Fluke larvae burrow through the liver, impacting stock health and production. The result is poorer production and growth rates, and reproductive losses – and a hole in your profits.

GET UP TO SPEED ON LIVER FLUKE AND HOW TO BEAT IT.

www.virbac.co.nz/fluke
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Right: Liver showing chronic Liver Fluke infestation.
In 1379, Jean de Brie was the first to describe “liver rot” without directly attributing it to the liver fluke, although its presence was noted. Since then, many researchers have studied this parasite whose biological description is well known but whose abilities to adapt to changes in cattle management and anthelmintic treatment is still surprising us today!

Although there are more effective anthelmintics and the epidemiology is better understood it is still likely that seasonal variations and geographical risks are predisposing to preventable subclinical effects.

This technical manual provides more detailed knowledge about the significance and impact of this parasite. Where possible it references New Zealand data but also provides relevant information from research conducted elsewhere but applicable to the New Zealand situation.

Liver fluke, Fasciola hepatica, is a major parasite of livestock in temperate regions throughout the world, including New Zealand. Liver flukes infect upwards of 300 million cattle and 250 million sheep worldwide.

In New Zealand no formal research has been conducted to assess National level costs overall but this manual will discuss herd level impacts in cattle herds. Indications are that it costs around $100m per year in Australia (Boray 2009) identifying the significance of impact of the disease.

Fluke-infected sheep and cattle often demonstrate no clinical disease, but subclinical blood loss, tissue damage and impairment of appetite, can lead to reductions in growth and weight gain, milk production and fertility. Animals that become heavily parasitised, however, can develop severe clinical disease and may die. Young animals are particularly vulnerable.

While liver flukes can have devastating effects on animal health and performance, they are relatively easily controlled. They have a complex life-cycle that is closely linked with particular habitats and heavily influenced by season. This means that we can design highly effective strategic control programmes that suppress fluke numbers to levels with minimal economic impacts. The key to success is using the best products at the best times.

The FlukeKill™ programme, a Virbac initiative, guides you through treatment timing and product choice. The program is supported by research completed by world renowned authorities on liver fluke, aiming to limit the economic impact of the liver fluke in a highly effective and sustainable way.
Liver fluke disease is regionalised due to climatic and geographical factors. The data displays the positive rate of samples submitted for liver fluke for districts with more than 20 samples submitted. Obviously these samples are likely to have been submitted where liver fluke was suspected and therefore do not indicate prevalence but give some indication of relative frequency of diagnosis in different districts.

Liver fluke was first recorded in New Zealand at Hawke’s Bay in 1896. In 1908 it was reported in Nelson and on the West Coast of the South Island.

By 1945, Hawke’s Bay was the most important endemic area, with smaller foci at Poverty Bay, Opotiki and Ngaruawahia in the North Island and the Owen Valley, Lake Rotoiti, Omakau and Wanaka in the South Island. Following increasingly frequent reports of fluke on farms previously regarded as fluke-free, the prevalence of infestation in slaughtered cattle was surveyed in 1969 and the distribution of infested farms was determined in 1970.

Liver fluke had spread to Northland and the west coast of the North Island and to pockets as far south as Eketahuna.

There were additional foci in Marlborough, Nelson and Westland and just south of Timaru. Cattle in the North Island had a 7.5% infestation rate compared to 0.7% for the South Island and a New Zealand average of 5.8%. Corresponding figures for sheep were 4.4%, 0.4% and 3.0%.

Mitchell’s summary in 1995 in Surveillance provides good historical information on various surveys to that time. A more comprehensive survey on slaughtered stock in 1984 – 85, concluded that the tentative prevalence in the North Island cattle had risen to about 12.8% overall based on studies of over 16,000 lines of stock. Trace back from the survey also indicated a geographical spread of the disease since the studies in the 1970s. South island cattle prevalence was only about 2% overall focused on the West Coast and Marlborough Tasman.

In 1984 an independent survey conducted by Edington and cited by Charleston et al. (1990) indicated average prevalence of over 31% and 35% for the Kokiri slaughterhouse servicing the West Coast. It was also noted that a Northland survey (Kearns) identified a significant increase in the fluke herd prevalence to about 10% from 3.8% in 1969-70. The article notes that most of the increases were due to increased geographical spread of areas affected in these regions.

Referencing the sheep situation it was noted that Hawkes Bay was stable at around 10.5%, vbut doubled in Auckland to 12.6% and trebled in Taranaki to 16.9%. In the SI it was noted that prevalence had increased to 18.1% in Nelson and 29.4% in West Coast making them the highest regional prevalence in the country.

A. The young flukes reach the liver within about a week of being ingested.
B. They penetrate the liver capsule and migrate through the liver tissue, feeding on blood and growing rapidly.
C. Young flukes from penetration to five weeks old are referred to as early immature flukes, while from five weeks old they are known as immature flukes.
D. About eight weeks after ingestion they leave the liver and enter the bile ducts to become adult flukes. They are generally about 2-3cm long when fully mature.
E. They begin producing eggs about 10-12 weeks after ingestion. While most flukes are eliminated within a year of infection, some have been known to survive several years in cattle and more than seven years in sheep. The eggs travel with the bile from the gall bladder into the intestine and excreted in faeces. Eggs can accumulate in the gall bladder and may be released for weeks after the flukes have been killed.
**FLUKE SNAILS**

Only snails in the family *Lymnaeidae* are suitable as intermediate hosts for the liver fluke. This is a different family of snails from those that carry stomach flukes. *Lymnaeid* snails are characterised by having a shell with a clockwise spiral and fleshy, triangular tentacles.

*Lymnaeid* snails thrive in areas with very shallow, slow-flowing water. Ideal habitats include springs, small creeks, dam overflows and irrigation channels. When conditions are very dry, the snails can bury into the mud and become dormant, potentially surviving for many months in that state.

In New Zealand, the main host is a snail called *Lymnaea columella* (sometimes *Pseudosuccinea columella*), which inhabits ponds and marshes and even found on irrigated pasture and in wet cattle-pugged pasture.

*Above: L.columella* (sometimes called *Pseudosuccinea columella*)

---

**THE INFLUENCE OF LIVESTOCK FEEDING BEHAVIOUR**

Cattle are particularly prone to liver fluke infections because they often feed in the wet areas that suit the snail intermediate host, which are therefore the areas with the highest level of contamination with metacercariae, the infective fluke stage.

Sheep are less prone to exposure because they usually avoid feeding in wet areas unless conditions are very dry and they are chasing green feed. However sheep tend to graze pasture to very low levels so when they do graze risk areas are likely to ingest quite high doses. During late summer and autumn, the most likely time for infection, pastures dry off in many regions and grazing stock will tend to look for green pick in the wet areas.

Similarly, animals will tend to feed more in wet areas in times of drought. Unlike most parasites, infection levels of fluke can increase in dry conditions.

*Above: Stock that drink and graze in wet areas are more likely to come in contact with the water snail.*

---

**LIVER FLUKE: A RAPIDLY MULTIPLYING PARASITE**

- **1 animal**
  - **150 liver flukes**
  - **50 000 eggs per day**
  - **7 500 000 miracidia**
  - **4 000 cercariae**
  - **30 000 000 000 metacercariae** (infective larvae)

One animal can hold an infection of up to 300 mature flukes. Each fluke can lay up to 50 000 eggs per day. Eggs hatch to form first stage flukes. These miracidia multiply inside the snail to create up to 4 000 cercariae each. The cercariae leave the snail, encyst on vegetation, forming infective metacercariae.
While both the liver fluke and its snail intermediate host require a wet environment to complete their lifecycles, temperature plays more of a role in influencing liver fluke populations than rainfall does.

Both the flukes and the snails thrive over the warmer months of the year. Heading into winter, when the average daily temperature drops below 10°C, fluke eggs stop hatching, development of the larval flukes in the snails slows down and the snails become inactive.

The infective larvae already on the pasture will die out over time and this will happen more quickly when there is very cold weather (e.g. a series of heavy frosts). However in New Zealand’s North Island, this is unlikely to occur in Northland, Bay of Plenty and Hawke’s Bay. This means that in colder areas the fluke life-cycle will effectively come to a halt over winter and the opportunity for cattle to pick up new infections diminishes. By the end of winter most of the flukes in the animal will be mature because they haven’t been acquired in the previous few months.

As temperatures become warmer in spring, the fluke snails become active again, potentially releasing parasites that they have carried through the winter. In addition, fluke eggs begin to hatch again, so that snails can quickly become infected if the livestock are carrying appreciable numbers of flukes. The fluke population builds up throughout the warmer months, with peak pasture contamination with metacercariae occurring in late summer/early autumn. This is often the time that clinical disease is observed.

In New Zealand situations the hot dry regions such as Northland and Hawke’s Bay have higher prevalence probably due to animals grazing wetter areas and the West Coast region in the South Island suffers higher prevalence due to extensive wet areas with suitable habitat for the intermediate host snails.

While adult liver flukes impact on the health of livestock through their blood-feeding habits in the bile ducts, it is the immature and early immature stages in the liver that cause the most damage. The type of disease seen as a result of liver fluke infection is often divided into three categories based on the amount of liver damage caused by the young flukes. Those categories are acute, subacute and chronic.

**LIVER FLUKE: RISK BY REGION**

*Liver Fluke risk in New Zealand by region.*

| High risk | Medium risk | Low risk |

**DRY AREAS**

During intense dry periods stock are forced to drink and eat from wet areas that may harbour liver fluke, increasing the chance of infestation.

**WET AREAS**

Farms with persistent wet areas, unfenced waterways and that are prone to dry periods of weather all run the risk of liver fluke infestation.
LIVER FLUKE INFESTATION

FUNCTIONS OF A HEALTHY LIVER

The liver is the organ that is central in supporting general health, vitality, production and reproduction.

It has around 500 different functions essential to health and production.

- **Supports almost every other organ**
- **Fights infections**: cleans the blood particles of infections, including bacteria etc.
- **Filters out toxins**: neutralises and destroys toxins that are harmful to the animal.
- **Stores essential elements**: such as vitamins and minerals (including trace minerals).
- **Hormones**: responsible for the manufacture, regulation and breakdown.

*Right: A healthy liver.*

EFFECT OF LIVER FLUKE ON THE ANIMAL

Liver fluke cause severe damage to the liver, resulting in:

- Haemorrhage and blood loss
- Anaemia
- Liver scarring
- Reduced appetite
- Possible death
- Protein loss
- Loss of liver function
- Reduced immunity
- Reduced reproduction
- Reduced production

*Top right: Bottle jaw. Bottom right: Anaemia and lethargy in cattle from liver fluke.*
**DAMAGE TO BODY ORGANS**

Once ingested, young fluke emerge from cysts in the small intestine, they penetrate the intestinal wall and enter the abdominal cavity. They migrate through the animal to the liver.

*In cattle, ± 25 % of the metacercaria ingested will reach the liver, the rest migrate through the body and cause damage to other organs.*

*Right: Bleeding caused by migrating liver fluke.*

**DAMAGE CAUSED BY IMMATURE FLUKE**

The most significant damage to the liver is caused by the migrating immature stages.

The immature fluke stages will often outnumber the mature stages.

*Below: Damage caused by migrating liver fluke from ± 2 weeks to adult stage.*

**DAMAGE CAUSED BY MATURE FLUKE**

Adult fluke live in the bile ducts where they feed on the blood of the host, which can cause anaemia. They also create thickening and calcification of the bile ducts which in turn can create blockages.

*Below: Thickening calcification and blocking of bile ducts.*

*Bleeding spots.*

*Thickening of the bile ducts.*

*Necrosis.*

*Calcification of the bile ducts.*
LIVER FLUKE DISEASE

**ACUTE DISEASE**

This form of the disease occurs where a large number of metacercariae are ingested over a short period of time. This results in the animal’s liver receiving many puncture wounds as the early immature flukes invade the liver. This damage can lead to the death of the animal through massive blood loss (bleeding into the body cavity) and the onset can be rapid, with the animal rarely showing signs of illness prior to its death.

Deaths are generally seen 1-2 weeks after the animals have gained access to wet areas. Young animals are particularly prone to this form of the disease because even minor blood loss can have a major impact on them.

**SUBACUTE DISEASE**

The subacute form of the disease is seen where animals acquire a moderate number of flukes or a large number of flukes over an extended period of time. This means that there isn’t enough acute damage at any one point in time to cause the animal’s immediate death. There is, however, massive damage to the liver that can lead to the animal wasting away quickly. Deaths occasionally occur around eight weeks after first infection when the immature flukes are at their largest, particularly in young animals, but in most cases the issue will have been identified and treated before the animals deteriorate to that point.

The scarring and fibrosis that result from the liver damage can lead to permanent damage and under-performance of the animal, including compromised immunity and metabolic inefficiency.

**CHRONIC DISEASE**

This form of the disease results from the ongoing acquisition of smaller numbers of flukes and is the form seen most commonly in adult cattle. Animals may waste away over an extended period of time, becoming emaciated, lethargic and anemic as a result of tissue damage and blood loss.

This form is particularly important in sheep which generally don’t develop good immunity and liver damage can occur over multiple seasons.

Other physiological responses include suppressed appetite and reduced feed conversion efficiency. They will often develop a distended abdomen and bottle jaw (indicators of a fluid imbalance associated with the loss of red blood cells).

*The majority of animals, however, will show no obvious signs of infection and will simply not perform as well as they should.*

A fluke burden of as few as 30 flukes is sufficient to retard an animal’s performance and an infection rate of 10% of the herd is considered to be the threshold where economic impacts become significant.
IMMUNITY TO LIVER FLUKE INFECTION

Can animals protect themselves from liver fluke?

There is little evidence that livestock can mount resistance to their first challenge from liver fluke. A form of resistance can develop over time but this is physiological and often associated with extensive prior damage to the liver, often involving hardening and calcification of the bile ducts. Unfortunately, this type of resistance is not a protective immune response, having little ability to control immature flukes. Although fluke numbers can be suppressed, liver damage and consequently production loss will occur.

Cattle develop a level of resistance by the time they are adults, but sheep develop little to no immunity. As a result the most severe disease is often seen in young cattle and older sheep.

With the help of Virbac Animal Health, Professor Terry Spithill and his team at La Trobe University plan to develop a vaccine that allows livestock to develop a protective immune response to liver fluke. Professor Spithill, who has more than 30 years experience in parasite immunology, including investigating the genetics of triclabendazole-resistant fluke, says “A successful vaccine that provides protection will kill invading immature parasites before significant liver damage occurs, and consequently reduce production loss caused by liver fluke.”

However, with a vaccine for liver fluke some time away, all classes of animal still require an effective liver fluke control programme. Professor Spithill says, “Not only do animals have little ability to mount a protective immune response to the first liver fluke infection, there is good evidence that fluke infection actually suppresses the animal’s immune system and immune responses to other diseases may be altered”.

PROF. TERRY SPITHILL

Professor Terry Spithill is the co-director of The Centre for AgriBioscience at La Trobe University. His major area of research investigates host immune responses to parasites, parasite immune evasion mechanisms, drug resistance, and parasite proteomics with the aim to develop vaccines or drugs to control parasitic diseases.

Right: Professor Terry Spithill
The economic impacts of liver fluke infection include reduced growth rates and weight gains, reduced milk production, reduced fertility, liver condemnation, secondary bacterial infection, mortality, and increased drenching costs (Boray, 1985; Dargie, 1986).

**LOWER GROWTH RATES AND WEIGHT GAINS**

Studies have shown that even subclinical infections of as few as 30-40 flukes can reduce weight gains by 8-9%, while higher levels of infection have reduced weight gains by 28%.1 2

While the greatest impact occurs in the first 16 weeks of infection, the performance of animals can be impaired for the rest of their lives, even after the flukes have been removed2. Young animals are particularly vulnerable and may never reach their genetic potential regardless of subsequent management.

**IMPAIRED PERFORMANCE**

Several studies conducted in the USA have demonstrated that treatment of fluke-infected cattle with an effective flukicide at induction produces a positive cost-benefit result and improved productivity.

The studies showed increases in weight gains between 5.9% and 9.5%, compared with animals carrying fluke burdens.3

**LOWER CARCASS VALUE**

In addition to reduced growth in the feedlot, abattoirs will condemn livers that show visible damage. Recent trials show that liver infection reduces cold carcass weight, carcass yield, marbling score and conformation.1 2 The reduced value of carcasses through liver condemnation and quality downgrades alone exceed the cost of an effective treatment.

**REDUCED FERTILITY**

Liver fluke infection has been reported to have a negative impact on cow fertility. Infections have been shown to reduce conception rates in heifers by up to 50% and delay puberty by up to 39 days.3 Managing fluke in heifers should be prioritised to limit production losses. In dairy cows, heavy fluke infection can also increase the inter-calving interval by 4.7 days.4

Non-milking heifers should be considered for multiple strategic treatments where necessary.

**BLACK DISEASE**

Black disease is a clostridial infection that occurs when *Clostridium novyi* proliferates within damaged liver tissue. Even light fluke infections can create enough damage for the disease to occur. While invariably fatal, the disease is rare these days because of the widespread use of effective clostridial vaccines.

---

LIVER FLUKE: CALF WEIGHT

Reduction of body weight in calves infected with liver fluke

<table>
<thead>
<tr>
<th>Flukes present in liver</th>
<th>Reduction in growth rate (grams/week)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 - 80</td>
<td>1200</td>
</tr>
<tr>
<td>200</td>
<td>1000</td>
</tr>
</tbody>
</table>

LIVER FLUKE: MILK PRODUCTION

Reduction of milk production in cows affected with liver fluke

<table>
<thead>
<tr>
<th>Loss of milk production in litres per cow per lactation</th>
<th>Range in production loss due to liver fluke</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 L to 300 L</td>
<td>-1200g</td>
</tr>
</tbody>
</table>

REDUCED MILK QUANTITY AND QUALITY

The effect of liver fluke infection on milk production is well documented and the parasite can be a significant impediment to dairy farming. A heavy infection can cost 0.7kg / cow per day in lost milk production and a 0.06% reduction in milk protein. While this has a direct impact on income for dairy farms, infection can also compromise growth rates in the offspring of infected beef cattle.

THE IMPORTANCE OF CONTROLLING YOUNG FLUKES

It is important to control the youngest stage of liver fluke possible. The longer the immature liver flukes are permitted to migrate through the liver tissue, the greater the damage and productivity losses they cause.

LIVER FLUKE: EFFECT ON GROWTH

Lack of body weight gain expressed as weight loss in grams per week on calves in differing severity of liver fluke infection.

A study by Dr Joe Boray (1999) clearly demonstrated the economic advantage in removing early immature flukes. As shown in the figure above, animals that were treated to remove early immature flukes 1-2 weeks post-infection (PI) had greater weight gains than animals treated 4-6 weeks PI or 8-12 weeks PI.

After 20 weeks, the average body weight of the early treated group was 8kg heavier than the group treated 4-6 week PI and 13kg heavier than the group treated to remove fluke after they had matured. Based on current stock prices, this could equate to as much as an additional $29 per head.

As with any animal health issue, it is important to define the problem prior to implementing a control programme. There is a range of tests available to detect liver fluke infections. We also now have the ability to determine prevalence of infection within dairy herds and to test the efficacy of treatments. It is important, however, to know the restrictions and capability of each test.

**EGG COUNTS**

Testing for liver fluke infection has traditionally been done by microscopic detection of fluke eggs in the faeces. While this test is highly reliable for detecting fluke infections in sheep, it is not very reliable for cattle. In cattle, liver flukes are irregular and intermittent egg layers and many flukes never reach the egg laying stage, despite developing and causing damage in the liver; so detection of eggs in the faeces is hit and miss (Vercruysse & Claerebout, 2001). Further, this test will only detect adult flukes, so it is a poor option for diagnosing acute and subacute forms of liver fluke disease.

**BLOOD AND MILK ANTIBODY ELISA**

The ELISA (Enzyme Linked Immuno-Sorbent Assay) is a test that detects the antibodies that cattle (and sheep) produce in response to liver fluke infection. The antibodies are found in the blood or milk of infected stock as quickly as 3 weeks after infection and the test is highly accurate (98%) for both types of sample (Cornelissen et al., 1999).

It is an ideal test for dairy herds because a sample can be taken from the milk vat and the result will indicate the presence of infection across the milking herd.

For beef cattle, blood samples are used for detection of fluke infection only i.e. not quantification. Blood samples are usually taken from a representative sample of ten animals, so numbers are insufficient to indicate the prevalence of infection.

Antibody levels are not indicative of the number of flukes present in the animals, so they cannot be used to assess the intensity of infection. The drawbacks of this test are that blood samples are difficult to collect and the test cannot be used to assess the efficacy of a treatment because the antibodies take several months to degrade even after all of the flukes have been removed from the animal.

**FAECAL ANTIGEN ELISA – RECENT DEVELOPMENT**

A test that detects F. hepatica antigens (proteins released by the parasite) in the faeces of the host animal has recently been validated for use in Australia. This test is highly accurate and can detect even a few flukes in sheep or cattle, but the flukes are detected only once they leave the liver and move to the bile ducts.

While there is an advantage associated with taking faecal samples rather than blood samples from beef cattle, the biggest advantage provided by this test is that it can be used as a post-treatment efficacy test. The antigens in the faeces disappear very soon (1-2 weeks) after the flukes have been removed, so a positive result 3-4 weeks after treatment indicates that flukes have survived the treatment and may be resistant to the chemical used.

**POST-MORTEM EXAMINATION**

Examination of the liver can be useful in a number of situations and used to determine how heavily animals are infected. Examination of the liver is the only way to determine if an animal has died from the acute form of liver fluke disease. Examination will reveal an otherwise healthy looking liver that is full of pinprick holes and leaking a lot of blood.

The incidence and severity of the chronic form of the disease can also be gauged by examination of the livers of slaughtered animals. Abattoirs will often provide feedback on the rate of liver condemnations in a particular line of animals, but it is important to confirm the cause of those condemnations to ensure that it is liver fluke causing the problems.

It is easy to determine the severity of fluke infection if animals are killed on-farm. Simply remove the liver and look for any signs of damage or scarring. Cut the liver and the bile ducts open and look for any flukes, which will be readily apparent (squeezing the liver may reveal flukes that were not obvious initially). Chronically infected cattle will generally have a brown tar-like deposit on the inside of the bile ducts and the wall of the duct will be thickened and calcified.

![Left: Chronically infected liver showing thickened ducts, tar-like deposit and adult flukes. Far left: Liver showing chronic infestation.](image)
Like all parasites of livestock, effective and sustainable control must be based on a sound understanding of the interaction between the parasite, its hosts, and the environment (Integrated Parasite Management). There are no chemicals currently registered in New Zealand for the widespread control of snails, so fluke control measures must focus on limiting exposure of the livestock to infection, and treatment of the animals to remove any parasites they do acquire.

### Non-chemical approaches

Non-chemical control of liver fluke populations focuses on reducing the exposure of livestock to wet areas that harbour the snail intermediate host and the infective stage of the fluke. One approach is to modify the wet areas to make them an unsuitable snail habitat. This could include improving drainage, to dry areas out, or modifying water courses to improve water flow. Another option is to fence the wet areas off so that animals cannot graze in those areas. Unfortunately for many producers, neither of these options is feasible or economically viable as a complete solution.

These approaches should not, however, be abandoned entirely. By reducing snail habitat and then fencing off the remaining wet areas, it is possible to manage those areas to minimise infection rates and the subsequent need for treatment of the animals. For instance, fluke-infested areas should not be used to graze young, highly susceptible stock. Where possible, those areas should only be grazed in late winter when the pasture contamination with infective metacercariae is likely to be at its lowest. It is also possible to identify and selectively treat only animals that have been grazing in the risky areas, reducing the amount of chemical treatment required.

### Chemical treatment

The effective control of the liver fluke through chemical treatment relies on two key factors: choice of product and timing of treatment. It is only by using the right product at the right time that maximum effect will be achieved.

There is a wide range of single active and combination products available for liver fluke control and the level of control offered varies remarkably. In order to get an approved label claim, the product needs to be at least 90% effective against each stage of fluke identified on the label.

Generally speaking, the younger the fluke is, the harder it is to kill, so while all flukicides will kill the adult flukes, few will kill the early immature flukes and only synergistic combination products reliably kill the 2-week-old early immature flukes.

### Efficacy: chemical and synergistic combinations

Efficacy of actives against flukes of different ages

<table>
<thead>
<tr>
<th>Active ingredients</th>
<th>Early Immature</th>
<th>Immature</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 weeks</td>
<td>4 weeks</td>
<td>6 weeks</td>
</tr>
<tr>
<td>Oxyclozanide</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Albendazole</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Clorsulon</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Nitroxynil</td>
<td>±</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Triclabendazole</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Triclabendazole + Oxendazole (FlukeCare® + Se )</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nitroxynil + Clorsulon + Ivermectin (Nitromec®)</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

± more effective in cattle than sheep.
SYNERGISTIC COMBINATION PRODUCTS

Synergy is said to occur only where the combination of chemicals has a greater effect than that expected from the activity of the individual chemicals.

In the case of flukicides, this can be seen where nitroxynil (kills adult and late immature flukes) and clorsulon (kills adult flukes only) are combined into one product (Nitromec® Injection). This combination increases effectiveness against early immature larvae which the individual agents by themselves do not possess.

While it might be expected that, at best, the product will provide control of adult and late immature flukes, the synergy between the two chemicals actually gives control of all stages including early immature flukes as young as 2-weeks-old. A similar synergistic effect can be seen where a combination of triclabendazole (TCBZ) and oxfendazole (FlukeCare® + Se) provides efficacy superior to triclabendazole alone.

Data from on-farm trial work has confirmed that the superior performance of the synergised combination translates to a productivity benefit for the producer.

Synergistic products have several advantages:

- Firstly by killing larvae at earlier stages you significantly reduce the level of liver damage and all its inherent effects on metabolism and immunity.
- Secondly there are less migrating larvae missed that continue on to adult and re-infect pasture.
- Potentially this greater efficacy allows better use of strategic liver fluke control [see later section] with longer periods between drenches, also preserving efficacy by lowering the risks of resistance development.

EFFICACY: CHEMICAL AND LIFE STAGE

*Efficacy of actives against flukes of different ages*

**Fluke eggs in gall bladder**
Ready for release into the digestive tract

**Adult fluke in bile duct**
Eggs layed ±10 to 12 weeks after infection

**8 week old immature fluke**
End of migratory phase, ready to enter bile duct

**4 week old early immature fluke**
Migratory phase, causing haemorrhage and scarring

**2 week old fluke**
Newly arrived from the gut
CONTROL METHODS

EFFICACY OF ACTIVES AGAINST FLUKES OF DIFFERENT AGES

The efficacy of triclabendazole compared to the synergistic combination of triclabendazole and oxfendazole against 2-week-old early immature flukes in cattle.

LEVEL OF CONTROL

Adult stage only
- Clorsulon
- Oxyclozanide
- Nitroxynil

From 4 weeks to adult (dose dependant)
- Closantel

All stages from 2 weeks to adult
- Triclabendazole

LIVEWEIGHT GAIN FOLLOWING TREATMENT

Results from a field trial conducted on Angus weaner heifers on the Southern Tablelands of NSW.

EFFICACY OF ACTIVES AGAINST FLUKES of different ages

Percent Efficacy

- Oral Triclabendazole
- FlukeCare® + Se

(n=20 per group, mean starting weight = 273kg)

Liveweight gain following treatment

Mean liveweight gain (kg)

Days after treatment

Fasinex 240 + Cydectin Pour On
FlukeCare® + Se + Cydectin Pour On

RESULTS FROM A FIELD TRIAL

- Virbac Study: AT82
- Virbac Study: AT84
- Walker et. al. (2004)
- Shi et. al. (1989)
- Hutchinson et. al. (2009)
- Boray (1982)
- Richards et. al. (1990)
- ---- 90%

KEY

- Migrating Stage
- Early Immature
- Immature
- Adult
- Eggs inside the gall bladder
FLUKECARE® + SE BLOOD PROFILE

- The oral product FlukeCare® + Se (Selenium) showed a typical blood plasma profile for an oral product.
- It peaked over 8 times higher than the pour-on product.
- The active was rapidly absorbed, peaking day 1 following treatment.
- The blood level of the triclabendazole in FlukeCare® + Se remained higher than the pour-on until day 5.

When the efficacy against 2-week-old and 4-week-old liver flukes was assessed for the two products, FlukeCare® + Se demonstrated superior control compared with the pour-on, as shown in the graphs above. Further, absorption through the skin is highly variable depending on the coat and skin condition of the animal. A recent study (Sargent, et al., 2009) showed that treatment of cattle in winter with a pour-on flukicide could reduce the efficacy of the product.

Field data has shown that the lower efficacy offered by pour-on triclabendazole treatment translates into lost production.

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DELIVERY METHOD – ORAL VS POUR-ON

Flukicides have historically been applied as oral (triclabendazole) or injectable (clorsulon, nitroxynil) products. In recent years, however, triclabendazole pour-ons have entered the market place.

While clearly having the advantage of ease of application, there is considerable doubt surrounding the ability of these products to perform as well as comparable oral products. In order for triclabendazole to achieve a high level of efficacy against the early immature and immature liver flukes, the drug must reach a high concentration in the liver. Triclabendazole given orally is absorbed from the gastrointestinal tract and quickly transported to the liver via the portal blood flow, achieving a high concentration of the drug quickly.

In contrast, triclabendazole applied topically needs to penetrate through the skin and then travel through the entire vascular system before it reaches the liver. Triclabendazole is quite a large molecule, so this is a highly inefficient method of delivery. The graph to the right shows the concentration of a marker for triclabendazole in the blood of cattle treated with (FlukeCare® + Se) (an oral triclabendazole + oxfendazole product) or a pour-on flukicide (triclabendazole at 2.5 times the oral dose + abamectin).

GROUP MEAN PLASMA TRICLABENDAZOLE SULPHOXIDE CONCENTRATIONS OVER TIME

Concentration of a marker for triclabendazole in the blood of cattle treated with FlukeCare® + Se (an oral triclabendazole + oxfendazole product) or a pour-on flukicide (triclabendazole at 2.5 times the oral dose + abamectin).
FlukeCare + Se® has proven efficacy over pour-on fluke (triclabendazole + abamectin) drenches.
- In both studies FlukeCare+Se® achieved ≥99% efficacy against 2 and 4 week old stages of fluke.
- The pour-on group showed only 8% efficacy on 2-week old stages.
- The pour-on group failed to demonstrate effective control at 4 weeks.
- Significant numbers of liver fluke survived the pour-on treatment.

Multiple comparative efficacy studies² have been undertaken trialling FlukeCare + Se® against reference oral fluke products.
- FlukeCare + Se® has consistently demonstrated efficacy of 99% or greater against all stages of fluke.
- Only FlukeCare + Se® offers dual active control of liver fluke resulting in significantly better control of the early immature stages of liver fluke.
- Competitor oral drenches do not achieve the same level of control of the early immature stages of liver fluke.


TREATING FOR OTHER PARASITES

Animals that are infected with liver flukes are often carrying other parasites as well, so it is important to consider the other parasite issues that are important at the time of fluke treatment. For instance, Brown stomach worm (Ostertagia ostertagi) is the most damaging roundworm of cattle and is found commonly in those areas where liver fluke is a problem.

Other roundworm species are also common and can cause production losses in young animals. It therefore makes good sense in many cases to treat for roundworms at the same time as treating for the liver fluke. This can be done by either using a product that includes a broad spectrum endectocide as well as a flukicide (e.g. Nitromec® Injection) or by using another worming product at the same time as the flukicide.

The second approach has the advantage of being able to incorporate a product with highly persistent activity against roundworms.

Moxidectin oral formulations are particularly effective as a broadspectrum complementary anthelmintic, showing greater efficacy than injectable and pour-ons¹.

In sheep where Haemonchus spp. are a problem Moxidectin is likely to be more effective than Ivermectin and Abamectin².
TREATING AT THE RIGHT TIME WITH THE RIGHT PRODUCT

Treatment timings within the FlukeKill programme are based on the biology of the fluke and likely parasite challenge to the livestock. There are two core treatments within the programme: late autumn/early winter and late winter/early spring. Depending on the area, seasonal conditions and the success of appropriate timing, an additional treatment may be appropriate in summer and, in some circumstances, a mid-winter treatment may also be recommended.

TREATMENT STRATEGY BY SEASON

Use a strategic control strategy throughout the year to limit the production losses caused by liver fluke, based on 3 options: Curative Treatment, Preventative Treatment and Optional Treatment.

TREATMENT STRATEGY IMPACT: TOTAL FLUKE CHALLENGE IN ONE YEAR

![Graph showing the impact of different treatment strategies on total fluke challenge over a year.]
LATE AUTUMN/EARLY WINTER TREATMENT

The autumn treatment is the most important treatment within the FlukeKill program. It is designed to clean out the flukes prior to animals facing the stresses of winter. For this treatment to be most effective, it should be administered following the onset of frosty weather when the opportunity for cattle to pick up new parasites starts to diminish.

Once the average daily temperature drops below 10°C, the snails become inactive and the development of the larval flukes slows down, so fluke cercariae are no longer being released from the snails to contaminate the pasture. Further, many of the metacercariae already on the pasture will have been killed by the frost. It is therefore better to err towards treating late rather than treating too early and having the animals reinfected prior to winter.

Livestock can, at this time, harbour flukes of all ages, so it is important to use a product that will give the best control of all stages of the flukes, including the early immature stage. FlukeCare® + Se and Nitromec® Injection are the most effective products available for use at these times.

LATE WINTER/EARLY SPRING TREATMENT

The spring treatment is an essential preventative treatment that helps to break the fluke life-cycle by removing any flukes that have infected the animals throughout the winter.

By preventing the contamination of the pastures with fluke eggs as temperatures warm up, the snail intermediate hosts do not immediately become infected as they become active. It is therefore essential that this treatment occurs prior to the spring break.

It is better with this treatment to err towards treating early rather than waiting until too late and having fluke reproduction promoted early in the yearly cycle.

Fluke numbers in animals may be low at the end of winter, particularly if the pre-winter treatment was timed effectively, but even a few flukes can easily seed the environment with larvae (miracidia) that actively hunt out snail hosts.

The spring treatment is therefore immensely important in suppressing the early expansion of the fluke population, which has a flow on effect throughout the rest of the fluke season, reducing overall fluke numbers and minimising productivity losses.

The spring treatment is even more important if timing for the late autumn/early winter treatment was too early or the winter was mild so that substantial numbers of flukes infected the animals following the pre-winter treatment.

Winters are sufficiently cold in most fluke areas that little reinfection occurs in the later stages of winter. Therefore, the flukes within the animals will have had the required time to mature into the adult stage.

However, where treatment has been delayed until after the spring break or in warmer coastal areas where snails have not gone dormant and reinfection has occurred throughout the winter period, it is essential that a product that controls all stages of the flukes (FlukeCare® + Se or Combat Nitromec® Injection) should be used.

TYPICAL HOT CLIMATE TREATMENT

TYPICAL COOL CLIMATE TREATMENT
**SUMMER/EARLY AUTUMN TREATMENT**

In our coldest areas, the warmer period of the year is quite short, so fluke numbers rarely exceed levels that require control beyond the two core treatments outlined earlier. In most fluke areas, however, the extended period of warm conditions allows fluke numbers to build up to damaging levels well before the late winter/early spring treatment occurs.

The summer treatment for liver fluke in January/February, can be important when conditions have been ideal for snail development and distribution. Often following a warm wet spring for example and then going into a dry summer - particularly on properties with known histories of fluke problems. This treatment will reduce the amount of damage - particularly in young stock, prior to the autumn, and should control all fluke stages.

**MID-WINTER TREATMENT**

In some overseas countries such as Australia, fluke infection can continue throughout the year, even in winter. This can occur in warm coastal areas where the fluke life-cycle continues unabated all year.

This is likely to be rare in New Zealand probably only occurs in Northland in seasons with very warm winters. It can also occur in areas where there is extensive snail habitat and heavy fluke challenge so that many metacercariae survive through at least the early part of winter. Areas where this may occur include irrigation flats and country that has a high number of springs and small streams.

In these cases a mid-winter treatment may also be required. Highly effective all stage treatments (FlukeCare® + Se or Nitromec® Injection) should be used for all mid-winter treatments.
**FlukeCare® + SE for Dairy Cows**

**CONTROL OF FLUKE AGED 2 WEEKS**

- Synergised formulation of triclabendazole and oxfendazole.
- Ideal late autumn/early winter or summer treatment.
- Controls damaging 2-week-old early immature flukes.
- Broad spectrum control of internal parasites.

**FLUKE EGG COUNT DATA**

For the effective treatment and control of the following species of gastrointestinal parasites (*includes third and fourth stage larva and inhibited immatures):  

<table>
<thead>
<tr>
<th>COMMON NAME</th>
<th>GENUS</th>
<th>SPECIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liver Fluke</td>
<td>Fasciola</td>
<td>hepatica*</td>
</tr>
<tr>
<td><strong>ABOMASUM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barber’s Pole Worm</td>
<td>Haemonchus</td>
<td>placei</td>
</tr>
<tr>
<td>Stomach Hair Worm</td>
<td>Trichostrongylus</td>
<td>axei</td>
</tr>
<tr>
<td>Small Brown Stomach Worm</td>
<td>Ostertagia</td>
<td>ostertagi*</td>
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<tr>
<td>Thin Necked Intestinal Worm</td>
<td>Nematodirus</td>
<td>colubri</td>
</tr>
<tr>
<td></td>
<td></td>
<td>formis</td>
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<tr>
<td></td>
<td></td>
<td>helvetianus</td>
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<tr>
<td><strong>SMALL INTESTINE</strong></td>
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<td></td>
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<tr>
<td>Black Scour Worm</td>
<td>Trichostrongylus</td>
<td>spp*</td>
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<td>Small Intestinal Worm</td>
<td>Cooperia</td>
<td>oncophera</td>
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<tr>
<td></td>
<td></td>
<td>punctata</td>
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<tr>
<td><strong>LARGE INTESTINE</strong></td>
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<td></td>
</tr>
<tr>
<td>Large Bowel Worm</td>
<td>Oesophagostomum</td>
<td>radiatum*</td>
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<tr>
<td><strong>LUNGWORM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Large Lungworm</td>
<td>Dictyocaulus</td>
<td>viviparous</td>
</tr>
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</table>

% reduction in total fluke count

FlukeCare® + Se

Non-synergised combination

<table>
<thead>
<tr>
<th>% reduction in total fluke count</th>
<th>FlukeCare® + Se</th>
<th>Non-synergised combination</th>
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</thead>
<tbody>
<tr>
<td>99%</td>
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<tr>
<td>46%</td>
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</table>

Average number of fluke eggs per gram of dung

FlukeCare® + Se

Non-synergised combination

<table>
<thead>
<tr>
<th>Average number of fluke eggs per gram of dung</th>
<th>FlukeCare® + Se</th>
<th>Non-synergised combination</th>
</tr>
</thead>
<tbody>
<tr>
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</tr>
<tr>
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</tr>
<tr>
<td>5</td>
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</tbody>
</table>
Synergised formulation of triclabendazole and oxfendazole.
- Ideal late autumn/early winter or summer treatment.
- Controls damaging 2-week-old early immature flukes.
- Broad spectrum control of internal parasites.

For the effective treatment and control of the following species of gastrointestinal parasites (*includes third and fourth stage larva and inhibited immatures):

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<tr>
<td>Liver Fluke</td>
<td>Fasciola</td>
<td>heptica*</td>
</tr>
<tr>
<td>ABOMASUM</td>
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<td></td>
</tr>
<tr>
<td>Barber’s Pole Worm</td>
<td>Haemonchus</td>
<td>contortus</td>
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<tr>
<td>Stomach Hair Worm</td>
<td>Trichostrongylus</td>
<td>axei</td>
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<tr>
<td>Small Brown Stomach Worm</td>
<td>Ostertagia</td>
<td>circumcincta</td>
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<tr>
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<td>spp.</td>
</tr>
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<td>Nematodirus</td>
<td>spp.</td>
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<tr>
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<tr>
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<td>Nodule Worm</td>
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<td>columbiaeanum</td>
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<td>Large Mouthed Bowel Worm</td>
<td>Chabertia</td>
<td>ovina</td>
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<tr>
<td>LUNGWORM</td>
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<td></td>
</tr>
<tr>
<td>Large Lungworm</td>
<td>Dictyocaulus</td>
<td>filaria</td>
</tr>
</tbody>
</table>
**LIVER FLUKE: EFFECT ON GROWTH**

Lack of body weight gain expressed as weight loss in grams per week on calves in differing severity of liver fluke infection.

- Synergised formulation of nitroxynil and clorsulon.
- Ideal late autumn/early winter or summer treatment.
- Controls triclabendazole resistant flukes.
- Controls damaging 2-week-old early immature flukes.
- Also contains ivermectin, providing broad spectrum control of internal and external parasites.

For the effective treatment and control of the following species of gastrointestinal parasites (*includes third and fourth stage larva and inhibited immatures*):

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<td>Stomach Hair Worm</td>
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<td>Black Scour Worm Intestinal Hair Worm</td>
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<td>Hookworm</td>
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<td>Strongyloides</td>
<td>papillosus*</td>
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<td>LARGE INTESTINE</td>
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<tr>
<td>Large Bowel Worm</td>
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<td>Whipworm</td>
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<td>Dictyocaulus</td>
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<td>Haematopinus</td>
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<tr>
<td>Little blue sucking louse</td>
<td>Solenopotes</td>
<td>capillatus</td>
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</tbody>
</table>

FlukeCare

Nitromec

ASK YOUR VET FOR MORE INFO

www.virbac.co.nz/fluke

ACVM Nos. A10203 and A10223