

# Hyperimmune Plasma Decreases Rhodococcal Pneumonia

Macarena Sanz, Iowa State University -One Year Grant

The study seeks to investigate the behavior of an analgesic agent approved for use in humans for the treatment of persistent pain, as a first step in assessing the utility of this drug for pain control in horses.



Rhodococcus equi (R. equi) is a leading cause of pneumonia in young foals worldwide, incurring significant costs for prevention and treatment while impacting the careers of racehorses and other equine athletes. Currently, there is no vaccine for R. equi, prompting many farms to utilize transfusions of R. equi-specific hyperimmune plasma (Re-HIP) shortly after birth to help prevent or mitigate pneumonia. However, the efficacy of this approach is controversial due to design limitations in previous studies such as the use of experimental infection instead of natural disease, lack of blinding to the treatment that can bias results, or not being big enough to properly assess the research question. As a result, foals in the U.S. often receive early antimicrobial treatments for rhodococcal pneumonia even after Re-HIP administration, contributing to the emergence of resistant R. equi strains which are difficult to treat and result in high mortality rates.

To address this issue, we propose a randomized, controlled, blinded field trial to test our hypothesis that intravenous administration of 1 L of Re-HIP to newborn foals decreases the cumulative incidence of pneumonia attributed to R. equi.

The study will be conducted at the Gestüt Lewitz Warmblood Stud in Germany, which foals 1,200-1,300 foals each season and has a documented history of high R. equi pneumonia incidence (26% of the foals had rhodococcal pneumonia and 93% had lesions in their lungs during 2023). The large number of foals at a single site is critical for our study, as we require 275 foals in each group to test our hypothesis with sufficient statistical power. As importantly, this farm does not treat foals solely based on ultrasonographic findings, allowing us to assess the real efficacy of Re-HIP on clinical and subclinical disease by monitoring untreated cases.

Since Re-HIP is not routinely used at this farm, a control group (no Re-HIP) can be included. This will be difficult to achieve in the U.S. where Re-HIP is routinely administered. Also, Dr. Venner's team at the Lewitz Stud includes experienced veterinarians proficient in clinical and thoracic ultrasonography scoring and with experience in field studies, supported by skilled farm personnel with extensive experience in foal management.

For this trial, healthy foals will be randomly assigned to receive either Re-HIP (275 foals) or no plasma (275 foals) within 48 hours of birth. Trained veterinarians, blinded to treatment groups, will monitor the foals weekly through physical examinations, white blood cell counts, and thoracic ultrasound scores until weaning at approximately six months of age. Foals without clinical signs of pneumonia but with ultrasonographic evidence of rhodococcal pneumonia will be closely monitored, while those showing clinical signs or having significant ultrasound lesions (score  $\geq 20$ ) will receive treatment as per farm protocol.

The primary objective of the study is to compare the number of foals that develop clinical signs of rhodococcal pneumonia and require treatment between the two groups. We will also assess the protective effect of Re-HIP on foals that become infected but do not exhibit clinical signs of disease (subclinical foals). Various statistical methods will be employed to analyze the data, focusing on differences in pneumonia development, treatment needs, thoracic ultrasound scores, and white blood cell counts for both clinical and subclinical cases.

We are uniquely positioned to accomplish this study. We have a team of experts leading the study, the farm management will cover labor and routine testing costs,

and MgBiologics has generously agreed to provide Re-HIP at a discounted rate, significantly reducing the project's financial burden. If our study confirms the effectiveness of Re-HIP, it could promote broader adoption of this practice on farms, leading to fewer affected foals and reduced disease severity. Additionally, we aim to encourage more diligent monitoring of foals receiving Re-HIP, which could help decrease the use of early-stage antibiotic treatments and mitigate the development of antibiotic-resistant *R. equi* strains.

**Importance to Industry:** *Rhodococcus equi* (*R. equi*) is a significant cause of pneumonia in young foals worldwide, resulting in considerable costs for prevention and treatment and impacting the performance of equine athletes. A vaccine is currently not available so many farms administer transfusions of *R. equi*-specific hyperimmune plasma (Re-HIP) shortly after birth to help mitigate the development of pneumonia. However, the effectiveness of this approach remains contentious due to design flaws in previous studies, such as reliance on experimental infections rather than natural cases, lack of blinding, and insufficient sample sizes.

As a result, foals in the U.S. often receive early antimicrobial treatments for rhodococcal pneumonia even after Re-HIP administration, contributing to the emergence of resistant *R. equi* strains that are difficult to treat and lead to increased mortality rates. Our study seeks to evaluate the effectiveness of Re-HIP in preventing pneumonia under real-world conditions using solid scientific methodology. To achieve this, 275 foals will be randomly assigned to receive Re-HIP within 48 hours of birth, while another 275 will not. These foals will be monitored until weaning at six months of age and the number of foals that develop clinical and subclinical pneumonia in each group will be compared between groups.

We are confident we have a unique opportunity to answer this important question. We have assembled a team of experts in *R. equi* research, identified a large farm with trained personnel to carry out the study, and partnered with a plasma company to reduce costs. If our hypothesis is confirmed, it could promote wider adoption of Re-HIP among current users and farms where this practice is not yet routine. Furthermore, it will encourage monitoring of subclinical foals after Re-HIP rather than relying on widespread antimicrobial treatments, thus reducing antibiotic usage and minimizing the risk of developing resistant *R. equi* strains on horse farms.