

TECHNICAL BRIEF



DUAL ACTIVE POUR-ON FOR CATTLE

Active Ingredients: Abamectin (10mg/ml) and Levamisole (200mg/ml)

The Formulation Challenge

Formulating combination parasiticides is no easy task. In the case of pour-on products the hurdles are even greater. Not only must the formulation remain within specification over the labelled shelf-life, it must also deliver the performance farmers expect with as few compromises as possible.

Macrocyclic lactone/levamisole based pour-ons are probably the most difficult to produce because the two active ingredients are so chemically incompatible. This incompatibility combined with the high concentration of levamisole renders many common formulation routes unworkable.

Even once a relatively stable formulation is developed the result may be that other formulation aspects have had to be neglected or compromised. Typical results include formulations that have such high viscosity that absorption is retarded or viscosity that is so low that there is a tendency for the formulation to run off the back of the animal.



The BOSS® Breakthrough

BOSS® Pour-on, is a new combination pour-on for cattle containing abamectin and levamisole in Alleva's new proprietary DMI-Sorb™ formulation system (patent pending).

The result of an extensive development process DMI-Sorb™ is a blend of solvents and additives designed to enhance macrocyclic lactone/levamisole formulation stability without compromising product performance. It achieves this by use of a novel primary solvent and careful balancing of solubility and viscosity characteristics. In simple terms this means:

- More effective transport of the active ingredients to skin level

- A reduced tendency to run from the back of the animal

- Enhanced dermal penetration

Performance You Can Trust

BOSS® Pour-on is the premier choice for treatment of young cattle. Clinical studies performed in New Zealand demonstrate that the product is highly effective against the common parasite species present on New Zealand farms. Efficacy levels of 100% against all species were obtained in the total worm count studies undertaken with this product. This level of efficacy gives peace of mind for parasite control and helps to delay the onset of parasite resistance. The product is effective in the control of endectocide resistant *Cooperia* species and species resistant to benzimidazole drenches. BOSS® Pour-on is also highly effective in the control of biting lice, sucking lice and lungworm.

BOSS® Pour-on was developed in New Zealand and all of the trial work performed to register the product was undertaken on New Zealand farms. The results from these studies are outlined below.

Waikato Total Worm Count Efficacy Study:

Efficacy of BOSS® Pour-on against a natural infection of gastrointestinal parasites in cattle. Efficacy determined by total worm counts in comparison with untreated control animals.

Table 1: Arithmetic mean worm counts and % efficacy of BOSS® Pour-on compared with an untreated control group.

Worm Spp	Control	BOSS Pour-on	% Efficacy
T. axei	192	0	100%
Ostertagia	1533	0	100%
Nematodirus	75	0	100%
Trichostrongylus	8	0	100%
Cooperia	5108	0	100%

Helensville Total Worm Count Efficacy Study:

Efficacy of BOSS® Pour-on against a natural infection of gastrointestinal parasites in cattle. Efficacy determined by total worm counts in comparison with untreated control animals.

Table 2: Arithmetic mean worm counts and % efficacy of BOSS® Pour-on compared with an untreated control group.

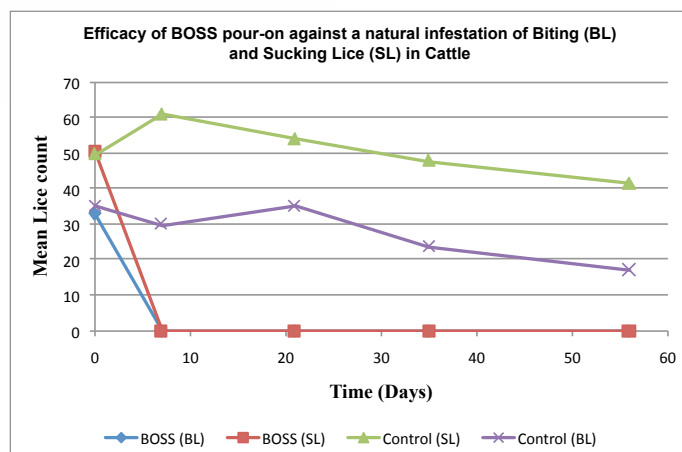
Worm Spp	Control	BOSS Pour-on	% Efficacy
T. axei	867	0	100%
Ostertagia	3950	0	100%
Nematodirus	100	0	100%
Trichostrongylus	83	0	100%
Cooperia	3875	0	100%
Haemonchus	50	0	100%
Trichuris	2	0	100%

Results:

Results from these studies demonstrate how effective BOSS® Pour-on is at controlling a gastrointestinal parasites burden. The product removed all parasites present in both studies. Efficacy levels as high as this are rarely seen with pour-on formulations.

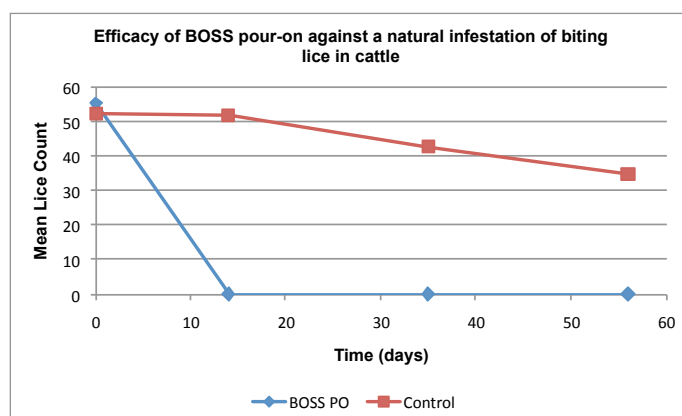
Waikato Lice Count Efficacy Study:

Efficacy of BOSS® Pour-on against a natural infection of lice in cattle. Efficacy determined by lice counts after treatment in comparison with untreated controls.



Helensville Lice Count Efficacy Study:

Efficacy of BOSS® Pour-on against a natural infection of lice in cattle. Efficacy determined by lice counts after treatment in comparison with untreated controls.



Results:

Results from these lice efficacy studies demonstrate that BOSS® Pour-on is highly effective at controlling a natural infection of biting and sucking lice in cattle. BOSS® Pour-on reduced lice numbers to non-detectable levels for 56 days post treatment in both studies.

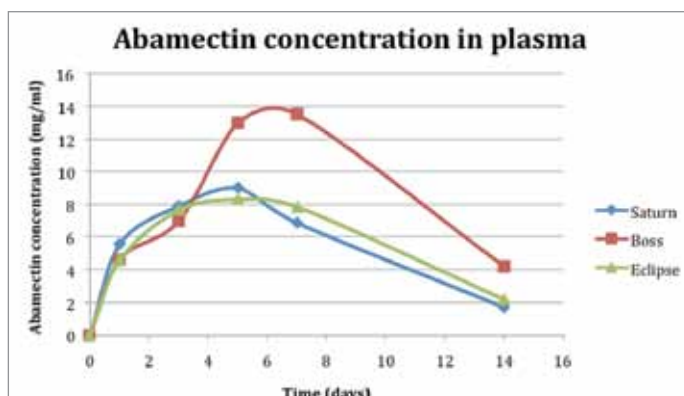
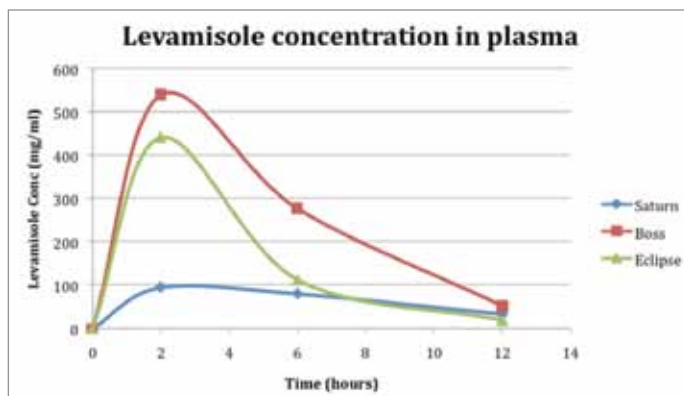
Pharmacokinetic Comparison Study:

A study was undertaken in which three groups of five cattle were treated with either BOSS® Pour-on, ECLIPSE® Pour-On (Merial-Ancare) or SATURN® Pour-On (Bayer-Bomac).

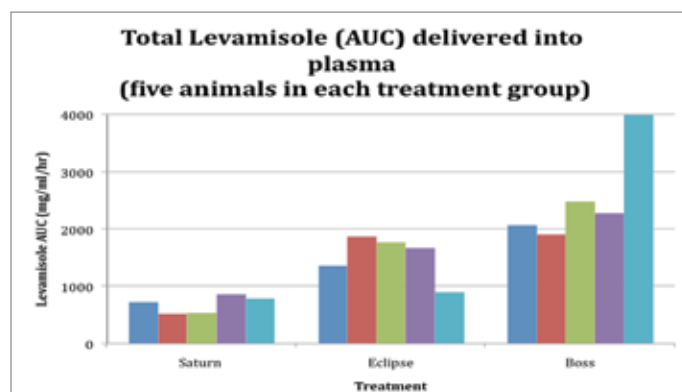
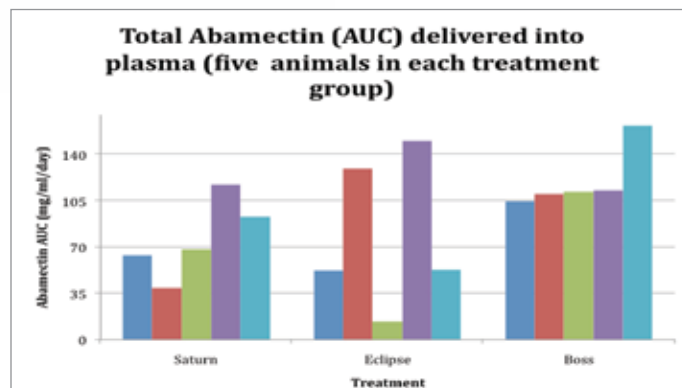
Group	Group 1	Group 2	Group 3
Treatment	BOSS® Pour-On (1ml per 20kg)	ECLIPSE® Pour-On (1ml per 20kg)	SATURN® Pour-On (1ml per 20kg)

The purpose of the study was to determine the effectiveness of each formulation in delivering the abamectin and levamisole active ingredients through the skin and into the blood.

The results confirmed that the average blood levels of both active ingredients were higher after treatment with BOSS® Pour-on than the alternate products.



When the results are viewed in terms of the amount of active ingredient delivered to individual animals it also reveals that with BOSS® Pour-on there was a reduction in the potential for delivery of lower levels of either abamectin or levamisole.



Variability is of therapeutic concern because for less sensitive species of parasites, we can assume that the use of a formulation associated with a highly variable bio-availability will probably lead to higher percentage failure and/or lack of persistence in preventing re-infection than a formulation with the same bioavailability, with a lower variability*.

What do these results mean for farmers who choose to treat their stock with BOSS® Pour-on?

In practical terms it means that they can have real confidence in achieving effective parasite control with BOSS® Pour-on. The risk of individual animals not receiving a therapeutic dose of each active ingredient is also likely to be reduced.

Result from study	Potential benefit	Leading to
<ul style="list-style-type: none"> Delivers higher average levels of both levamisole and abamectin into the blood 	<ul style="list-style-type: none"> Greater exposure of the parasite to both drugs 	<ul style="list-style-type: none"> Higher efficacy Greater efficacy against parasites which may already have established partial tolerance to less potent single-active or combination products Reduced risk of resistance Improved animal performance Improved long-term productivity
<ul style="list-style-type: none"> Reduced risk of individual animals not receiving a therapeutic dose 	<ul style="list-style-type: none"> Lower risk of poor or non-responding animals 	<ul style="list-style-type: none"> Higher efficacy Reduced risk of resistance Improved animal performance Reduced risk of pasture contamination by these animals before the mob is due for next treatment Improved long-term productivity

Rain study:

To demonstrate rain-resistance Alleva contracted a NZ research group to undertake an efficacy study which looked at the effect of simulated rain on the performance of BOSS® Pour-on. Four groups of 10 animals with positive faecal egg counts were treated with BOSS® Pour-on. Simulated rain was applied to one group prior to treatment and one group at 20 minutes after treatment. An additional group had simulated rain applied at 2 hours after treatment. These groups were compared to a group of animals that was treated with BOSS® Pour-on (not subject to simulated rain) and an untreated control group. All treatment groups had efficacy levels of >98% when compared to the untreated control group. There was no statistical difference between any of the treatment groups. This study demonstrated that rain did not reduce efficacy.

In the study the simulated rain was applied at a rate of 12.5mls over 26 minutes.

Product Safety

A clinical safety study was undertaken to determine the safety of BOSS® Pour-on in the target species. In this study BOSS® Pour-on was administered to weaned calves (3-6 months of age) at 3x the recommended dose rate with no adverse effects. However, these animals were treated under trial conditions and were not stressed. As with any formulation containing levamisole doses of 3x the recommend can cause levamisole toxicity. It is important to make sure the correct label dose of BOSS® Pour-on is calculated before administering the product.

General Information

Dose Rate:

1ml/20kg (10mg/ml abamectin & 200mg/ml levamisole)

With-holding periods:

42 days meat, 35 days milk

Active ingredients:

10g/L abamectin and 200g/L levamisole

Administration method:

Apply in a line down the middle of the back with the supplied applicator.

IMPORTANT: BOSS® Pour-on may only be applied with the BOSS® Pour-on applicator. This has been specially designed to apply high viscosity materials.

BOSS® Application Cleaning:

DO NOT USE WATER TO CLEAN THE BOSS® POUR-ON APPLICATOR. IF WATER IS USED THE APPLICATOR WILL CLOG AND CEASE TO FUNCTION. For correct applicator cleaning procedures please consult instruction supplied with the applicator.

Rain - resistance:

The efficacy of BOSS® Pour-On is not adversely affected if rain occurs shortly before or after treatment.

Storage:

Store below 25°C

Pack Sizes:

2.5L & 5L carry packs.



Dosage Table:

Live weight	Dose	2.5L Pack Treats	5L Pack Treats
101-120kg	6 mL	416	833
121-140kg	7 mL	357	714
141-160kg	8 mL	312	625
161-180kg	9 mL	277	555
181-200kg	10 mL	250	500
201-220kg	11 mL	227	454
221-240kg	12 mL	208	416
241-260kg	13 mL	192	384
261-280kg	14 ml	178	357
281-300kg	15 ml	166	333
301-320kg	16ml	156	312
321-340kg	17ml	147	294
341-360kg	18ml	138	277
361-380kg	19ml	131	263
381-400kg	20ml	125	250
401-420kg	21ml	119	238
421-440kg	22ml	113	227
441-460kg	23ml	108	217
461-480kg	24ml	104	208
481-500kg	25ml	100	200
501-520kg	26ml	96	192
521-540kg	27ml	92	185
541-560kg	28ml	89	178
561-580kg	29ml	86	172
581-600kg	30ml	83	166
601-620kg	31ml	80	161
621-640kg	32ml	78	156
641-660kg	33ml	75	151

Cattle in excess of 650 kg to be dosed at 1 mL per 20 kg bodyweight.

Product Benefits

- Dual active ingredients
- Convenient pour-on application
- Low run formulation
- Formulated using rain-resistant DMI-Sorb™ technology to enhance active ingredient delivery and absorption
- Broad spectrum activity – 100% effective against natural parasite infestations in New Zealand studies
- Effective against resistant species including endectocide resistant Cooperia
- More effective at delaying parasite resistance than single active products
- Developed for New Zealand conditions by a New Zealand owned company

BOSS® is a registered trademark of



Alleva Animal Health Limited,
15 Calman Place, Birkenhead,
Auckland.

*Alvinerie M, Sutra JF, Galtier P, Mage C; **Pharmacokinetics of eprinomectin in plasma and milk following topical administration to lactating dairy cattle.** Res Vet Sci. 1999 Dec;67(3):229-32.

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