Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza$_3$-Respiratory Syncytial Virus Vaccine

Modified Live and Killed Virus

Campylobacter Fetus-Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin

CattleMaster® 4+VL5

PRODUCT DESCRIPTION: CattleMaster 4+VL5 is for vaccination of healthy cattle, including pregnant cows, as an aid in preventing infectious bovine rhinotracheitis caused by infectious bovine rhinotracheitis (IBR) virus, bovine viral diarrhea caused by bovine viral diarrhea (BVD) Type 1 virus, disease caused by parainfluenza$_3$ (PI_3) virus and bovine respiratory syncytial virus (BRSV), campylobacteriosis (vibriosis) caused by *Campylobacter fetus*, and leptospirosis caused by *Leptospira canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae*, and *L. pomona*. CattleMaster 4+VL5 is a freeze-dried preparation of chemically altered strains of IBR and PI_3 viruses and modified live BRSV plus a liquid, adjuvanted preparation of inactivated cytopathic and noncytopathic BVD Type 1 virus strains, *C. fetus*, and cultures of the 5 *Leptospira* serovars identified above. The liquid component is used to rehydrate the freeze-dried component. Viral antigens are propagated on an established cell line. This product is adjuvanted with aluminum hydroxide to enhance immune response.

DISEASE DESCRIPTION: IBR, BVD, PI_3, and BRSV viruses are commonly associated with respiratory disease and/or reproductive failure in cattle. IBR virus infection is characterized by high temperature, excessive nasal discharge, conjunctivitis and ocular discharge, inflamed nose ("red nose"), increased rate of respiration, coughing, loss of appetite, and depression. Cattle infected during pregnancy may abort.

A characteristic of IBR virus (BHV1) is that it establishes a latent infection in sensory neurons, typically trigeminal ganglia or iliosacral dorsal root ganglia.[1] From these sites of latency, it can be reactivated when an infected animal is stressed or injured. Subsequently, the virus is shed and transmitted by contact to other cattle.

BVD virus may be transmitted in nasal secretions, saliva, blood, feces, and/or urine, and by direct contact with contaminated objects; it invades through the nose and mouth and replicates systemically. Infection during pregnancy may result in abortion, fetal resorption, or congenital malformation of the fetus. Moreover, if susceptible cows are infected with noncytopathic BVD virus during the first trimester of pregnancy, their calves may be born persistently infected with the virus. Exposure of those calves to certain virulent cytopathic BVD virus strains may precipitate BVD-mucosal disease. Clinical signs of BVD include loss of appetite, ulcerations in the mouth, profuse salivation, elevated temperature, diarrhea, dehydration, and lameness.

PI_3 virus usually localizes in the upper respiratory tract, causing elevated temperature and moderate nasal and ocular discharge. Although clinical signs typically are mild, PI_3 infection weakens respiratory tissues. Invasion and replication of other pathogens, particularly *Pasteurella* spp., is thereby facilitated and may result in pneumonia.

BRSV is the etiologic agent of a specific viral respiratory disease of cattle of all ages, including nursing calves. Infection is characterized by rapid breathing, coughing, loss of appetite, discharge from the nose and eyes, fever, and swelling around the throat and neck. In an acute outbreak, deaths may follow within 48 hours after onset of signs. Clinically, BRSV infection may be indistinguishable from other viral infections associated with the bovine respiratory disease complex. BRSV infection, like PI_3, facilitates invasion and replication of other respiratory pathogens. Exacerbation of clinical signs has been documented when concurrent BRSV and BVD or IBR infection exists.

Campylobacteriosis (vibriosis) is a bovine venereal disease transmitted during breeding, either through coitus or artificial insemination with contaminated semen. Although the disease is often subclinical, in cows it causes temporary infertility, irregular estrus cycles, delayed conception, and occasionally, abortion.

Leptospirosis may be caused by several serovars of *Leptospira*, of which *L. canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae*, and *L. pomona* are the most common affecting cattle. *Leptospira* localize in the kidneys, are shed in the urine, and cause anemia, bloody urine, fever, loss of appetite, and prostration in calves. Signs are usually subclinical in adult cattle. Infected pregnant cows, however, often abort, and dairy cows may exhibit a marked decrease in milk production. *Leptospira* spp. are known zoonotic pathogens.

SAFETY AND EFFICACY: In safety studies of the fractions of CattleMaster 4+VL5, no adverse reactions to vaccination were observed and vaccinated pregnant cattle delivered normal, healthy calves.

The latency and subsequent excretion of the IBR virus fraction of CattleMaster 4+VL5 was determined in a safety study in which cattle were inoculated intramuscularly with the attenuated, temperature-sensitive IBR virus component and subsequently given corticosteroid to reactivate latent herpesvirus. Vaccination resulted in a characteristic serological response that remained unaltered even after corticosteroid treatment, indicating a lack of viral reactivation. Also, no BHV1 was recovered from mucosal swabs collected postvaccination or postcorticosteroid treatment, nor was it transmitted to nonvaccinated sentinel calves commingled with the vaccinates for the duration of the study. Further, no BHV1 DNA or latency-related RNA was detected in trigeminal or iliosacral spinal dorsal root ganglia collected after the administration of corticosteroid. Both nucleic acids were detected in a single cervical ganglion sample, suggesting a direct or proximate intraneural injection. BHV1 given by IM injection could not be reactivated from trigeminal ganglia, the primary site of BHV1 latency, demonstrating a lack of efficient viral replication in those sensory neurons. Excluding possible injection into nervous tissue (from which reactivation was not observed), the IBR fraction of CattleMaster 4+VL5 given by the IM route showed no propensity to establish latent herpesvirus infections.

Efficacy of each fraction of CattleMaster 4+VL5 was demonstrated in challenge-of-immunity studies. Cattle vaccinated with any fraction of CattleMaster 4+VL5, followed by challenge with a disease-causing strain of that fraction, showed no signs or had significantly fewer clinical signs than nonvaccinated control cattle. Serologic studies also demonstrated no immunologic interference among the fractions of CattleMaster 4+VL5. Antibody response was not significantly different between cattle vaccinated with an individual fraction and cattle vaccinated with the combined fractions.

DIRECTIONS:

1. *General Directions:* Vaccination of healthy cattle, including pregnant cows, is recommended. Aseptically rehydrate the freeze-dried vaccine with the liquid component provided, shake well, and administer 5 mL intramuscularly. In accordance with Beef Quality Assurance guidelines, this product should be administered in the muscular region of the neck.
2. *Primary Vaccination:* Healthy cattle should receive 2 doses administered 2–4 weeks apart. To avoid possible maternal antibody interference with active immunization, calves vaccinated before the age of 6 months should be revaccinated after 6 months of age.
3. *Revaccination:* Annual revaccination with a single dose is recommended.
4. Good animal husbandry and herd health management practices should be employed.

PRECAUTIONS:

1. Store at 2°–7°C. Prolonged exposure to higher temperatures and/or direct sunlight may adversely affect potency. Do not freeze.
2. Use entire contents when first opened.
3. Sterilized syringes and needles should be used to administer this vaccine. Do not sterilize with chemicals because traces of disinfectant may inactivate the vaccine.
4. Burn containers and all unused contents.
5. Do not vaccinate within 21 days before slaughter.
6. Contains gentamicin as preservative.
7. Occasional hypersensitivity reactions may occur up to 18 hours postvaccination. Owners should be advised to observe animals during this period. While this event appears to be rare overall, dairy cattle may be affected more frequently than other cattle. Animals affected may display excessive salivation, incoordination, and/or dyspnea. Animals displaying such signs should be treated immediately with epinephrine or equivalent. In nonresponsive animals, other modes of treatment should be considered.
8. As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.
9. This product has been shown to be efficacious in healthy animals. A protective immune response may not be elicited if animals are persistently infected with BVD virus or incubating an infectious disease, are malnourished or parasitized, are stressed due to shipment or environmental conditions, are otherwise immunocompromised, or the vaccine is not administered in accordance with label directions.

REFERENCES:

1. Jones C: Alphaherpesvirus latency: Its role in disease and survival of the virus in nature. Adv in Vir Res 51:81–133, 1999.

Technical inquiries should be directed to Zoetis Inc. Technical Services, (888) 963-8471 (USA), (800) 461-0917 (Canada).

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Zoetis Inc.
Kalamazoo, MI 49007, USA