

# IMMUNOTHERAPUTIC ACTIVITY OF SETTLE™ (MYCOBACTERIAL CELL WALL FRACTION) IN TREATING *STREPTOCOCCUS ZOOEPIDEMICUS*-INDUCED ENDOMETRITIS IN MARES

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## Introduction

Endometritis in mares is an important disease that has large economic impacts in the horse industry (1, 2). In general, there are two groups of mares: those that are capable of clearing bacteria that contaminate the uterus following parturition or intrauterine manipulation; and those that are prone to infection, usually older or barren mares with a history of endometritis(3). Currently, equine endometritis is commonly treated with antibiotics. However, recent data(4) indicates that nonspecific immunostimulation with a mycobacterial cell wall formulation can restore homeostasis of the local inflammatory mechanisms and, consequently, assist in the prophylaxis or treatment of this condition. It is known that mycobacterial cell wall formulations (MCWF) possess adjuvant activity and have been used in many vaccine formulations. In the present study, we have evaluated the efficacy of a *Mycobacterium phlei* cell wall formulated as an emulsion (SETTLE™, Bioniche Animal Health USA, Inc., Athens GA) for the treatment of *Streptococcus zooepidemicus* (*S. zooepidemicus*) induced endometritis in susceptible mares.

## Material and methods

Thirty endometritis susceptible mares were selected from a herd of 896 mares. Endometritis was diagnosed by bacterial culture, exfoliate cytology, uterine biopsy, the presence of uterine fluid during diestrus and an ultrasound estrus fluid score of >2. All mares were treated with antibiotics to clear any existing infection. Upon clearance, estrus was induced with a 1 mL intramuscular injection of prostaglandin (Estroplan 250 µg/mL). When the onset of estrus was confirmed by ultrasound, each mare was infused with an intrauterine (IU) inoculation of  $1 \times 10^9$  cfu *S. zooepidemicus* to induce the endometritis. Twenty-four hours later, endometritis was confirmed by exfoliate cytology, bacterial culture, uterine biopsy and ultrasonography. Following the establishment of the endometritis, mares were allocated into four groups as follows: a) 10 mares treated with SETTLE™

(1500 µg MCW) by intravenous (IV) injection, b) 10 mares treated with SETTLE™ by IU instillation, c) 5 mares treated with an IV placebo and d) 5 mares treated with an IU placebo.

## Results and Discussions

The data indicate no statistically significant difference between the IV and IU routes of administration. For those mares treated with SETTLE™, there was a statistically significant decrease ( $p < 0.001$ ) in the number of polymorphonuclear leucocytes (PMN) found in biopsy samples at 24 hours and 7 days post-treatment when compared to the samples at pre-treatment. A statistically significant decrease was observed in the number of bacteria found at 24 hours and 7 days post-treatment ( $p < 0.001$ ). Furthermore, a statistically significant reduction ( $p < 0.001$ ) was observed in the volume of uterine fluid when comparing the mares at pre-treatment to the mares at day 7 post-treatment. One hundred percent of the control mares still had a bacterial endometritis at day 7, whereas those mares treated with mycobacterial cell wall formulation were cured of the endometritis in 55% of the cases after 24 hours and 75% after 7 days. The known ability of MCW to enhance the non-specific immunological response during the early phase of mare infection has proven to have a significant therapeutic effect. The immediate reduction in the uterine bacterial load unequivocally suggests that SETTLE™ is a fast, safe and effective treatment for equine endometritis.

## References

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*Original publication reference: Rogan, D. et al. (2004). Immunotherapeutic activity of a mycobacterial cell wall formulation in treating Streptococcus zooepidemicus-induced endometritis in mares. In Press (Modern Vaccines/Adjuvants Formulation, Prague, September 15-17)*