of oxygen to tissue) can occur.

Normally, methaemoglobin levels are <1%. Some drugs such as local anaesthetics can cause methaemoglobinaemia and it can also be inherited, and these individuals will have levels higher than 1%.

Symptoms are proportional to the methaemoglobin concentration in the blood and include skin colour changes (with blue or greyish pigmentation) and blood colour changes (brown or chocolate colour) at methaemoglobin levels up to 15%. Moderate methaemoglobinaemia (< 30 % of total haemoglobin oxidised) causes discomfort (e.g. headache) with severe methaemoglobinaemia (> 50 %) being possibly life threatening. Levels of methaemoglobin above 70% in the blood are usually fatal.

### How is sodium nitrite used for possum control in current trials?

Sodium nitrite has a bitter taste so it has to be encapsulated before possums and pigs will eat it. It has been shown to be effective at killing captive possums and pigs when mixed into cereal and paste baits at 10%.

Research has focused on sodium nitrite use in ground control operations where baits are put into covered bait stations using standard ground baiting methods. Bait stations for possums, as an example, would be laid in a grid of approximately 80 per 100 hectares and set up at 100 m intervals on lines paced 150 m apart in areas where vegetation is sparse and 100 m apart in areas of thicker scrub. Pre-feeding with non-toxic bait in the bait stations is important. This involves the placement of approximately 200 g of non-toxic paste bait in each station. Pre-feed baiting would typically be carried out three times a week for two to three weeks before toxic baiting. Then the toxic bait, in quantities of 100-200 g of bait dependent on the density of possums present (higher quantities would be used in areas with higher densities), would be placed in each bait station and toxic bait "take" checked and replenished if needed.

For feral pig baiting a specially designed bait stations has been developed, with a lid that excludes non-target species. Toxic bait balls are placed in the bait station following prefeeding.

A solid grain based bait, also consisting of 10% MSN and weighing approximately 15 g each, is also being developed.

### What are the target species for sodium nitrite?

Sodium nitrite is not sufficiently toxic to kill rodents.

The more common proposed use of the new sodium nitrite bait will be for possum control, delivered from bait stations where possum are the main target or where rodents have been controlled by other toxins such as diphacinone.

A less common discrete use may be the targeting of unwanted feral pigs that for whatever reason are difficult to hunt and shoot or kill by "dogging". Toxin bait is only likely to be used for pig control where shooting and dogging is not easily undertaken and where farmers are having problems controlling pigs on their farms or where conservation programmes are underway.

### Why use sodium nitrite?

In large, remote and rugged areas of countryside, where access for ground-based control is difficult, aerial application of pesticide is the most effective way to control possums. At present sodium fluoroacetate (1080) is the only pesticide licensed for aerial distribution on the mainland. Solid bait containing sodium nitrite could be used in some situations, but it needs to be proven to be effective in ground control operations first, and it will take several years to assemble the data required for registration of sodium nitrite bait for aerial use.

In ground control operations, sodium nitrite has the potential to be one of many tools that can be used, and to be integrated with 1080, cyanide, cholecalciferol, anticoagulants and traps. The choice of which poison, trap and bait to use is based on a range of factors including the non-target species in the area, community interest, cost and weather, and whether possums may be 'bait shy' from earlier control activities in the area.

Possums killed by eating sodium nitrite baits are less likely to cause secondary poisoning of dogs. In addition sodium nitrite has an antidote. Use of sodium nitrite baits on or adjacent to farmland where working dogs are present will have advantages.

Sodium nitrite is the only toxin registered for the control of feral pigs.

### What are the welfare implications of using sodium nitrite?

One of the drivers for developing sodium nitrite has been animal welfare. A humane death has been identified as a very important aspect and is a key to the effectiveness of sodium nitrite bait for possum and pig control).

When delivered at a lethal dose, rapid induction of high levels of methaemoglobin quickly induces death with minimal symptoms of distress.

Research has shown the symptoms of poisoning are similar in both pigs and possums. The onset of symptoms of poisoning and time to death are relatively swift in comparison to other toxins. The sequence of behavioural changes in animals is consistent with our understanding of the toxicology of sodium nitrite, namely that the compound is rapidly absorbed and quickly induces methaemoglobinaemia.

In sub-lethally dosed animals there was prompt recovery from sub-lethal poisoning which is consistent with a compound that has a plasma elimination half–life of less than one hour in most animals.

### Are there restrictions on the use of sodium nitrite?

Sodium nitrite for possum and pig control is to be treated as a controlled substance. There are comprehensive and rigorous regulations and operating procedures that govern its use in New Zealand. It is managed in compliance with 1996 Hazardous Substances and New Organisms Act (HSNO) regulations, which cover packaging, transport, exposure limits (from workplace to environment) disposal, emergency management, record keeping to track all sodium nitrite containing baits and labelling.

Possum control operations using sodium nitrite may require Medical Officer of Health approval. Local authorities may require that resource consent be obtained under the Resource Management Act as for 1080 application, particularly if it is further developed for aerial use.

The Animal Health Board, Department of Conservation and pest control professionals also have strict codes of practice covering operating procedures that incorporate their experience in risk management and best practice built up over four decades of using toxins in New Zealand. The Department of Conservation has also produced a comprehensive 'Quality Conservation Management' system for all its pest control operations, to ensure high operational standards.

The Department of Conservation's consent is required for all pesticide operations on lands administered by the Department, and regional councils closely monitor all operations.

## Do other countries use sodium nitrite for animal pest control?

Sodium nitrite is being researched and registered for use in Australia. In Australia it is being developed as an additional feral pig active.

### Does sodium nitrite persist or accumulate in the soil?

Sodium nitrite is highly water–soluble. This means that if any bait falls out of a bait station the sodium nitrite will be easily leached into the soil by rain. Any sodium nitrite leaching from uneaten baits is broken down into non-toxic naturally occurring substances. Consequently, sodium nitrite does not accumulate in the soil, as some pesticides do.

Ammonia, nitrite and nitrate are the common ionic forms of inorganic nitrogen in ecosystems. These ions can be present naturally, as part of the nitrogen cycle, as a result of atmospheric deposition, nitrogen fixation by bacteria and biological decay of organic matter. Hence nitrite occurs naturally in soil and putrefaction processes caused by oxygen-free conditions convert nitrites in soil into nitrogen gas or into gaseous compounds such as nitrous oxide or nitric oxide. In addition bacteria of the genus Nitrobacter oxidise nitrites to nitrates, which are reduced to nitrogen by anaerobic bacteria in soil and sediment.

The amount of sodium nitrite used in baits should not impact on background naturally occurring levels in the environment. Sodium nitrite is reported to be photo-oxidised with a half-life of 82.3 days.

### Will sodium nitrite pollute water supplies?

Sodium nitrite is initially being developed for use in bait stations. Baits will be placed in the stations away from waterways so contamination is most unlikely.

A large amount of research and monitoring has also been undertaken to answer this question with regard to 1080, and 1080 and sodium nitrite will be similar with regard to solubility and leaching characteristics; hence research on 1080 is relevant.

Between 1990 and 2012 water was monitored for 1080 residues following large-scale control operations, each using aerially sown 1080 baits. Most of the samples contained no detectable 1080. Trace amounts of 1080 were found in approx 3.5% of the water samples tested but, in most of these, the 1080 was below the two parts per billion maximum level recommended by the Ministry of Health for drinking water.

If sodium nitrite were used in aerial application significant contamination of waterways from this source would be most unlikely because of the small amounts used.

If bait were to enter waterways, algae, bacteria and hydrolysis will all play a role in the breakdown of nitrites.

First, the salt sodium nitrite dissociates liberating nitrous oxide. The NO2 reacts with water. Being the conjugate of a weak acid, the nitrite ions will accept a proton from water to form nitrous acid (weak) and hydroxide ions (basic).

This is the net ionic equation for the hydrolysis of sodium nitrite.

### How toxic is sodium nitrite to humans?

The Acceptable Daily Intake for nitrite is for up to 0.07 mg/kg/day. The sodium nitrite food standard limit for processed meat is < 500 mg/kg.

The oral lethal dose for humans has been estimated to vary from 33 to 250 mg nitrite/kg.

Sodium nitrite has the potential to kill and cause sub-lethal effects in humans; the organs most affected would be those with high oxygen demands such as the brain and the heart. A 15-kg child would have to eat about  $\frac{1}{2}$  gm of sodium nitrite powder or 5 gm of bait to get a lethal dose. An 80-kg adult would have to eat 2.6 gm sodium nitrite powder or 26 gms of baits to receive a lethal dose.

It is very important that young children are kept away from bait stations and from bait. Hence baits must be used in appropriately designed bait stations and located with limited access (i.e. up off ground) thereby limiting access to young children and small animals. As with all other toxic baiting practice bait should be placed in such a way and with appropriate signage to prevent access.

As explained above, human exposure to dangerous levels of sodium nitrite from drinking contaminated water is most unlikely.

Sodium nitrite at sub-lethal doses is known to be rapidly eliminated by different animals. Should there be exposure (by ingestion) to the bait, then elimination of sodium nitrite residue would probably occur within 12 hours at worst, and most likely within 1-6 hours of any game species or livestock ingesting a sub-lethal amount of bait. There would be no risk or negligible risk of procurement of contaminated game meat which might be harvested at a later date.

### What are the symptoms of sodium nitrite poisoning?

The current acceptable amount of nitrite in the daily human diet is up to 0.06 mg of nitrite per kg of body weight per day. For a person weighing 70 kg, this would be about 4.2 mg per day. In instances where human overexposure to sodium nitrite is suspected, the symptoms would include a fall in blood pressure and methaemoglobinemia, difficulty breathing and weakness. If poisoning is suspected or medical advice is needed, have a product label at hand and call the NATIONAL POISON CENTRE [0800 764 766] or a doctor.

## What is the treatment for sodium nitrite poisoning?

Methaemoglobinaemia can be treated with supplemental oxygen and methylene blue. A 1-2% solution (1-2gm/100 ml) can be administered at 1 to 2 mg/kg intravenously slowly over five minutes followed by an intravenous flush with normal saline. This may need to be repeated in severe cases. Methylene blue restores the iron in haemoglobin to its normal (reduced) oxygen-carrying state.

Cases of nitrite poisoning in dogs and cats have been treated successfully with methylene blue. For cats a single dose of 1.5 mg/kg has been found to be safe and effective in reversing methaemoglobinaemia.