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# Persistent efficacy and production benefits following use of extended-release injectable eprinomectin in grazing beef cattle under field conditions

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ABSTRACT

Seven studies were conducted in commercial grazing operations to confirm anthelmintic efficacy, assess acceptability, and measure the productivity response of cattle to treatment with eprinomectin in an extended-release injectable formulation (ERI) when exposed to nematode infected pastures for 120 days. The studies were conducted under one protocol in the USA in seven locations (Arkansas, Idaho, Louisiana, Minnesota, Missouri, Oregon, and Wisconsin). Each study had 67–68 naturally infected animals for a total of 475 (226 female, 249 male castrate) Angus or beef-cross cattle. The animals weighed 133–335 kg prior to treatment and were approximately 3–12 months of age. The studies were conducted under a randomized block design based on pre-treatment body weights to sequentially form 17 replicates of four animals each within sex in each study. Animals within a replicate were randomly assigned to treatments, one to Eprinomectin ERI vehicle (control) and three to Eprinomectin ERI (5%, w/v eprinomectin). Treatments were administered at 1 mL/50 kg body weight once subcutaneously anterior to the shoulder. All animals in each study grazed one pasture throughout the observation period of 120 days. Cattle were weighed and fecal samples collected pre-treatment and on 28, 56, 84, and 120 days after treatment for fecal egg and lungworm larval counts. Positive fecal samples generally were cultured *en masse* to determine the nematode genera attributable to the gastrointestinal helminth infection. *Bunostomum*, *Cooperia*, *Haemonchus*, *Nematodirus*, *Oesophagostomum*, *Ostertagia*, and *Trichostrongylus*, when present, were referred to as strongylids. At all post-treatment sampling intervals, Eprinomectin ERI-treated cattle had significantly ($P < 0.05$) lower strongylid egg counts than vehicle-treated controls, with ≥95% reduction after 120 days of grazing. Over this same period, Eprinomectin ERI-treated cattle gained more weight (43.9 lb/head) than vehicle-treated controls in all studies. This weight gain advantage was significant ($P < 0.05$) in six of the studies with the Eprinomectin ERI-treated cattle gaining an average of 42.8% and the control cattle gaining 33.1% of their initial weight. No adverse reactions were observed in the treated animals.



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## 1. Introduction

The overall impact of internal parasitism in grazing cattle is assessed by productivity, which can be measured as weight gain, feed conversion, carcass composition or quality, reproductive performance or milk production. Whether the level of infection observed is clinical or subclinical, productivity losses can be the result of many factors working in synergy. Decreased feed intake, impaired nutrient utilization, and alterations in metabolism and immune status are factors associated with parasitism that can affect productivity. The effect on the parasitized cattle and the loss of productivity are not only evident during the first grazing season, but may also affect the productivity of those animals for the second and subsequent seasons (Holste et al., 1986; Hawkins, 1993; Forbes et al., 2004; Sutherland and Scott, 2010).

Preventive and therapeutic anthelmintic programs involving scheduled dosing, formulations with prolonged duration of activity, and sustained release devices have been developed. The goal of these programs was to remove an established parasite infection and prevent re-infection, reduce pasture contamination early in the grazing season, and maintain low numbers of infective larvae on the pasture for the duration of the season. An additional benefit of formulations with prolonged activity or sustained release is the reduction in frequency of animal handling resulting in reduced animal stress and labor costs.

Eprinomectin is a macrocyclic lactone belonging to the second generation avermectin group of endectocides for cattle. Eprinomectin in a 0.5% pour-on formulation at 0.5 mg/kg body weight has been shown to be highly efficacious against adult and immature gastrointestinal nematodes (Shoop et al., 1996; Gogolewski et al., 1997a,b; Pitt et al., 1997; Williams et al., 1997; Yazwinski et al., 1997; Batty et al., 1999; Epe et al., 1999; Cramer et al., 2000; Dorny et al., 2000; Höglund et al., 2003). Subsequently, an extended-release injectable (ERI) formulation of eprinomectin has been developed for the therapeutic and persistent control of nematode infections in cattle (Soll et al., 2013; Rehbein et al., 2013). The ERI formulation incorporates eprinomectin into poly(D,L-lactide-co-glycolic)acid (PGLA), which forms an extended-release biodegradable drug delivery matrix when injected subcutaneously.

The objective of these studies was to confirm 120-day persistent efficacy, acceptability, and productivity response to eprinomectin extended-release injection solution when administered subcutaneously at 1 mg/kg body weight in a single injection to beef cattle in commercial grazing operations.

## 2. Materials and methods

The studies were conducted under one protocol in the USA at seven locations (Arkansas, Idaho, Louisiana, Minnesota, Missouri, Oregon and Wisconsin). Study personnel involved in collecting post-treatment data were blinded to treatment assignments for the study duration. The studies were designed and conducted to comply with the regulatory requirements of both the FDA/CVM and the European Medicines Agency/Committee for Medicinal Products for Veterinary Use, and according to relevant guidelines for Good Clinical Practices (GCPs) and for establishing the efficacy of cattle anthelmintics.

### 2.1. Experimental animals

A total of 475 (226 female, 249 male-castrate) Angus or beef-cross cattle, weighing approximately 133–335 kg prior to treatment (Day −5 to Day 0), and aged approximately 3–12 months were utilized in seven studies (67–68 animals per study) in a variety of locations in the USA. The animals had not been treated previously with an avermectin or milbemycin product. Animal descriptions and details are provided in Table 1. All cattle were exposed to a natural parasitic infection by grazing for several weeks on pasture contaminated by cattle nematodes prior to treatment. In one study the cattle were held in a dry lot for 30 days prior to treatment. Nematode parasite infections were confirmed on the basis of positive fecal examinations prior to treatment.

### 2.2. Experimental design

All studies were conducted using a randomized block design based on pre-treatment bodyweight. Seventeen replicates of 4 cattle each were formed sequentially, within sex, based on pre-treatment (Day −5 to Day 0) bodyweights. Within replicates each animal was randomly allocated to treatment: one to the Eprinomectin ERI vehicle (control) group at 1 mL/50 kg bodyweight and three to the Eprinomectin 5% (w/v) ERI group at 1 mL/50 kg bodyweight (1.0 mg eprinomectin/kg). This allocation scheme resulted in a total of 17 controls and 51 treated in each study, except for a single replicate in the Idaho study which consisted of only three animals (one control and two treated), 50 Eprinomectin ERI-treated total.

Treatments were administered at 1 mL/50 kg bodyweight once on Day 0 by subcutaneous injection in front of the shoulder using individual sterile syringes and needles. Dose volumes were rounded to the next 1 mL above the calculated dose volume if the bodyweight was between the 50 kg increments.

Fecal samples were collected pre-treatment (between Day −7 and 0) and on Days 28, 56, 84, and 120 from all the animals for fecal egg (quantitative flotation techniques) and lungworm larval (Baermann technique) counts. Fecal egg count methods involved single centrifugation–flotation procedures with sodium chloride as the flotation medium in Idaho and Oregon and with magnesium sulfate in Arkansas. A double centrifugation–flotation with sucrose was conducted in Louisiana, Minnesota, Missouri, and Wisconsin. The sensitivities of the methods in eggs per gram were as follows: 0.2 in Idaho, Oregon and Wisconsin; 0.3 in Louisiana; 0.5 in Minnesota; 2.0 in Arkansas and 0.2/0.5 in Missouri. A coproculture procedure using the Baermann technique for larval recovery was employed for the identification of the larvae of gastrointestinal nematodes. In general, positive fecal samples were cultured *en masse* to determine nematode composition by genera. Samples of fecal composites