

Package Insert
 SALMONELLA TYPHIMURIUM ANTIBODY, EQUINE ORIGIN
 ENDOSERUM®
 U.S. Veterinary License No. 345

GRAM NEGATIVE ENDOTOXEMIA IN HORSES

When administered to horses, ENDOSERUM® increases circulating levels of IgG anti-endotoxin antibodies. Administration of ENDOSERUM® should be considered when clinical signs and/or laboratory data indicate impending or ongoing Gram negative endotoxemia in adult horses or foals. Specific indications include foals that have failed to receive adequate passive transfer of Gram negative maternal antibodies via colostrum, horses recovering from abdominal surgery, horses suffering from Gram negative bacteremia, Gram negative metritis, Gram negative diarrhea and gastrointestinal disorders due to carbohydrate overload. Because of the severe responses Gram negative endotoxins cause in horses, early diagnosis and treatment are of utmost importance.

HOW ENDOSERUM® IS PRODUCED

ENDOSERUM® is produced from blood harvested from healthy horses that have been hyper immunized with a combination vaccine. The vaccine is composed of a bacterin made from a mutant of *Salmonella typhimurium*; a toxoid made from the *Salmonella typhimurium* endotoxin and aluminum trioxide adjuvant. When the antibody titers of the donor animals are sufficiently increased to equal the potency of the USDA approved antibody, blood is collected and the serum is harvested. It is then processed and tested for potency, safety, and sterility before being shipped to equine clinicians. ENDOSERUM® is heated to inactivate complements and destroy IgE antibodies; a preservative, merthiolate, is added; and it is filter sterilized.

HOW CROSS PROTECTION IS ACHIEVED

The cross protection provided by ENDOSERUM® occurs because the naked core mutant bacterin contained in the vaccine stimulates the immune system to produce antibodies against the core portion of the cell wall. The core portions of the cell wall in virtually all Gram negative bacteria are very similar; therefore, antibodies produced in response to the core antigen can theoretically provide protection against virtually all Gram negative endotoxins. The application of such cross protection is relatively new to clinical veterinary medicine.

The combination vaccine used to hyper immunize the donor horses is Salmonella typhimurium Bacterin-Toxoid. It was tested by challenging vaccinated and non-vaccinated animals with an intravenous bolus of *Salmonella typhimurium* endotoxin (the homologous challenge) and *E. coli* endotoxin (the heterologous challenge), respectively. Vaccinated animals exhibited little or no significant responses to either endotoxin challenge, and the non-vaccinated animals (controls) exhibited significant responses to both challenges when compared to vaccinated on the basis of a colic/depression index. Retrospective measurements of IgG antibodies in both control and vaccinated animals correlated with colic/depression data, i.e., lower titer values were accompanied by high scores while high titers were accompanied by low colic/depression response. Demonstration of protection from the heterologous challenge confirmed cross protection in horses that has, heretofore, been demonstrated primarily in humans and laboratory animals.

In both ENDOSERUM® and vaccine efficacy tests the difference between the controls and the antibody protected animals challenged with endotoxin exceeded the statistical significance required by USDA.

HOW DOSAGE IS DETERMINED

Recommended dosage for treatment of an anticipated acute endotoxemic episode via IgG antibodies is 0.7 ml ENDOSERUM® per pound of body weight.

Horse Size	ENDOSERUM® Dose
1000 lbs.	700 ml
800 lbs.	525 ml or 1 - 500 ml unit
150 lbs.	105 ml or 1 - 100 ml unit

Because immunoglobulin may be rapidly depleted during Gram negative diseases, it is recommended that the administration be repeated if signs of endotoxemia recur or persist.

Recommended dosage for treating FPT by increasing total IgG levels is determined by the foal's extracellular fluid volume or body weight and the amount of IgG increases desired.

ENDOSERUM® Dose

Foal Size	To raise IgG 200 mg/dl	To raise IgG 400 mg/dl
50 lbs.	350 ml	700 ml
75 lbs.	525 ml or 1 - 500 ml unit	1050 ml or 2 - 500 ml units
100 lbs.	700 ml	1400 ml

HOW ENDOSERUM® IS ADMINISTERED

ENDOSERUM® is to be warmed to room temperature, diluted in an equal or larger volume of sterile physiological saline or lactated Ringer's solution, and administered intravenously. It is very important for the administration to be completed in NO LESS THAN 30 MINUTES. If administration results in coughing, shaking or shivering, administration should be slowed or temporarily ceased. Because immunoglobulin may be rapidly depleted during Gram negative diseases, it is recommended that the administration be repeated if signs of endotoxemia recur or persist. If an allergic response occurs, epinephrine or its equivalent should be administered.

ENDOSERUM® should be stored at 2 - 7° C (34 - 45° F). Freezing is not recommended although frozen samples tested for potency have not been damaged by one freezing.

SAFETY OF THE ANTIBODY

Hundreds of horses received ENDOSERUM® during the developmental stage and during the USDA efficacy and safety studies. Those involved in the USDA safety testing were located in six different geographical areas of the United States. As stated above, it is very important to administer the diluted ENDOSERUM® slowly.

IMMVAC®, Incorporated
 6080 Bass Lane
 Columbia, MO 65201
 (573) 443-5363
 (800) 944-7563