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

Modified Live and Killed Virus

Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin

CattleMaster® GOLD FP® 5 L5

PRODUCT DESCRIPTION: CattleMaster GOLD FP 5 L5 is for vaccination of healthy cattle, including pregnant cows, as an aid in preventing abortion caused by infectious bovine rhinotracheitis (IBR, bovine herpesvirus Type 1), persistently infected calves caused by bovine virus diarrhea (BVD) virus Types 1 and 2, respiratory disease caused by IBR, BVD (Types 1 and 2), parainfluenza$_3$ (PI$_3$), and bovine respiratory syncytial virus (BRSV) and leptospirosis caused by *Leptospira canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae,* and *L. pomona*. CattleMaster GOLD FP 5 L5 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 BVD virus (Types 1 and 2) and inactivated 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 a unique combination of adjuvants including Amphigen®. The BVD fraction of CattleMaster GOLD FP 5 L5 is further processed by a proprietary system to help assure consistency of the formulation.

DISEASE DESCRIPTION: IBR and BVD are commonly associated with reproductive and respiratory disease while BRSV and PI$_3$ are predominantly associated with respiratory disease. 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 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 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.

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. *Leptospira* spp. are known zoonotic pathogens.

SAFETY AND EFFICACY: In safety studies of the fractions of CattleMaster GOLD FP 5 L5, no significant adverse reactions to vaccination were observed and vaccinated pregnant cattle delivered normal, healthy calves. Safety was demonstrated in pre-breeding and pregnant cows in all 3 trimesters. Transient local swelling was occasionally observed at the injection site.

The latency and subsequent excretion of the IBR virus fraction of CattleMaster GOLD FP 5 L5 was determined in a safety study in which cattle were vaccinated 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 intramuscular (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 GOLD FP 5 L5 given by the IM route showed no propensity to establish latent herpesvirus infections.

Efficacy of each fraction of CattleMaster GOLD FP 5 L5 was demonstrated in challenge-of-immunity studies. Cattle vaccinated with any fraction of CattleMaster GOLD FP 5 L5, followed by challenge with a disease-causing strain of that fraction, had significantly fewer clinical signs than nonvaccinated control cattle.

Efficacy of the IBR and BVD Type 1 and 2 fractions of CattleMaster GOLD FP 5 L5 were additionally demonstrated in challenge-of-immunity, fetal protection studies. The effectiveness of the IBR fraction of CattleMaster GOLD FP 5 L5 in preventing IBR-induced abortion was demonstrated by vaccinating susceptible heifers approximately 5 and 2 weeks prior to breeding. The vaccinated heifers, along with a group of nonvaccinated controls, were challenged with virulent IBR virus (Cooper strain) at approximately 180 days postbreeding. Following challenge, > 90% of vaccinated cows gave birth to healthy calves whereas >90% of the nonvaccinated controls aborted.

A similar study design was used to demonstrate the effectiveness of CattleMaster GOLD FP 5 L5 in preventing persistently infected calves with both BVD Types 1 and 2. In these studies, cows were challenged at approximately 82 days postbreeding using virulent strains of BVD. In nonvaccinated controls, challenge with BVD Type 1 resulted in 100% fetal infection, and challenge with BVD Type 2 resulted in greater than 85% fetal infection. Conversely, 100% of calves born to cows vaccinated with CattleMaster GOLD FP 5 L5 were protected from persistent infection following challenge by both BVD Types 1 and 2.

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 subcutaneously.
2. *Primary Vaccination:* Healthy cattle should receive an initial 2 doses 3 weeks apart. As an aid in preventing IBR-induced abortion and BVD persistently infected calves, administer a 5-mL dose at approximately 5 and 2 weeks prior to breeding. 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. Transient local reactions may be observed at the injection site.
5. Burn containers and all unused contents.
6. Do not vaccinate within 21 days before slaughter.
7. Contains gentamicin as preservative.
8. Routine handling of lactating dairy cattle, including administration of vaccines such as CattleMaster GOLD FP 5 L5, has been associated with transient reduction of milk production.
9. As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.
10. 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.

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

Modified Live and Killed Virus

CattleMaster® GOLD FP® 5

PRODUCT DESCRIPTION: CattleMaster GOLD FP 5 is for vaccination of healthy cattle, including pregnant cows, as an aid in preventing abortion caused by infectious bovine rhinotracheitis (IBR, bovine herpesvirus Type 1), persistently infected calves caused by bovine virus diarrhea (BVD) virus Types 1 and 2, and respiratory disease caused by IBR, BVD (Types 1 and 2), parainfluenza$_3$ (PI_3), and bovine respiratory syncytial virus (BRSV). CattleMaster GOLD FP 5 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 BVD virus (Types 1 and 2). The liquid component is used to rehydrate the freeze-dried component. Viral antigens are propagated on an established cell line. This product contains a unique combination of adjuvants, including Amphigen®, to enhance the immune response to its fractions. The BVD diluent of CattleMaster GOLD FP 5 is further processed by a proprietary system to help assure consistency of the formulation.

DISEASE DESCRIPTION: IBR and BVD are commonly associated with reproductive and respiratory disease while BRSV and PI_3 are predominantly associated with respiratory disease. 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 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 BVD virus strains may precipitate BVD-mucosal disease. Both BVD Types 1 and 2 can show a variety of clinical signs. The signs may be mild and not readily apparent. Clinical signs may include severe immune suppression, diarrhea, anorexia, depression, fever and respiratory disease. If infected with some Type 2 strains of BVD, severe thrombocytopenia may occur and hemorrhaging may be seen.

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.

SAFETY AND EFFICACY: In safety studies conducted with CattleMaster GOLD FP 5, no significant adverse reactions to vaccination were observed and vaccinated pregnant cattle delivered normal, healthy calves. Safety was demonstrated in prebreeding and pregnant cows in all 3 trimesters. Transient local swellings, attributable to the adjuvant formulation, were occasionally observed at the injection sites.

The latency and subsequent excretion of the IBR virus fraction of CattleMaster GOLD FP 5 was determined in a safety study in which cattle were vaccinated 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 intramuscular (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 GOLD FP 5 given by the IM route showed no propensity to establish latent herpesvirus infections.

Efficacy of each fraction of CattleMaster GOLD FP 5 was demonstrated in challenge-of-immunity studies. Cattle vaccinated with any fraction of CattleMaster GOLD FP 5, followed by intranasal challenge with a disease-causing strain of that fraction, had significantly fewer clinical signs than nonvaccinated control cattle.

Efficacy of the IBR and BVD Types 1 and 2 fractions of CattleMaster GOLD FP 5 were additionally demonstrated in challenge-of-immunity, fetal protection studies. The effectiveness of CattleMaster GOLD FP 5 in preventing IBR-induced abortion was demonstrated by vaccinating susceptible heifers approximately 5 and 2 weeks prior to breeding. The vaccinated heifers, along with a group of nonvaccinated controls, were challenged with virulent IBR virus (Cooper strain) at approximately 180 days postbreeding. Following challenge, >90% of vaccinated cows gave birth to healthy calves whereas >90% of the nonvaccinated controls aborted.

A similar study design was used to demonstrate the effectiveness of CattleMaster GOLD FP 5 in preventing persistently infected calves with both BVD Types 1 and 2. In these studies, cows were challenged at approximately 82 days postbreeding using virulent strains of BVD. In nonvaccinated controls, challenge with BVD Type 1 resulted in 100% fetal infection, and challenge with BVD Type 2 resulted in greater than 85% fetal infection. Conversely, 100% of calves born to cows vaccinated with CattleMaster GOLD FP 5 were protected from persistent infection following challenge by both BVD Types 1 and 2.

DIRECTIONS:

1. *General Directions:* Vaccination of healthy cattle, including pregnant cows, is recommended. Aseptically rehydrate the freeze-dried vaccine with the liquid vaccine provided, shake well, and administer 2 mL subcutaneously.
2. *Primary Vaccination:* Healthy cattle should receive an initial 2 doses 3 weeks apart. As an aid in preventing IBR-induced abortion and BVD persistently infected calves, administer a 2-mL dose at approximately 5 and 2 weeks prior to breeding. 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. Transient local reactions may be observed at the injection site.
5. Burn containers and all unused contents.
6. Do not vaccinate within 21 days before slaughter.
7. Contains gentamicin as preservative.
8. Routine handling of lactating dairy cattle, including administration of vaccines such as CattleMaster GOLD FP 5, has been associated with transient reduction of milk production.
9. As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.
10. 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.

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Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza$_3$ Vaccine

Modified Live Virus

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

PregGuard® GOLD FP® 10

INDICATIONS: PregGuard GOLD FP 10 is for vaccination of healthy cows and heifers prior to breeding to prevent persistently infected calves caused by bovine virus diarrhea (BVD) virus Types 1 and 2 and as an aid in preventing abortion caused by infectious bovine rhinotracheitis (IBR, bovine herpesvirus Type 1) virus; respiratory disease caused by IBR, BVD Types 1 and 2, and parainfluenza$_3$ (PI$_3$) virus; BVD Type 2 testicular infection; campylobacteriosis (vibriosis) caused by *Campylobacter fetus;* and leptospirosis caused by *Leptospira canicola, L. grippotyphosa, L. hardjo, L. icterohaemorrhagiae,* and *L. pomona.* A 12-month duration of immunity has been demonstrated against IBR-induced abortion and persistently infected calves caused by BVD Types 1 and 2. PregGuard GOLD FP 10 may be administered to pregnant cattle provided they were vaccinated, according to label directions, with any Bovi-Shield GOLD® FP or PregGuard GOLD FP vaccine within the past 12 months. PregGuard GOLD FP 10 may also be administered to calves nursing pregnant cows provided their dams were vaccinated within the past 12 months as described above. **To help ensure safety in pregnant cattle, heifers must receive at least 2 doses of any Bovi-Shield GOLD FP or PregGuard GOLD FP product with the second dose administered approximately 30 days prebreeding.**

PRODUCT DESCRIPTION: The freeze-dried vaccine is a preparation of modified live virus (MLV) strains of IBR, BVD (Types 1 and 2), and PI$_3$. The *Campylobacter* bacterin is an inactivated suspension of *C. fetus*. It is combined with an inactivated *Leptospira* bacterin prepared from whole cultures of the agents indicated. The *Campylobacter-Leptospira* bacterin is supplied as a diluent for the IBR-BVD-PI$_3$ vaccine.

DIRECTIONS:

General Directions: Vaccination of healthy cattle is recommended. Aseptically rehydrate the freeze-dried vaccine (PregGuard GOLD FP 10) with the liquid bacterin provided (Vibrio/Leptoferm-5®), shake well, and administer 2 mL intramuscularly. In accordance with Beef Quality Assurance guidelines, this product should be administered in the muscular region of the neck.

Primary Vaccination: Administer a single 2-mL dose to all breeding cows and heifers approximately 1 month prior to breeding or being added to the herd, followed 2–4 weeks later by a single dose of Vibrio/Leptoferm-5.

Revaccination: Annual revaccination with a single dose of PregGuard GOLD FP 10 is recommended.

Good animal husbandry and herd health management practices should be employed.

PRECAUTIONS:

Do not use in pregnant cows (abortions can result) unless they were vaccinated, according to label directions, with any Bovi-Shield GOLD FP or PregGuard GOLD FP vaccine within the past 12 months. Do not use in calves nursing pregnant cows unless their dams were vaccinated within the past 12 months as described above. Do not vaccinate calves under 3 months of age. **To help ensure safety in pregnant cattle, heifers must receive at least 2 doses of any Bovi-Shield GOLD FP or PregGuard GOLD FP product with the second dose administered approximately 30 days prebreeding.**

Store at 2°–7°C. Prolonged exposure to higher temperatures and/or direct sunlight may adversely affect potency. Do not freeze.

Use entire contents when first opened.

Sterilized syringes and needles should be used to administer this vaccine. Do not sterilize with chemicals because traces of disinfectant may inactivate the vaccine.

Burn containers and all unused contents.

Do not vaccinate within 21 days before slaughter.

Contains gentamicin as preservative.

Vaccination of stressed animals should be delayed.

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.

As with many vaccines, anaphylaxis may occur after use. Initial antidote of epinephrine is recommended and should be followed with appropriate supportive therapy.

This product has been shown to be efficacious in healthy animals. A protective immune response may not be elicited if animals are 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.

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