

# Treatment Options for wombats with Mange- Second report from the Wombat Protection Society of Australia Mange Clearing House

The current paper reviews and critiques information about acaricides that have been used or could potentially be used to remove the mite *s.scabiei* from naturally reared free wombats. The means by which these conclusions are reached are contained in the body of the paper. 10 per cent Sulphur in oil, self applied by the wombat via a distribution device hung over burrows rates as the method which best meets the criteria set down in paper number one.

The first report into Mange researched available literature, critiqued existing studies and looked at impediments to action. Its' main conclusions are contained in the summary given below.

- 1.Sarcoptic mange is caused by a mite that can be easily eradicated using a variety of acaricides. These acaricides exist naturally, eg; sulphur, lemon juice, eucalyptus/tea tree oil or are synthesised eg; ivermectin, selamectin, benzyl benzoate, and used in commercially registered products eg; revolution, ivomec or cydectin, amongst others.
- 2.The intensity of mite infestation correlates with the severity of clinical signs seen in infested animals.
- 3.If left, in general, sarcoptic mange progresses, mites increase incrementally and the affected wombat dies. We know this death is slow and painful and avoidable.
- 4.The death of an heavily infested wombat in its burrow, if shared with another wombat, is the most likely means by which an intense load of mites will be transferred to another wombat, sufficient, irrespective of previous contact to the mite and possibility of immunity, to cause sarcoptic mange in that animal.
- 5.Mites do not live long off their host and burrows, even if infested via the death of a wombat from sarcoptic mange , will be mite free within three weeks. Leaving wombats with sarcoptic mange to die is unethical and likely to lead to more wombats dying from mange.
- 6.Treating wombats with early stages of clinical signs will lead to complete resolution of mange and the wombat will be healthy and not more likely to become reinfested, probably less so.

From what we know, we recommend;

1. Action to eradicate mange in wombats should be taken.
2. Wombats with clinical signs of mange should be treated with an acaricide.
3. Wombats with severe mange should be targeted for treatment and need, in addition to acaricidal treatment, antibiotics to assist secondary infections and thus prevent their deaths. Treatment of these animals is particularly important not only to prevent their suffering but to ensure no other wombat becomes infested.
4. Carers of hand reared wombats turning these animals from captive to free should avoid burrows where a wombat has died from sarcoptic mite infestation for at least three weeks.
5. Carers of wombats with severe mange should avoid allowing that animal to die and if it does should ensure no other wombat has contact with its bedding, housing or burrow for a period of at least three weeks.

## ERADICATION OPTIONS

There are many methods that can be used to eradicate *sarcoptes scabiei*, the mite that causes mange in wombats. This review is by no means a full coverage of those methods. Some techniques have been selected because they have been referred to previously in the limited literature concerning scabies/mange, for example in Lee Skerratt's 2001 Phd. thesis where ivermectin injections were used to completely resolve all clinical signs of scabies/mange in wombats. Others have been selected because they present a good match with the criteria set by the first report into scabies/mange and are considered to potentially do the most good and the least harm. We include non prescription treatments such as sulphur and oil which are considered safe for use without supervision. Others are included because members or websites mention the use of such products on wombats. Phosmet, contained in the now withdrawn Novartis product poron, and the now unavailable (in Australia) product porect, are included for that reason. The miticide Ectodex, containing amitraz, is included because it too appears on a mange related site and there are new warnings not to use such products with other products such as Ivermectin (we found one mange treatment procedure still on websites in Australia recommending the use of both these products in a single treatment program). Similarly where other veterinary medications we are aware of are used on wombats, for example valium, for sedation and they are in conflict with a particular scabies/mange treatment, for example the ivermectin group, we make mention of these. The inclusion of any product or treatment in this review should not be considered in anyway to constitute an endorsement of that product for use on wombats. Individual eradication programs will need to consider a range of factors before deciding on treatment methods.

While we will use our evaluation schema developed previously to provide a ranking for possible interventions, the individual circumstance of the proposed use situation must be taken into account and methods determined from those variables. Readers are reminded that NO products anywhere in the world are registered for use on wombats and all uses of any manufactured product are off label uses. In some States there may also be legal issues pertaining to using any product or treatment method on a native animal and contact regarding this with appropriate authorities in each State is recommended.

Cost of treatment is another when trying to have an impact on a widespread problem like scabies/mange in wombats. Currently there are no State funded projects looking into the issue and most costs of treatment are borne by those who volunteer their time and energy in the attempt to save wombats. This leads to uses of products that are not only off label but often in variance with the product formulation, for example, using an oral version of a product as a pour on. While this can be technically done in some cases, it must be remembered that dose rates for injections, oral use and pour-ons vary, as do the amounts of certain components in different formulations of products. It is important when using any restricted product that an appropriate authority, such as a veterinarian, prescribe and oversee the management of its use to avoid mistakes. We have noted that website information often fails to indicate that product formulations vary and we know of one case where the use of a formulation for pigs rather than that for poultry may have been responsible for the death of a wombat.

There will also be issues specific to wombats that need to be taken into account and may not have been considered in provided product information. Wombats, for example are hind gut fermenters and as such are likely to excrete metabolites of products much more slowly than would be the case with usual experimental animals.

Many products shouldn't be used on young or suckling animals, hence joeys in pouches could be affected by applications on female wombats.

Many commercially available products are used in other ways, such as insecticides for crops. A great deal of the adverse impact information which exists about various chemicals comes from testing of these uses of these chemicals and specific, limited use of animals products do not necessarily result in the same adverse outcomes. For example, using a product as a foliar spray over many acres of sunflower crops has a different effect on non target species such as bees than does the use of the same product in much smaller doses such as a spot on or in injectable form on an animal. Similarly, it needs to be recognized that often the tests undertaken to register a product differ from country to country and product type to type. There are big differences in determining safety factors for products used as drugs versus those used as crop pesticides. We urge you to follow through and read the references before quoting adverse impacts of particular chemicals. We remind you that no study has been based on outcomes for wombats.

Acaricides that exist in nature without modification cannot be copyrighted and therefore less testing of such substances occurs and literature information is scarce. It is registration boards that determine the type of testing required. In the first step of making any of the macrocyclic lactone acaricides, which happen to be antibiotic as well as acaricidal, naturally occurring bacteria are fermented. Were the resulting product used directly, it would be organic, be able to be registered as organic and as such could not be "owned", unless the fermentation process was novel and copyright. In the next stage chemical reactions and procedures are used to change the final product's molecular structure to a substance that is considered synthesized because it wouldn't, in that format, be found in nature. This product can be owned.

Companies choose how they register products in particular countries, dependant on market forces and registration requirements of that country. If a particular product is already registered and in use, for example, for scab or scabies or mange, a company whose product also covers the same mites but is effective against fleas, for which no other product is registered, may not bother to include its miticidal properties in their registration. Frontline, containing the miticide, Fipronil is an example of this. In Australia, Frontline is registered for fleas and ticks but not mites. Similarly, products that are registered elsewhere (U.S.A. and U.K. for example) may have limited registrations in Australia. Synthesised products often have multi type uses, all the avermectin acaricides are antibiotics as well, though in many cases their manufacturers have not applied for registration of the substance as an antibiotic.

This is a huge area of study and it is well beyond the scope of this paper to include all chemicals, all means of application and all data concerning impact of chemical use. We have done our best and used information from as many countries and as many applications as we could locate, while still focusing on the main aim of this work- to locate and critique available substances that can be used to eradicate mange in the wild wombat population in Australia.

As with the first report into scabies/mange, we ask for input and feedback and see this report as a starting point that should change and develop as information and field trials become available.

## WHICH WOMBATS TO TREAT

The first report covered how mange is recognized and diagnosed. In terms of the least invasive means of deciding whether to treat an animal showing apparent signs of scabies/mange, we recommend the "maybe mange" approach, described here by Marvistavet.

"Since negative test results do not rule out mite infection, a "Maybe Mange" test is frequently performed. This consists simply of treating for sarcoptic mange and observing for resolution of the signs within 2-4 weeks." We believe the "maybe mange test", used with a safe acaricide is appropriate and overcomes stress that would be otherwise associated with other means of detecting mange such as capture for skin scrapings/skin biopsies.

This research would recommend treating any wombat showing clinical signs of mange and to treat prophylactically those not showing clinical signs, given products or treatments are selected which do no harm. The evaluation of the potential for harm was established in the first report and the criterion developed is listed below.

- 1. The degree of interference with the wombat's normal routine and lifestyle. The better treatment will not interfere, or limits the degree of interference with the normal routine and behaviour of the naturally raised free wombat.**

In regard to this there are methods of treating mange that do not involve capture or confinement the wombat for that purpose. These methods rank above other methods requiring capture. A self administered spot on would rank 5, above one needing to be administered by a person, which would rank 4, above catching the wombat and dosing it orally, which would rank 3, above capturing the wombat and injecting substances into it once, which would rank 2, above having to recapture the animal progressively to give injections which would rank 1, above confining and removing the animal for that purpose from its usual environment.

- 2. The degree of likely impact on the longer term health of the animal. The better treatment has no new negative impacts on the long term well being of the wombat.**

Here we look at how long the product stays in or on the wombat and whether any residual effects, impact on gut flora, reproductive rates, levels of toxicity and other adverse event reports such as mutagenicity, phylogenicity of the product exist or are on record. Rankings start with 5 and for each area of concern one point is deducted.

- 3. The degree of ease with which the treatment can be supplied to the wombat. The better treatment is simple, safe and able to be provided by a range of people.**

This section is ranked giving remote, self applied products the higher recommendation, those requiring contact with the animal such as injectable a lower ranking and those requiring specialized training due to toxicity or some other reason lower ratings.

- 4. The universality of treatment. The better treatment will be able to be used on wombats whatever their stage of mange development and should cause no harm to any other wombat that may come in contact with the treatment modality.**

Some products specifically are not recommended for young or sick animals or animals that are lactating. Where these factors are known they are included in the evaluation of the product. Each product starts with five and a point deducted for any precautions.

- 5. The unintended consequences of treatment. The better treatment should have no or as few unintended consequences to those using the treatment, other animals that may inadvertently come in contact with the treatment and the environment in general.**

These effects include impact on other creatures such as dung beetles or effects from run off from product use on aquatic creatures. Once again it is often broad acres use of foliar or soil preparation uses of these chemicals that cause these problems where use as a spot on or injectable is not as problematic, however where these outcomes are known they are taken into account.

### References

Skerratt,L. Sarcoptic Mange in The Common Wombat, *Vombatus Ursinus* , Melbourne University.2001.pp.1-290.Available on line from Melbourne University Library.

Wombat Protection Society of Australia Mange Report 1 . 2007 Available on site [www.wombatprotection.org.au](http://www.wombatprotection.org.au) Research section.

Marvistavet;

[http://www.marvistavet.com/html/body\\_sarcoptic\\_mange.html](http://www.marvistavet.com/html/body_sarcoptic_mange.html)

## TREATMENTS FOR MANGE/SCABIES

### Lemon Juice

We have had two reports for successful mange mite removal using lemon juice. One is the straight application of juice to the mite affected area and the other, believed to be derived from a herbal remedy involved letting lemons steep in a bucket of water until mouldy and then using this solution as a wash. It was successfully used on dogs exhibiting clinical signs of mange in N.S.W. according to member 694301 and 694373 and one of the Society's Directors, Macpherson, reports its use in the Northern Territory in 2002 to remove scabies mites from camp dogs. In Arnhem land these dogs are known as "skin dogs" due to alopecia caused by mite infestation. Due to the need to throw buckets of water at wombats to deliver this treatment method it is considered likely to impact on their normal behaviour and rates lower than a self application method. As no testing could be found with lemon juice alone distributed from a self applicator, comment about this cannot be made. It is also possible that the mould spores produced by the rotting lemons are involved in its miticidal activity but this has not been documented. 3,5,3,5,5 =21

### **Oil-To Remove Crusting**

Oil of some type to remove and soften crusting associated with mange should not be considered a treatment in and of itself, although there is some evidence that oil will smother mites.

Davis and Skerratt recommended baby oil or if this had not softened the crusting Glycerine and raw sugar.(Davis and Skerratt). As part of a treatment procedure.

### **References**

Davis,C and Skerratt,L. Mange Update.Reproduced from Wildcry-newsletter of the Wildlife Care Network. 1995.

### **Sump Oil**

Sump oil was apparently used on pigs to remove mites . According to member number 694374 this was still being used on pig farms up into the 1990s. It is likely to be the combined effect of oil smothering live mites and sulphur in the engine oil that had effect. Sump oil while a history of its efficacy and use exist and its use on animals consumed by people exists, would not be recommended due to the likelihood of heavy metals and carcinogens in the product, given that other products can be found which do not include these concerns. It would also involve capturing the wombat for this treatment and possibly doing so on a number of occasions. 2,3,3,3,3 =15

### **Sulphur, precipitated in oil**

Sulphur is an element represented by the symbol S. In recent times there have been various spellings of the word sulphur and these now include as correct sulfur. According to the Wikipedia it is an abundant, tasteless, multivalent, non metal. It is an essential element for life and is found in amino acids, eg; cysteine and methionine. (Wikipedia) . Sulphur is an essential element of protein, biotin and vitamin B1. It is part of the chemical structure of the amino acids methionine, cysteine, taurine and glutathione. It is required for the synthesis of collagen ,needed for skin. (Zest). It is

an essential component of all living cells. S-S sulphur bonds between peptide chains give proteins their strength and these are found in hair and feathers.(Wikipedia).

It is used commercially, amongst other uses, as an insecticide and fungicide. The smell occasionally associated with a sulphur compound is not due to sulphur itself but the compound, usually hydrogen sulphide also known as rotten egg gas.

Sulphur has been used as an insecticide and fungicide for thousands of years, one of the earlier mentions of it was by Homer in the 8<sup>th</sup> Century B.C. as what he referred to as "pest averting sulfur". It is still recommended as a scabies cure for infants, mixed in its precipitated powder form ( 5 to 6 per cent) into petroleum jelly and applied as a cream twice daily for a week. (Miller-Keane,1997,p.1444). In the only systemic study of mange in wombats, author Lee Skerratt writes "organic or metabolized products of sulphur appear to have acaricidal activity and for many years sulphur was the drug of choice when treating scabies" (Skerratt,2001,p.32). Skerratt also reports on an early explorer becoming infested with scabies from a wombat and resolving this with sulphur.

Sulphur occurs in its elemental form near hot springs and volcanic regions in many parts of the world and in underground deposits beneath quicksand in the U.S.A. To extract the later, a procedure known as the Frasch process, was invented around 1867. Elemental sulphur is also present in salt domes in Mexico and evaporates in Eastern Europe and Western Asia. It can be reconstituted by the action of anaerobic bacteria on sulphite minerals, especially gypsum, and through the process of hydrodesulphurisation of oil and gas, and it is also present in meteorites. (Wikipedia,p.4)

Sulphur is available in onions, skunk smell and brassicas (Wikipedia) as well as grapefruit, dried beans, cabbage, eggs, fish, garlic, kale, meats, soybeans, turnips , wheatgerm, horsetail.(Sulfa\*Derm)

Sulphur in its elemental form is odorless and harmless, it is when compounded or in the process of breaking down that odor arises. Sulphur is consumed in large quantities through food, the average person, according to Lenntech takes in 900mg of sulphur each day.

Sulphur dioxide is used in food additives and is meant to be safe in small amounts except to insects where it prevents respiration (due to them having no lungs), but hydrogen sulphite is more toxic than cyanide and quickly deadens smell resulting in exposures which can kill.(Wikipedia). Airborne sulphur compounds when mixed with water cause what has become known as acid rain. Sulphur as gas, in compounds in the air, due to industrial processes, causes damage; in animals this is mainly brain damage through malfunctioning of the hypothalamus and damage to the nervous system. Brain, heart and kidney damage, foetal and congenital effects can be caused by sulphur products and sulphur poisoning can be passed through mother's milk. Internal enzyme systems of animals can also be affected. (Lenntech). These effects are through inhalation of sulphur compounds in the air, not through transdermal or oral intake of sulphur.

Sulphur exists in many commercial products including Sulfa\*Derm cream where the active ingredient is 99.96% Pure volcanic ash sulphur. This is used as a bactericide, for dermatitis, rashes and ringworm, acne and fungal/yeast infections.

According to Zest's table of toxicity for dietary and mineral intake there is no toxicity associated with a high sulphur intake.

A number of members of the Wombat Protection Society have used sulphur mixed with oil to successfully treat scabies/mange and remove mange mites on wombats with no reported negative or side effects. Members 694374, 694324, and 694321 have used this method. There are two ways such treatments have been employed. The first involves captive wombats having the oil and sulphur mix rubbed over their bodies to a point of fur saturation over a long period of time, using the oil to assist remove the keratotic plaques and feeding the wombat small doses of sulphur mixed into feed. This method causes saturation of fur with oil and may lead to thermo-regulatory issues so it is only used on captive wombats able to be monitored and temperature controlled. 1,3,2,5,5=16

The second method using the same mixture of sulphur and oil is to hang an applicator device over a burrow that delivers a small quantity of sulphur and oil onto the top of the wombat each time it enters and leaves the burrow. Using the wombat's natural grooming process, over a period of time, the oil and sulphur is gradually distributed over the entire body. This method does not involve saturating the animal so thermoregulation is not an issue.

In trials with a hand reared captive wombat, given a 5ml delivery of sulphur and oil daily for a week as a pour on, no matting or sticking of hair occurred and after 24 hours in each case the mixture was well distributed throughout the fur despite it only being applied to the neck region. It also made no difference if this amount was squirted along the back. Wombats generally only enter and leave burrows a few times at most nightly, and a delivery device of 5mls will not result in the animal becoming saturated. 4,4,5,5,5=23

It should be noted that some proponents of this method believe that scabies/mange is the result of other environmental factors as well and merely eradicating the mange mite will not ensure the ongoing health of the wombat per se. It is also important to note that a wombat with severe mange (more than 75% of body affected by plaques, following Skerratt,2001) would, in most circumstances also require antibiotics to survive, however, there may be benefits to other wombats which may share the burrow of such of wombat in removing the mites from it , even if it dies.

Sulphur has also been claimed to detoxify and enhance immune response (Zest) so it would seem that no further harm is likely to be done to a wombat with severe mange which may die using the self application method and this method probably protects other wombats that may share a burrow with it.

The delivery device is a plastic screw top jar filled with 500mls of a carrier oil such as advocado, neatsfoot or a vegetable oil, into which is mixed 50grams sulphur and agitated to make a 10% suspension. The sulphur does not fully dissolve into the oil but rather is suspended and delivered via the oil onto the wombat. This container has a small hole 1/8" drilled into the lid and is screwed onto an upturned lid such as a milo lid employing washers between the two lids. This is hung from a chain by a spike over the top of burrows at wombat height. The solution runs out onto the lid and remains there airlocked until the wombat's movement tips the amount on the lid down its back at which time the lid refills.

## References

Lenntech Sulphur – S <http://www.lenntech.com/Periodic-chart-elements/S-en.htm>

Miller-Keane (Eds) Encyclopedia and Dictionary of Medicine, Nursing and Allied Health. Sixth Edition. 1997.

Skerratt,L. Sarcoptic Mange in The Common Wombat, *Vombatus Ursinus*. Doctoral Thesis, Department of Veterinary Science. Melbourne University.2001.pp.1-290.Available on line from Melbourne University Library.

Sulfa\*Derm Product Information. [Http://www.safe2use.com/safe-products/sulfer\\_cream.htm](Http://www.safe2use.com/safe-products/sulfer_cream.htm)

Wikipedia. Sulphur. <http://en.wikipedia.org/wiki/Sulfur>

Zest. <Http://www.anyvitamins.com/sulfur-info.htm>

## MACROCYCLIC LACTONE ACARICIDES

These include two classes of acaricides, avermectin acaricides and milbemycin acaricides. Ivermectin,(ivomec) selamectin (revolution)and eprinomectin (eg;ivomec eprimec) are avermectin acaricides and moxidectin (cydectin) is a milbemycin acaricide.Macrocyclic lactone acaricides are also classed as antribiotic acaricides. This section covers these commonly used miticides.

## IVERMECTIN

Ivermectin is contained in a wide array of products used for combating a wide variety of infestations, including scabies. IVOMECC®, HEARTGARD30 & ACAREXX are commercial names for products containing ivermectin. In the only systemic study undertaken into mange on wombats Lee Skerratt successfully proved that Ivomectin by injection could be used to eradicate infestations of the mite (2001). Ivomectin is contained in a number of formulations and formats including pour-ons, chewables, injectable, tablet and spot ons. It is present in different amounts depending on the product formulation, so a sheep drench (worming medicine taken orally) contains a different amount of ivermectin per ml than does a pour-on for cattle (a substance squirted down the back).

According to Marvistavat, In the mid-1980's, ivermectin was introduced as probably the most broad-spectrum anti-parasite medication ever. It is effective against most common intestinal worms (except tapeworms), most mites, and some lice. It is not effective against fleas, ticks, flies, or flukes. It is effective against larval heartworms (the "microfilariae" that circulate in the blood) but not against adult heartworms (that live in the heart and pulmonary\arteries). It is commonly used for the treatment of a variety of mange mites including treatment of sarcoptic, notoedric or demodectic mange.

In dogs,side effects generally do not occur with any anti-mange doses of ivermectin except in Collies, Shetland sheepdogs, Australian shepherds, and Old English sheepdogs, though some individual animals that are not members of these sensitive

breeds may also be prone to side effects. Collies with Ivermectin sensitivity have been found to have a mutant gene for what is called the "P-glycoprotein."

In dogs, side effects of concern are: dilated pupils and drunken gait that can progress to respiratory paralysis and death if medication is not withdrawn and supportive care is withheld.

## INTERACTIONS WITH OTHER DRUGS

Ivermectin should not be used in combination with valium or related tranquilizers. It should not be used in conjunction with Amitraz (Mitaban<sup>®</sup>) dips nor with Amitraz tick prevention collars (Preventic<sup>®</sup> collars). Amitraz is also contained in a wash available in Australia called Ectodex and previously was suggested as part of a mange treatment for wombats in combination with Ivermectin. (see Mange Update, ... website). This should be avoided. These medications (containing Amitraz) are all members of the monoamine oxidase inhibitor group and when they used together their effects add together creating sedation and adverse neurologic effects.

## CONCERNS AND CAUTIONS

Ivermectin use in pregnancy and lactation is not considered to be a problem. It is possible to test an individual animal's response to Ivermectin by using a low dose of ivermectin. According to Shipstone (2000) Ivermectin is able to cross the blood-brain barrier and cause neurotoxicity in some dogs. Collies and Old English sheepdogs are predisposed. Toxicity effects include ataxia, mydriasis, tremors, stupor, salivation, bradycardia and respiratory arrest. Toxic side effects are noted at 100-200ug/kg so Shipstone advises a regime beginning with 50ug/kg and gradually increasing to 300ug/kg. He also compares milbemycin (see moxidectin) favourably due to its lower toxicity in general and specifically in ivermectin sensitive animals, but claims it is prohibitive due to cost. In his studies he used this orally at a dose rate of 200 to 400ug/kg per day.

The following information about Ivermectin was written by Shipstone ,2000 referring to *Demodex* , a mite that affects dogs. Three types , a follicular mite *D canis*, a short bodied mite *D cornei* and a long bodied mite (unnamed) have been described. He says that the published literature recommends a dose of 600ug/kg daily but he found that 300ug/kg daily was effective. Shipstone uses the cattle injectable formulation administered orally (p241) at 300ug/kg daily until two negative skin scrapings are found one month apart and continues treatment for at least two months after the initial negative skin scrape is obtained.

Davis (1995) using advice from Lee Skerratt used Ivomec<sup>®</sup> at the rate of 1ml/10 kilos body weight directly onto the skin over the shoulder area on days three, ten and seventeen. Ivomec<sup>®</sup> pour-on product information warns not to underdose and that applications should not occur prior to rainfall.

The wombat Protection society recently corresponded with members using ivomec as a spot on / pour on product and noted that there is a difference in the amount of active ingredient in different products. The sheep drench, is 0.8grams to the litre or 1000mls. This is the equivalent of 0.08% w/v which is how Merial explain it on their web site. The cattle pour on Ivomec Pour- On<sup>®</sup> for cattle, (note also there is another cattle pour on product called ivomec eprinex<sup>®</sup> containing another ingredient) is 5mg/ml and is used at a rate of 1ml per 10kg. A 40kg wombat would receive 4mls which is 20mg of ivermectin. To deliver the same amount of ivermectin using sheep

drench you'd need to use 25mls. We reiterate the caution given in the beginning of this paper, It is important when using any restricted product that an appropriate authority, such as a veterinarian prescribe and oversee the management of its use to avoid mistakes.

### **IVERMECTIN RESISTANCES/**

It is also important to recognize that off label uses and uses of ivermectin type products with animals other than those specified by the manufacturers can cause additional problems. Veale noted that in Victoria " farmers often purchase any product containing avermectin/milbemycin intended for sheep use and apply it goats. This is occurring despite manufacturer's warnings that moxidectin, in particular, is not recommended for goats. Scott et al demonstrated that the clearance of ivermectin from the plasma of goats after oral administration was faster than from sheep"p.304,2002. Veale comments that an ivermectin resistant strain of *Ostertagia* sp isolated from goats was infective for sheep and that *Trichostrongylus* spp may also pass from goats to sheep. This study was "the first report in Australia of the recovery of *Trichostrongylus* spp nematodes after treatment of ruminants with the avermectin/milbemycin ( macrocyclic lactone) antihelminthics."p.304.

In addition to the development of resistances there is also evidence that dung beetles, and hence by association the possibility of a wide array of insect life being affected by the excretion of these monocyclic lactones in the faeces of treated animals. The avermectins (abamectin, ivermectin and doramectin) and particularly ivermectin, have " been shown to have adverse effects on the development and survival of more than 20 species of scarabeine dung beetles and dung feeding flies. Sublethal effects have also been displayed in progeny and include reduced fecundity, impaired mating and developmental abnormalities.". Wardhaugh,K.G. '98,p.259 .In comparison,the milbemycins (moxidectin) when used in accordance with the manufacturer's instructions, appear to have minor effects on dung feeding insects.(ibid.p.259).,these will be covered further on in this paper.

Ivermectin as an Injectable using Skerratt (2001) 0,2,1,3,1 =7  
Ivermectin as a Pour On 4,2,1,3,1 =11

### **References**

Davis,C and Skerratt,L. Mange Update. Reproduced from Wildcry-newsletter of the Wildlife Care Network. 1995.

Marvistavet [http://www.marvistavet.com/html/body\\_sarcoptic\\_mange.html](http://www.marvistavet.com/html/body_sarcoptic_mange.html)  
[http://www.marvistavet.com/html/body\\_ivermectin.html](http://www.marvistavet.com/html/body_ivermectin.html)

Pipano,E. Recent Developments in the Control of Ectoparasites and endoparasites of dogs and /Cats with selamectin. Israeli Journal of veterinary Medicine vol 58, No.2 2003. [http://www.isvma.org/article/58\\_2\\_1.htm](http://www.isvma.org/article/58_2_1.htm)

Shipstone,M. Generalised demodicosis in dogs, clinical perspective. Australian Veterinary Journal. Vol 78. No.4. April 2000.pp.240-242  
Veterinary Medicines containing Organophosphates. UK Parliament Publications.  
<http://www.publications.parliament.uk/pa/ld199596/lhansrd/vo960125/text/60125w01>

Rendell,R.Dr. in New Zealand Veterinary journal. Ivermectin/ Moxidectin Resistances, quoted in <http://www.farmacomm.com/>

Veale,Pi. Resistance to Macrocyclic Lactones in Nematodes of goats. Australian Veterinary journal. Vol.80, No.5 May 2002.

Wardhaugh,K.G. and Ridsdill-Smith,T.J. Antiparasitic drugs, the livestock industry and dung beetles- cause for concern.? Australian Veterinary journal. Vol 76. No.4, April 1998.

Wombat Protection Society of Australia. Correspondence with Members. Mange Clearing house 2007.

## EPRINOMECTIN

Eprinomectin is the main content in Ivomec® Eprinex™ Pour-On and is registered against a number of endo and ecto parasites for use in dairy and beef cattle. It's U.S.A. registration includes Mange Mites *Chorioptes bovis* and *Sarcoptes scabiei* .It was approved for use in the U.S.A. in 1997. It was registered by Merck /research /laboratories in America and is made by Merial Australia pty.Ltd. It is effective in killing a wide array of ecto and endo parasites, flies and worms. Ivomec eprinex® pour-on is a clear non aqueous solution containing 5mg per ml of eprinomectin. It is applied by pouring the substance onto cows running a strip down their back. Its dose rate is 1ml per 10 kilos of body weight.

In cattle, radiolabelled eprinomectin was absorbed slowly after topical administration. The absorbed radiolabel was taken up mainly by the liver and to a lesser extent by the kidney, fat, and muscle. The radiolabel disappeared from these tissues with half-lives of 7.8 and 8.6 days, except for muscle beneath the application site in which the half life was 36 days.

After oral administration of eprinomectin, the approximate LD<sub>50</sub> values were 70 mg/kg bw for mice and 55 mg/kg bw for rats. Eprinomectin is moderately hazardous after acute **oral** exposure.

In U.S. studies of Eprinomectin against *s.scabiei* on cows, treated once and compared to controls via weekly skin scrapings and mite counts, researchers found that by day 21 a standard dose of eprinomectin achieved 100% efficacy controlling mange mites.(NADA data).

The World Health Organisation has produced a report on eprinomectin and in this report notes that most of the substance leaves the body via faeces and residual amounts left within the body remain as unchanged eprinomectin.

Eprinomectin as pour on – 3,3,3,3,3=15

## References

Ivomec Eprinex Product Information.  
[http://ivomec.us.merial.com/cowcalf/products/products\\_eprinex.asp](http://ivomec.us.merial.com/cowcalf/products/products_eprinex.asp)

TOXICOLOGICAL EVALUATION OF CERTAIN VETERINARY DRUG RESIDUES IN FOOD  
WHO FOOD ADDITIVES SERIES 41 Prepared by: The 50th meeting of the Joint  
FAO/WHO Expert Committee on Food Additives (JECFA)  
World Health Organization, Geneva 1998

[NADA 141-079 www.fda.gov/cvm/FOI/933.htm](http://www.fda.gov/cvm/FOI/933.htm) - 209k  
[www.inchem.org/documents/jecfa/jecmono/v041je02.htm](http://www.inchem.org/documents/jecfa/jecmono/v041je02.htm) - 74k - [Cached](#)

## SELAMECTIN

Selamectin is the active chemical in Revolution, which is a topically applied as a (spot on) and used for Cats and dogs. In cats, Pfizer, the manufacturer, claim it kills adult fleas and prevents eggs hatching, prevents cat heartworm disease, treats and controls ear mites and treats and controls roundworms. In dogs it is approved for use against adult fleas, flea eggs, heartworm, ear mites, sarcoptic mites and the American dog tick (in USA). The recommended topical dose rate is 6mg/kg of body weight and it comes in a variety of weight ranges including 20.1kg-40kg in which there are three pack and six pack versions. There does appear to be an expiry date associated with the product, with a minimum of 12 months indicated by the manufacturer.

It is advertised as a prescription only medicine, not an insecticide (see Pfizer, dog, 2007) and is sold for dogs as a once monthly spot on. Pfizer comments its low volume allows it to be placed in one spot and this is achieved on dogs by parting the hair at the base of the neck and placing the pre-measured tube there and squeezing all contents onto the one spot.

Selamectin, along with Ivermectin is one of the avermectin acaricides. These and the milbemycin acaricides ( which include moxidectin) are classed as a macrocyclic lactones . Despite Pfizer's comments , Selamectin is both an acaricide and an insecticide. (Wood,A.) It binds to glutamate gated chloride channels in the parasites' nervous system, causing them to open. It is absorbed through the skin and distributed via blood. According to the Nolan (2004) it concentrates in the sebaceous glands and active concentrations are found in plasma for at least 30 days. Most is excreted unmetabolised in faeces, and a small amount is excreted in urine. According to a press release by Environmental protection agency (America) Revolution is recommended as a replacement for the banned chlorpyrifos Dursban where it is registered as a parasiticide not an insecticide and was formulated specifically for dogs and cats.(EPA News Release)

Selamectin is a semi synthetic modification of doramectin produced from a bio-engineered new strain of *streptomyces avermitilis* which has a half life of 11 days in dogs and 8 in cats. Applied topically it has a substantially longer half life than when applied intravenously .

Adverse Effects noted by Pfizer (2007) include up to 1% of dogs and cats experiencing digestive upset and 1% cats having hair loss at the applicator site. It should not be used on sick, debilitated or underweight animals. For humans it may be irritating to skin and eyes.

According to Nolan (2004) a 10x dose given to dogs and cats starting at six weeks old for 7 monthly treatments produced no adverse reactions, given orally at normal dose rate to cats 2 out of 6 vomit and a 3x normal doses produced no problems in

reproductive female dogs or heartworm positive dogs. 3 monthly doses of 5x normal dose rate produced no adverse effects in ivermectin sensitive collies

### **Efficacy against mites**

Forty two dogs with naturally acquired infestation of *S. scabiei* obtained from commercial dog kennels where an outbreak followed an inadvertent introduction of infested dogs (USA) or from a private hunting kennel which experienced an outbreak of scabies (Europe) were treated on day 0 and day 30 with selamectin at the recommended dose and or with an inert vehicle mixture. Counts of *S.scabiei* from skin scrapings were performed every 14-15 days up to 60 days after treatment. *S.scabiei* mites were reduced 93.5 % (USA) and 98.1 % (Europe) on the first count after treatment and by 100 % for all remaining counts. There was a clear reduction of the severity of the clinical signs for the selamectin treated dogs compared with those treated with the vehicle mixture (22).

In another study dogs and cats presented at veterinary clinics in the USA and Europe were treated against scabies infection with selamectin or other insecticides containing phosmet or amitraz or N-(mercaptomethyl) phthalimide S-(0,0-dimethyl phosphoro-didithioate). No *S. scabiei* were detected in over 95 % of the selamectin treated dogs, 30 days after a single dose and no mites were recovered from any of the selamectin treated dogs after the second treatment. A dramatic improvement in all six clinical signs of *S. scabiei* (pruritus, erythema, crusting, papulae, alopecia and pyodermatitis) was observed in the course of treatment. Similar results were achieved with the control products while repeat treatments were necessary to control the infestation. When a dog is diagnosed with *S. scabiei* infestation it is recommended that all dogs in contact also be treated irrespective of whether they are showing clinical signs (23).Pipano (2003).

In controlled studies Selamectin in Revolution was safely used in animals receiving other typical veterinary products such as vaccines, antihelminthics, antiparasitics, antibiotics, steroids, collars, shampoos and dips.

Storage conditions store below 30 degrees C 86F. (prnewswire)

Selamectin in Revolution Spot on- 3,4,3,4,4=18

### **References**

Nolan,Dr. University of Pennsylvania. [Parasit@vet.upenn.edu](mailto:Parasit@vet.upenn.edu)  
<http://cal.vet.upenn.edu/dxendopar/drug%20pages/selamectin.htm>

Pipano,E. Recent Developments in the Control of Ectoparasites and endoparasites of dogs and /Cats with selamectin. Israeli Journal of veterinary Medicine vol 58, No.2 2003. [http://www.isvma.org/article/58\\_2\\_1.htm](http://www.isvma.org/article/58_2_1.htm)

PRN New Wire <http://www.prnewswire.com/cgi-bin/stories.pl?ACCT=104&STORY+/www/story/06-15>

Revolution flea and Heartworm control IPET International. [http://www.ipet-int.com/category\\_12\\_2.htm](http://www.ipet-int.com/category_12_2.htm)

**Pfizer Product Information- Cats**

<http://www.revolution4cats.com/display.asp?country=US&lang=EN&drug>

**Pfizer Product Information – Dogs**

<http://www.revolution4dogs.com/content.asp?country=US&species=CN>

Wood, Alan. Compendium of Pesticide Common Names. Classified Lists of Pesticides. 2006. [http://www.alanwood.net/pesticides/class\\_pesticides.html](http://www.alanwood.net/pesticides/class_pesticides.html)

## MOXIDECTIN

Moxidectin, like Ivermectin and Selamectin is a Macrocyclic lactones and an antibiotic acaricide. It is in a separate class called milbemycin acaricides (Wood). Moxidectin is found in a range of veterinary medicines including Advocate, a spot on for dogs (in combination with imidacloprid); Pro Heart an anti heartworm treatment for dogs, Quest a horse wormer and Cydectin, for cattle.

Moxidectin is used in treatments prescribed for dogs, cats, horses cattle and sheep for endo and ecto parasites and can include oral, topical and injectable applications according to the Wikipedia. It works by binding to parasite's glutamate-gated chloride ion channels. This disrupts neurotransmission that paralyzes and kills the parasite. According to the Committee for Veterinary Medicinal Product of the European Agency for the Evaluation of Medicinal Products Moxidectin is intended for the treatment of endo- and ecto-parasites in cattle and sheep at the recommended dosage of 0.2mg/kg bw administered by oral or subcutaneous routes. It is also used as a topical pour on.

In horses the recommended dose is 0.4mg/kg bw administered once orally. It is considered to have a NOEL (no observable effects level = no adverse effects observed) of 0.3mg/kg bw/day. This study on horses found that peak serum concentration was attained 6 hours post dose, that oral and intravenous routes gave approximately the same rate of elimination of moxidectin from the animals, that is elimination half life is approximately 80 hours and by 168 hours post dose 77.3% is excreted, 77% by faecal route and 0.3% in urine. Horses fed moxidectin orally at the recommended rate and later slaughtered were found to contain moxidectin in fat at the rates of 222ug/kg at 28 days reducing to 131ug/kg at 49 days. In other tissues tested the residual was below measureable levels, less than 10ug/kg. (1999,p.2)

It has been used to eliminate demodex mange mites from dogs. Shipstone (2000) compares milbemycin (moxidectin) favourably to ivermectin due to its lower toxicity in general and specifically in ivermectin sensitive animals, but claims it is prohibitive due to cost. In his studies he used this orally at a dose rate of 200 to 400ug/kg per day, but noted facial angio-oedema in 12.5% of treated dogs. (p.242).

It has been used to eradicate knemidocoptic mange (scaly face) in budgerigars in a study by Toparlak et al (1999) where Cydectin injectable was used as a spot on at the rate of 0.1ml Cydectin per bird. Cydectin's active constituent is 10mg/ml moxidectin and in this study 0.1ml (1mg moxidectin) equivalent 25-29mg/kg was used as a spot on on birds with 0.1ml dropped onto the skin between feathers on the bird's neck. This rate is much higher than the recommended rate of 0.2mg/kg bw for cattle but the authors whose study appears in the Turkish Journal of Veterinary Science report no side effects for the birds and complete resolution of all clinical signs, including itching stopped within 10 days and spongy lesions healed in 30-40 days after one treatment. They found no better efficacy with two treatments. The authors' comment that this treatment was quicker and had better outcomes than treatment with ivermectin.

Moxidectin is contained in ProHeart a heart worm prevention treatment for dogs. . ProHeart is considered able to treat external parasites ( fleas,ticks and mites) and internal parasites ( intestinal worms, lungworms, heartworms).

The Injectable form of proheart has been withdrawn from sale due to potential side effects according to Dr. D.Ruben The injectable form of ProHeart is blamed for the death of "Tobie", a Border Collie and cautions are now given to people using heartworm treatment with dogs that may be ivermectin sensitive such as herding dogs which apparently carry a gene that responds to ivermectin.

Wooster et al (2001) reported in the Australian Veterinary Journal, tested ivermectin and moxidectin against two field isolates of a worm that parasitises sheep, *H.contortus* in a study which suggests that resistance to these chemicals is developing. The millibemycins (moxidectin) when used in accordance with the manufacturer's instructions, appear to have minor effects on dung feeding insects. Wardhaugh,K.G. '98,p.259 .

In an assessment for registration as an organic product (denied as the product was considered synthesized) the technical advisory panel agreed that moxidectin did not appear to have carcinogenic, developmental or teratogenic impact. Bacterial assays indicate it is not a mutagen mammalian tests are inconclusive. It appears to not effect earthworms and fauna remains present in dung pats of treated versus untreated animals.(TAP,p5-6,2003)

Moxidectin alone in Cydectin Pour On for Cattle- 3,4,3,4,4 =18

#### **PRODUCTS COMBINING MILBEMYCINS WITH OTHERS**

Advocate is a patented combination of Imidacloprid (contained in Advantage) and Moxidectin used to eliminate parasitic infestations and to prevent new infestations in dogs ,according to its maker, Bayer Australia. Bayer say that it provides continuous protection following one "spot on" application which lasts for a month. In dogs fleas, heartworm and gastrointestinal worms are eliminated, ear mites and demodex (a skin mite) are controlled and Bayer claim that sarcoptic mange is 100% eliminated after a single treatment. There are three types of Advantage for dogs 4-10kilos, 10-25kilos and over 25 kilos. These products contain Imidacloprid at 100grams/L and Moxidectin 25grams/L.

Given it appears to be the moxidectin that has the impact on mange mites, some might consider it questionable to bother using moxidectin in combination with any other chemical. Following our scale of doing the least harm we would not advise adding further chemicals to one which removed the mite unless some other benefit were conferred. In dogs, where target parasites are often in combination or not responsive to moxidectin, a mixed product might be justified, however we note that the products containing moxidectin for dogs ( eg; ADVOCATE ) in combination with IMIDACLOPRID do so to target the mange mite which imidacloprid (alone in Advantage) apparently does not.It means that ADVOCATE would rank lower on our assessment scale because it combines moxidectin with another unnecessary chemical, imiprochlorid given the basis of this study is to target the sarcoptes mite alone.

Advocate, spot on for dogs - 3,3,3,2,2 =13  
low ranking primarily due to imidacloprid

We include information covering the mixed product, ADVOCATE and the Imiprochlorpid alone product, ADVANTAGE, so that readers can make their own judgement regarding available product information and adverse effects.

## References

Advantage Product Information. Bayer Health Care. Bayer Australia Limited. Product Information.

Australian Veterinary Journal. Letters. Vol 80, No.5, May 2002. NRA ruling re ProHeartSR-12 injectable. See also Aust.Vet.Journal 80, No.3 p.128.

BAYER: <http://www.bayeranimal.com.au/default.aspx?page=50&ItemId=38>

FDA Study. NADA 141-051 <http://www.fda.gov/cvm/FOI/1056.htm>

MOXIDECTIN Summary Report 2 .The Committee for Veterinary Medicinal Products of the European Agency for the Evaluation of Medicinal Products. Veterinary Medicines Evaluation Unit. April 1999

Summary of TAP Reviewer's Analyses **Moxidectin** was petitioned for use as a broad spectrum topically applied antiparasitic  
[www.ams.usda.gov/nop/NationalList/MoxidectinFinalTAP.pdf](http://www.ams.usda.gov/nop/NationalList/MoxidectinFinalTAP.pdf) - 231k -

Toparlak,M., Tuzer,E., Gargili,A. and Gulanber,A. Therapy of Knemidocoptic Mange in Budgerigars with Spot on Application of Moxidectin. In Turkish Journal of Veterinary and Animal Sciences. 23 (1999) 173-174.

Ruben,D.Dr. Pro-Heart. [http://www.petplace.com/drug-library/moxidectin-proheart/page\\_1.aspx](http://www.petplace.com/drug-library/moxidectin-proheart/page_1.aspx)

Shipstone,M. Generalised demodicosis in dogs, clinical perspective. Australian Veterinary Journal. Vol 78. No.4. April 2000.pp.240-242

Tobie. <http://www.dogadversereactions.com/moxidectin/memorial24.html>

Rendell,R.Dr. in New Zealand Veterinary journal. Ivermectin/ Moxidectin Resistances, quoted in <http://www.farmacomm.com/>

Veale,Pi. Resistance to Macrocyclic Lactones in Nematodes of goats. Australian Veterinary journal. Vol.80, No.5 May 2002.

Wardhaugh,K.G. and Ridsdill-Smith,T.J. Antiparasitic drugs, the livestock industry and dung beetles- cause for concern.? Australian Veterinary journal. Vol 76. No.4, April 1998.

Wood, Alan. Compendium of Pesticide Common Names. Classified Lists of Pesticides. 2006. [http://www.alanwood.net/pesticides/class\\_pesticides.html](http://www.alanwood.net/pesticides/class_pesticides.html)

Wooster, M.J., Woodgate, R.G. and Chick B.F. Veterinary Health research Pty. Ltd. West Armidale N.S.W. Australian Veterinary Journal. Vol.79 No.12 Dec.2001  
<http://www.ava.com.au/avj/0112/01120840.pdf>

## IMIDACLOPRID

Imidacloprid is found in a variety of commercial crop insecticides including Admire, Confidor, Gaucho, Premier, Provado, Marathon, Merit, Pre-empt, Winner, Hachikusan (Japan) and animal products such as Advantage and Advocate. It is the sole ingredient in Advantage and is combined with moxidectin in Advocate. To be effective animals treated with Imidacloprid should not be washed using shampoo (see Wikipedia, p.3). Advantage is 100g/L of Imidacloprid alone and according to its manufacturer, Bayer, it is for the treatment and prevention of fleas *Ctenocephalides* spp on dogs, cats, rabbits and ferrets. One application on the skin lasts for a month on dogs and up to a month on cats. Larval flea stages are killed in the surroundings of Advantage treated pets. For the control of lice *Trichodectes canis*, *Lingognathus setosus* on dogs for up to 6 weeks. There are six types of Advantage including the Blue pack for dogs weighing 25 to 50 kilos. This is applied by dividing the dose between the shoulder blades, on the midline of the back between the hips and on one point between. (Bayer product information).

Imidacloprid is a systemic, chloro-nicotinyl insecticide which works by interfering with the transmission of stimuli in the insect nervous system. It causes a blockage in the nicotinic neuronal pathway which "is more abundant in insects than in warm blooded animals (making the chemical selectively more toxic to insects than warm blooded animals). This blockage leads to the accumulation of acetylcholine, an important neurotransmitter, resulting in the insect's paralysis and eventually death."(ETN).

It is effective on contact and via stomach action and is widely used as a crop insecticide where it is available as dustable powder, granular, seed dressing, soluble concentrate, suspension concentrate and wettable powder where it is applied in ranges from 0.05 to 0.125 pounds/acre.

It is considered moderately toxic, the lethal oral dose to half the tested animals (LD50) is 450mg/kg body weight (bw) in rats and 131mg/kg in mice and 24 hour dermal LD50 is greater than 5000mg/kg in rats. It is considered non irritating to the eyes and skin- tested on rabbits and non sensitizing to skin- tested on guinea pigs. The No observable effect level (NOEL) broke down with rats at 5.7mg/kg/day in male rats (this represents 100ppm) and 7.6mg/kg/day in females. At 100ppm reproductive effects of decreased pup weight are noted in baby rats. At 300ppm weight decreases were found in female rats, thyroid lesions in males and at 900ppm thyroid lesions in females. (ETN) In dogs the NOEL was 1250ppm (41mg/kg) and included increased blood cholesterol levels and liver stress measured by elevated liver cytochrome p-450 levels.

Imidacloprid is considered weakly mutagenic testing positive for causing changes in human lymphocytes and Chinese Hamster Ovary Cells, (ETN) however PAN reports that new techniques in DNA testing since registration with ADMIRE have shown an

increased frequency of adducts ( the binding of a chemical to DNA) and that these were five times more common in calf thymus cells exposed to imidacloprid compared to unexposed cells.(Buffin,p.1).

It is considered to have minimum carcinogenic risk, however some of the inert products used in combination with it such as crystalline quartz silica found in Merit 0.5G is carcinogenic to humans.(Buffin, p.1) and Napthalene contained in Leverage2.7 causes nasal cancers, anemia, liver damage, cataracts and skin allergies. (Cox,2001,p.16)

It has a number of ecological impacts including toxicity to game birds where the LD50 of 152/mg/kg for bobtail quail and 31/mg/kg in Japanese Quail has been shown. (ETN,p.2) These effects are mainly based on seed treated being eaten by birds and studies have shown birds learn to avoid treated seed. It causes abnormal behaviour at below toxic levels- including the inability to fly and eggshell thinning at 61mg/kg (Buffin,p.2)

Toxicity to fish is considered moderate with lethal concentration causing death of half the test animals (LC50)after 96 hours ranging from 211mg/l for rainbow trout to 280mg/l for carp. Aquatic invertebrates are also effected with the EC50 (effective concentration, death of 50% of test animals) 85mg/l for Daphnia leading to the conclusion that it may be very toxic to aquatic invertebrates.(ETN,p.2).

It is highly toxic to bees (ETN,p3) . In a number of countries it has been banned from use on certain crops due to the impact on bees, including Gaucho suspended from use on sunflowers in France, and beekeepers elsewhere report losses of 50-80%.(Buffin in PAN,p.3). It is acutely toxic to earthworms killing some at concentrations as low as 2 and 4 ppm in soil (Cox,2001,p.18) .

Resistance in insects has been noted and of even more concern is cross resistance. Thrips selected for their resistance to the organophosphate insecticide diazinon were also found to be resistant to imidacloprid.(Buffin,p.2).

Imidacloprid has a half life in soil ranging from 48 to 190 days and is greater than 31 days in groundwater at pHs above 5.(ETN,p.3) but "it can have a half life in soil under aerobic conditions as long as 997 days, which is the cause of concern over possible water contamination as it gradually leaches out"...The manufacturer maintains that, when applied according to instructions, such long term contamination is only found as the result of "repetitive application over several years".(Wikipedia).

According to the Wikipedia 96% of the chemical is eliminated from the body within 48 hours but there are reports of it degrading into toxic, persistent, 2-chloropyridine.

Over exposure to agricultural products included reduced activity, incoordination, tremors,diarrhea and emaciation lasting up to 6 days after imidacloprid exposure alone and 12 days after imidacloprid plus inerts. (Cox,2001,p.16).

Overdose (to flea control product) was characterized by reduced activity, convulsions and labored breathing and cats are effected by an unidentified inert ingredient in Advantage spot on with kittens showing toxicity when Advantage is applied above recommended dose rates as a spot on. Death, coma and incoordination were observed in kittens given five times the recommended dose of Advantage and when fed Advantage or its inert ingredients vomiting, salivation and depression were noted in cats. (Cox,2001,p.16)

Advantage and other products containing imidacloprid 3,2,2,2,0=9

Buffin,D. Imidacloprid. PAN UK Journal of Pesticides.  
<http://www.pan-uk.org/pestnews/Actives/imidaclo.htm>

Wood, Alan. Compendium of Pesticide Common Names. Classified Lists of Pesticides. 2006. [http://www.alanwood.net/pesticides/class\\_pesticides.html](http://www.alanwood.net/pesticides/class_pesticides.html)

Cox,C. Imidacloprid. Journal of Pesticide Reform/ Spring 2001 Vol 21, No.1.pp.15-21.

ETN- Extoxnet Extension Toxicology Network- Pesticide Information Profiles. Project of cornell University, Oregon State University, University of Idaho, University of California and the Institute for Environmental toxicology.  
<http://extoxnet.orst.edu/pips/imidaclo.htm>

PAN-Pesticide A Network. Imidacloprid see Buffin,D.

BAYER Website- Imidacloprid  
<http://www.bayeranimal.com.au/default.aspx?page=50&ItemId=38>

Wikipedia entry Imidacloprid. March 2007.  
<http://en.wikipedia.org/wiki/Imidacloprid>

## **PORON/PORECT**

Porcine products, poron, porect, phosmets, Novartis. Found and mentioned in Yahoo search for porect, Novartis product list, article on Mange authored by Clare Davis- "Mange Update" reproduced from WildCry- newsletter of the Wildlife Care Network. On Wrin site. Additional input- correspondence with Clare Davis, Novartis , discussion with Jackie French.

According to correspondence with Novartis, Poron is no longer available and has been withdrawn from sale. Porect has been used on wombats but according to Clare Davis was a once only use due to potential liver toxicity. Correspondence with Novartis indicates Porect is not a current Novartis product in Australia, it is however listed on the U.K. list of Veterinary Medicines containing Organophosphates as being registered in the U.K. as Young's Poron 20 for Cattle with the active ingredient Phosmet as is Porect for pigs ,again with Phosmet as the active ingredient. It would appear any supplies of either in Australia are out of date and the products longer available.

These product contained phosmet which according to the Wikipedia is a non systemic, organophosphate insecticide used on plants and animals. It is highly toxic to bees. It is listed on the US Emergency Planning List of Extremely Hazardous Substances. A recent ( controversial) report by Mark Purdey suggests it may be linked to spongiform encephalopathies (eg BSE) .

According to Alan Wood it is used in acaricides ( organophosphate acaricide; phthalimide acaricide) and insecticides (isoindole organothiophosphate insecticides; phthalimide insecticides). It is called phthalophos in Russia and PMP in Japan.

World Health Organisation lists it as a class 11, moderately hazardous chemical. It is a cholinesterase inhibitor. Signs of poisoning are similar to all organophosphates and include dizziness, sweating, laboured breathing, nausea, papillary constriction, muscle cramp and excessive salivation. Can be absorbed through skin, eyes become red, ingestion leads to abdominal cramps, convulsions, diarrhoea, unconsciousness and vomiting. PAN rates it as a "Bad Actor Chemical", considers it possibly carcinogenic, it is a cholinesterase inhibitor and is considered by PAN to be a possible ground water contaminant.

Its' effects on other living organisms include growth and mortality impact on amphibians, mortality of annelids, accumulates in and effects behaviour of and kills crustaceans, effects fish biochemistry, accumulates in fish and causes mortality, insects are affected by accumulation, intoxication and mortality, molluscs behaviour and morphology are affected, it leads to intoxication and mortality of molluscs and zooplankton, it accumulates in zooplankton and phytoplankton and effects the later's physiology.

Advice re use on wombats was that it was good to use as a once only product on free wombats and should only be used monthly on captive wombats. (ref. Clare Davis). Cautionary advice re liver toxicity was given but cannot be documented. Given it is no longer available in Australia, this information has been included due to previous references to its use on wombats. Novartis information indicates any remaining product left in Australia would be out of date and it should not be used. As a result this product receives a zero rating.

=0

## References

PAN Pesticide Data Base – Pesticide Action Network <http://www.pesticideinfo.org> 2006 Phosmet.

Letter via E-mail to Wombat P.S.A. March 2007 Novartis

Yahoo Search Porect March 2007- Article 5 "mange" and 6 Products from Novartis

Phosmet Wikipedia Entry March 2007 <http://en.wikipedia.org/wiki/Phosmet>  
Mange update by Clare Davis- reproduced from Wildcry-Newsletter of the Wildlife Care Network on <http://www.wombatechidna.id.au/mange.html>

Compendium of Pesticide Common Names-  
[http://www.alanwood.net/pesticides/class\\_pesticides.html](http://www.alanwood.net/pesticides/class_pesticides.html) phosmet  
Wood, Alan. Compendium of Pesticide Common Names. Classified Lists of Pesticides. 2006. [http://www.alanwood.net/pesticides/class\\_pesticides.html](http://www.alanwood.net/pesticides/class_pesticides.html)

## FIPRONIL

Main ingredient in Frontline Spot On for Dogs and Cats, Topspot, Frontline Plus, Chipco Choice, combat, Maxforce, Termidor  
Marketing in Australia for fleas and Paralysis and Brown Dog ticks on Dogs.

Frontline Plus for dogs contains Fipronil 100g/L and S-Methoprene 90g/L and its manufacturer Merial advises it is for use on dogs 8 weeks and older. Merial say it prevents the development of flea eggs and larvae and pupae( see Methoprene) for up to 3 months after treatment. It is supplied in pre-dosed pipettes for 20-40kg dogs at 2.68mL and for 40-60kg dogs in 4.02mL pipette which are applied to a place the animal won't lick. In Australia the product is registered for the brown dog tick *Rhipicephalus sanguineus*, biting lice *Trichodectes canis* and the paralysis tick *Ixodes holocyclus* Merial product information) but Fipronil controls mites (PAN page1).

The N.P.T.N. fact sheet of the U.S. Environmental Protection Agency calls Fipronil a phenylpyrazole insecticide, these act by disrupting normal nerve function. Fipronil acts by blocking the GABA- gate chloride channels of neuron in the central nervous system. Neural excitation caused by contact causes the insect's death.1997.p.1.

Information from PAN, the Pesticides Advisory Network of the U.K. follows. Fipronil is an insecticide discovered and developed by Rhône-Poulenc between 1985-87 and placed on the market in 1993. Although effective against a variety of pests, there are concerns about its environmental and human health effects. Actively marketed in many industrialised and developing countries its, worldwide use is increasing. Fipronil is a member of the phenyl pyrazole class of pesticides, which are principally chemicals with a herbicidal effect. Fipronil, however, acts as an insecticide with contact and stomach action. It is sparingly soluble in water; is stable at normal temperatures for one year but not stable in the presence of metal ions and is degraded by sunlight to produce a variety of metabolites one of which (fipronil-desulfinyl (MB 46513) is extremely stable and is more toxic than the parent compound.

Fipronil under the trade name Frontline or Top Spot is also used to control fleas, ticks and mites on domestic animals and as a pour-on or dip for cattle to control ticks. In the UK, provisional approval for five years has been granted for fipronil use as a public hygiene insecticide.

#### **Mode of action**

Fipronil is an extremely active molecule and is a potent disruptor of the insect central nervous system via the (-aminobutyric acid (GABA) regulated chloride channel. Despite the fact that the GABA channel is important in nerve transmission in both vertebrate and invertebrate animals, and that fipronil does bind to the GABA receptor in vertebrates, the binding is 'less tight' which offers a degree of selectivity.

#### **Environmental fate**

Field persistence is low-moderate in water and soil (half-life 10-130 hours (h) in water and 45-530 h in soil) with three major degradates formed in soil – RPA 20076 (amide), MB46513 (fipronil-desulfinyl), and RPA 104615 and two major metabolites in water, including MB 45950 (sulfide). Under aerobic conditions in soil several metabolites have been identified, including RPA 200766 and MB 46136 (sulfone).

Fipronil residues tend to stay in the upper 15 cm of soil and exhibit low potential to leach to groundwater.

In aquatic environments, fipronil residues rapidly move from the water to the sediment with over 95% of the residues being found in or on the sediments within one week of application.

#### **Acute toxicity**

Fipronil is classed as a WHO Class II moderately hazardous pesticide and has a rat

acute oral LD50 (the dose required to kill half a population of lab animals) is 97 mg/kg(35). It is less toxic to mammals than to some birds, fish and most invertebrates.

Fipronil has moderate acute toxicity by the oral and inhalation routes in rats. Dermal absorption in rats is less than 1% after 24 h and toxicity is considered to be low. In contrast, it is of moderate dermal toxicity to rabbits.

#### **Chronic effects**

Fipronil is neurotoxic in both rats and dogs, there are indications of developmental neurotoxicity and chronic carcinogenicity in the rat and in two dog studies.

There has been a low incidence of severe skin reactions to Frontline Spray treatment, Top Spot for Cats and Top Spot for Dogs, mostly resulting in skin irritation and/or hair loss at the site of application. There is some suggestion that dogs are more severely affected than cats.

Fipronil is carcinogenic to rats at doses of 300 ppm in males (12.68 mg/kg/day) and females (16.75 mg/kg/day), causing thyroid cancer related to disruption in the thyroid-pituitary status. However fipronil was not carcinogenic to female mice when administered at doses of 30 ppm.

Fipronil is associated with reproductive effects in rats fed 95.4% fipronil continuously in the diet at 300 ppm based on clinical signs of toxicity, decreased litter size, decreased body weights, decrease in the percentage of animals mating, reduction in fertility index, reduced post-implantation survival and offspring postnatal survivability, and delay in physical development.

#### **Human health**

There have been very few studies undertaken with human subjects, although human cells have been used in some carcinogenicity studies in which no adverse effects were detected.

Fipronil has been classified as a Group C (Possible Human) Carcinogen based on an increase in thyroid follicular cell tumours in both sexes of the rat. In contrast, thyroid tumours induced by fipronil in rats are not considered of relevance to human health in the UK.

Two Top Spot products were determined by the New York State Department of Environmental Conservation to pose no significant exposure risks to workers applying the product. However, concerns were raised about human exposure to Frontline spray treatment in 1996 leading to a denial of registration for the spray product. Commercial pet groomers and veterinarians were considered to be at risk from chronic exposure via inhalation and dermal absorption during the application of the spray, assuming that they may have to treat up to 20 large dogs per day.

#### **Effects on wildlife**

##### *Laboratory toxicity tests*

Fipronil is highly toxic to certain groups of gallinaceous birds (Acute LD50 for Bobwhite quail = 11.3 mg/kg), while being relatively innocuous to passerines (LD50 for field sparrow = 1120 mg/kg) and wildfowl (LD50 for Mallard duck > 2150 mg/kg)(49).

The LD50 of fipronil for the fringe-toed lizard (*Acanthodactylus dumerili*) [Lacertidae] has been estimated at 30 µg a.i./g body weight in laboratory tests, indicating that it is highly toxic. Mortality was delayed and lizards died during the four weeks after treatment. Locomotor activity, prey consumption and body weight remained significantly lower in lizards fed fipronil treated prey than in the control group for 2-4 weeks after treatment.

Toxicity of fipronil to fish varies with species. It is very highly toxic to bluegill sunfish, highly toxic to rainbow trout and to European carp. It is very highly toxic to one of the African tilapia (*Oreochromis niloticus*) . Fipronil affects larval growth in

rainbow trout at concentrations greater than 0.0066 ppm.

Fipronil is also toxic to a wide range of aquatic invertebrates, very highly toxic to shrimps and other crustacea and very highly toxic to oysters.

Fipronil is highly toxic to bees and termites. It had the highest acute toxicity for the parasitoid *Bracon hebetor* [*Hymenoptera: Braconidae*]. Fipronil was given the highest hazard ranking for beneficial tenebrionid beetles of six insecticides tested in the Locustox study. It is virtually non-toxic to earthworms.

**Frontline;** The use of fipronil is in combination with methoprene (see next) in products available in Australia 3,2,3,2,0 =10

## References

PAN Fipronil <http://www.pan.-uk.org/pestnews/actives/fipronil.htm>

Frontline Plus Product Information from Merial Australia 2006

National Pesticide Telecommunications Network FIPRONIL Information Sheet Oregon State University and the U.S. Environmental and Protection Agency 1997(EPA).<http://ace.orst.edu/info/nptn/>

## METHOPRENE

**Methoprene is the second ingredient in Frontline made by Merial Australia. It is also contained in products that include Atosid, Apex, Diacan, Dianex, Kabat, Minex, Pharorid, Precor and ZR-515.**

According to Extoxnet , "Methoprene is mimics the action of an insect growth regulation hormone. It is used as an insecticide because it interferes with the normal maturation process. In a normal life cycle, an insect goes from egg to larva, to pupa, and eventually to adult. Methoprene artificially stunts the insects' development, making it impossible for insects to mature to the adult stages, and thus preventing them from reproducing." The Wikipedia describes methoprene as a juvenile hormone which stops pupae from developing into adult insects. Hence it is not effective against adults, but is effective against larval forms of insects and mites. It is used most widely as a mosquito larvacide Altosid which is used to prevent West Nile virus.

Extoxnet information includes; "To be effective, it is essential that this growth inhibitor be administered at the proper stage of the target pest's life cycle. Methoprene is not toxic to the pupal or adult stages. Treated larvae will pupate but adults do not hatch from the pupal stage. Methoprene is also considered a larvicide since it is effective in controlling the larval stage of insects. Methoprene is used in the production of a number of foods including meat, milk, eggs, mushrooms, peanuts, rice, and cereals. It is also used in aquatic areas to control mosquitoes and several types of ants, flies, lice, moths, beetles, and fleas. It is available in suspension, emulsifiable and soluble concentrate formulations, as well as in briquette, aerosol, and bait form." In Frontline it is a "spot on" product, coming in preprepared weight based doses to be applied at a point between the shoulders according to Merial frontline's Australian makers product information. It is registered for use on cats and dogs for flea control.

**According to Extoxnet**, Methoprene is practically nontoxic when ingested or inhaled and slightly toxic by dermal absorption. The oral LD50 for methoprene in rats is greater than 34,600 mg/kg, and in dogs is greater than 5000 mg/kg .It is slightly toxic by skin exposure, with reported dermal LD50 values of greater than 2000 to 3000 mg/kg in rabbits. Methoprene is not an eye or skin irritant, and it is not a skin sensitizer . The inhalation LC50 for methoprene in rats is greater than 210 mg/L [155]. No overt signs of poisoning have been reported in incidents involving accidental human exposure to methoprene .

No methoprene-related effects were observed in 2-year feeding trials with rats given doses of 250 mg/kg/day, nor in mice given 30 mg/kg/day . At higher ingested amounts over a longer period some liver changes were seen in mice. Experimental data indicate that no reproductive hazards are associated with methoprene. There have been no teratogenic effects in animals dosed with methoprene .Methoprene does not appear to be mutagenic. Experimental data suggest that methoprene is not carcinogenic.

In mammals, methoprene is rapidly and completely broken down and excreted, mostly in the urine and feces . Some evidence suggests that methoprene metabolites are incorporated into natural body components. Methoprene is excreted unchanged in cattle feces in amounts that are sufficient to kill some larvae that breed in dung .

Methoprene is slightly toxic to birds. These effects appeared as soon as 2 hours after treatment and persisted for up to 2 days and included slowness, reluctance to move, sitting, withdrawal, and incoordination . Methoprene is slightly to moderately toxic to fish. Methoprene is very highly toxic to some species of freshwater, estuarine, and marine invertebrates, while the acute LC50 values are greater than 100 mg/L in freshwater shrimp, and it is greater than 0.1 mg/L in estuarine mud crabs. Methoprene had very little effect, if any, on exposed non-target aquatic organisms including waterfleas, damselflies, snails, tadpoles, and mosquito fish . Tests with earthworms showed little if any toxic effects on contact . It is nontoxic to bees . Methoprene is of low persistence in the soil environment. In soil, microbial degradation is rapid and appears to be the major route of its disappearance from soil. Methoprene also readily undergoes degradation by sunlight and is rapidly and tightly absorbed to most soils. It is slightly soluble in water . Methoprene degrades rapidly in water. Studies have demonstrated half-lives in pond water of about 30 and 40 hours at initial concentrations of 0.001 mg/L and 0.01 mg/L, respectively . At normal temperatures and levels of sunlight, technical Altosid is rapidly degraded, mainly by aquatic microorganisms and sunlight . Altosid is biodegradable and nonpersistent, even in plants treated at very high rates.

Methoprene is not available on its own and is therefore not given a separate rating.

## References

Frontline Plus Product Information from Merial Australia 2006

EXTOXNET Extension Toxicology Network Pesticide Information Profile Methoprene.  
<http://extonet.orst.edu/pips/mrthopre.htm>

WIKIPEDIA- Methoprene <http://en.wikipedia.org/wiki/Methoprene> March 2007

## AMITRAZ

Amitraz is a topical parasite control agent, its action is apparently not fully understood, but it is suspected to work by interfering with the nervous system of susceptible parasites. It is supplied as a topical solution (19.9%) and in tick collars (9%). Veterinary formulations include Mitaban (Upjohn), Preventic (Allerderm/Virbac) and Taktic (Hoescht) and Ectodex (50g/L amitraz) as well as generic brands.

The following information about Amitraz was written by Shipstone ,2000 referring to *Demodex* , a mite that affects dogs. Three types , a follicular mite *D canis*, a short bodied mite *D cornei* and a long bodied mite (unnamed) have been described. Topical Amitraz, a monoamine oxidase inhibitor in a xylene base is registered for use as a miticide in Australia. The dose and frequency of application of amitraz affects reported efficacy (80% at 600mg/L weekly, 67% at 300mg/L weekly and 25% at 600mg/L fortnightly. The registered use rate in Australia is 500mg/L applied 3-5 days. Long haired animals should be clipped to allow increased penetration of the active ingredient to skin level and all crusts and exudates should be removed using an antimicrobial shampoo such as benzyl peroxide or chlorohexidine.

The animals needs to be totally dried before application and allowed to air dry following application.

Ectodex contains 50g/L of Amitraz and is registered for mange mites and some specific ticks on dogs by Intervet New Zealand. It cautions against use in Chihuahuas, puppies under three months and in animals affected by heat stress.

In a treatment regime worked out by Lee Skerratt and Clare Davis and published in WildCry the newsletter of Wildlife Care Network, Amitraz as Ectodex was suggested for use on day two after bathing the wombat . This contradicts information provided by Shipstone re ensuring the animal is dry before applying Amitraz, but given the Skerratt/Davis regime also involved other miticidal interventions and not Ectodex alone , this perhaps explains the variation.

Ectodex's manufacturer also advises wearing full chemical contamination wear while using the product.

Toxicity includes transitory sedation, bradycardia, hypothermia, hypotension, bloat, polyuria, hyperglycaemia and vomiting have been noted, particularly in animals 5kg and less. These symptoms can be treated using yohimbine ( Parnell Lab.Aus.) or atipamezole (Novartis).(Shipstone 2000) and effects can last up to 72 hours and ingestion of flea collars can lead to poisoning.(Ruben,D)  
Amitraz is toxic to fish .

Rating; Miticide and Ectodex are washes needing repeated applications; 1,3,1,1,1=7

## References

Davis,C and Skerratt,L. Mange Update.Reproduced from Wildcry-newsletter of the Wildlife Care Network. 1995.

Ectodex EC Acaricidal Dog Wash. Product Information.Intervet. 49 George Stree Auckland, New Zealand.

Ruben,D. PetPlace Product Information. [http://www.petplace.com.drug-library/amitraz-mitiban-preventic/page\\_1.aspx](http://www.petplace.com.drug-library/amitraz-mitiban-preventic/page_1.aspx)

Shipstone,M. Generalised demodicosis in dogs, clinical perspective. Australian Veterinary Journal. Vol 78. No.4. April 2000.pp.240-242

There are many other products that have not been included within this list. If people caring for wombats would like a particular product researched and evaluated by the criteria used in this report they are welcome to contact the Wombat Protection Society of Australia and an analysis will be made. We recognize that other easily accessible products including malathion ( in Malawash) and benzyl benzoate , used in many human scabies treatments as well as carbaryl and coal tar products are available . Due to their method of application or other factors already canvassed in the report, these have not been examined individually as it was felt they would receive lower rankings than those already examined.

### **Summary of Rankings**

**Precipitated sulphur in oil-self application method -23**  
**Lemon juice/fermented- 21**  
**Moxidectin in Cydectin pour on for cattle - 18**  
**Selamectin in Revolution spot on for dogs -18**  
**Precipitated sulphur in oil –applied by human-16**  
**Eprinomectin as pour on in Ivomec-Eprinex-15**  
**Moxidectin combined with Imidacloprid in Advocate spot on for dogs-13**  
**Ivermectin as Ivomec Pour on –11**  
**Fipronil alone or in combination with Methoprene in Frontline spot on for dogs-10**  
**Imidacloprid alone in Advantage spot on for dogs -9**  
**Ivermectin as an injectable – 7**  
**Amitraz in washes; mticide/ectodex-7**  
**Phospmets in poron or porect in any form -0**