

## Bovine Rhinotracheitis-Virus Diarrhea-Parainfluenza<sub>3</sub>-Respiratory Syncytial Virus Vaccine

Modified Live Virus

Leptospira Canicola-Grippotyphosa-Hardjo-Icterohaemorrhagiae-Pomona Bacterin

### **Bovi-Shield® FP™ 4+L5**

**PRODUCT DESCRIPTION:** Bovi-Shield FP 4+L5 is for vaccination of healthy cows and heifers prior to breeding as an aid in preventing abortion caused by infectious bovine rhinotracheitis (IBR, bovine herpesvirus Type 1) virus; persistently infected calves caused by bovine virus diarrhea (BVD) Types 1 and 2; respiratory disease caused by IBR, BVD Types 1 and 2, parainfluenza<sub>3</sub> (PI<sub>3</sub>) and bovine respiratory syncytial virus (BRSV); and leptospirosis caused by *Leptospira canicola*, *L. grippotyphosa*, *L. hardjo*, *L. icterohaemorrhagiae*, and *L. pomona*. Bovi-Shield FP 4+L5 may be administered to pregnant cattle provided they were vaccinated, according to label directions, with Bovi-Shield FP 4+L5, Bovi-Shield FP 4+VL5 or PregGuard® FP 9 prior to breeding. Bovi-Shield FP 4+L5 may also be administered to calves nursing pregnant cows provided their dams were vaccinated prior to breeding as described above. Bovi-Shield FP 4+L5 is a freeze-dried preparation of modified live virus (MLV) strains of IBR, BVD, PI<sub>3</sub>, and BRSV viruses, plus a liquid bacterin containing the 5 *Leptospira* serovars identified above. The liquid bacterin is used to rehydrate the freeze-dried vaccine. Viral antigens are propagated on an established cell line.

**DISEASE DESCRIPTION:** IBR, BVD, PI<sub>3</sub>, 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.

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<sub>3</sub> virus usually localizes in the upper respiratory tract, causing elevated temperature and moderate nasal and ocular discharge. Although clinical signs typically are mild, PI<sub>3</sub> 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<sub>3</sub>, 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. grippityphosa*, *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 Bovi-Shield FP 4+L5, no adverse reactions to vaccination were observed.

Four studies were conducted to demonstrate the safety of Bovi-Shield FP 4+L5 when administered to pregnant cows vaccinated prior to breeding with Bovi-Shield FP 4+L5, Bovi-Shield FP 4+VL5 or PregGuard FP 9. An intensive safety study was conducted in which susceptible heifers were vaccinated prior to breeding with either a placebo, a single dose of Bovi-Shield FP 4+VL5 30 days prior to breeding, or Bovi-Shield 4 150 days prior to breeding followed by Bovi-Shield FP 4+VL5 30 days prior to breeding. At approximately 160 to 220 days of pregnancy, each heifer received 10 doses of Bovi-Shield FP 4+L5. Administration of 10 doses of Bovi-Shield FP 4+L5 did not adversely affect pregnant heifers which had been vaccinated prior to breeding with Bovi-Shield FP 4+VL5.

**Table 1.** Effects of administration of 10 doses\* of Bovi-Shield FP 4+L5 to pregnant heifers.

Prebreeding Vaccination	No. Heifers	No. Abortions	No. of Healthy Calves	No. of Calves Positive for Pre-Nursing VN Antibodies		
				IBRV	BVDV-1	BVDV-2
Placebo†	20	6	14	0	9	7
Bovi-Shield FP 4+VL5	29	0	29	0	0	0
Bovi-Shield 4/ Bovi-Shield FP 4+VL5	30	0	30	0	0	0

\* A single dose of Leptoferm-5® was used to restore 10 doses of Bovi-Shield FP 4.

† At the time of administration of 10 doses of Bovi-Shield FP 4+L5, 11 of 20 placebo-vaccinated animals were negative for neutralizing antibodies to IBRV and 19 of 20 placebo-vaccinated animals were negative for both Type 1 and Type 2 BVDV antibodies.

In 3 field safety studies, cows were vaccinated prior to breeding with either Bovi-Shield FP 4+L5 or PregGuard FP 9 and then vaccinated with either Bovi-Shield FP 4+L5 or a placebo during the first, second or third trimester of pregnancy. Cows vaccinated with Bovi-Shield FP 4+L5 had abortion and calving rates similar to the placebo-vaccinated cows.

**Table 2.** Calving rates (normal calves delivered/total delivered) from cows confirmed pregnant.

Study	Controls	Vaccinates
First Trimester	261/263 (99.2%)	263/264 (99.6%)
Second Trimester	225/236 (95.3%)	220/235 (93.6%)
Third Trimester	148/149 (99.3%)	195/196 (99.5%)
Total	634/648 (97.8%)	678/695 (97.6%)

Efficacy of each fraction of Bovi-Shield FP 4+L5 was demonstrated in challenge-of-immunity studies. Cattle vaccinated with any fraction of Bovi-Shield FP 4+L5, 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 demonstrated no immunologic interference among the fractions of Bovi-Shield FP 4+L5. The effectiveness of Bovi-Shield FP 4+L5 in preventing IBR-induced abortion was demonstrated by vaccinating susceptible heifers approximately 4 weeks prior to breeding. The vaccinated heifers, along with a group of nonvaccinated controls, were challenged with virulent IBR virus (Cooper strain) at approximately 190 days postbreeding. Results are summarized in the following table.

<b>Group</b>	<b>No. of Pregnant Heifers</b>	<b>No. of Abortions<sup>3,4</sup></b>	<b>Percent of Abortions<sup>4</sup></b>
Vaccinates <sup>1</sup>	20	1/20 <sup>3</sup>	5.0%
Vaccinates <sup>2</sup>	20	0/20	0.0%
Controls	11	10/11 <sup>4</sup>	91.0% <sup>4</sup>

<sup>1</sup> Vaccination with a single dose 1 month prior to breeding. Seronegative heifers with no history of vaccination with any product containing IBR or BVD vaccine viruses were selected for use in the efficacy studies.

<sup>2</sup> Vaccination with 2 doses at 5 months and 1 month prior to breeding.

<sup>3</sup> One stillbirth (IBR positive). Nineteen of 20 normal.

<sup>4</sup> Nine abortions (IBR positive). One calf appeared healthy at birth, subsequently became ill (IBR positive). One of 11 animals normal.

Similar study designs were used to demonstrate the effectiveness of the BVD fraction contained in Bovi-Shield FP 4+L5 in preventing fetal infections associated with both Types 1 and 2 BVD. In these studies, vaccinated heifers, along with a group of nonvaccinated control heifers, were challenged with virulent strains of either BVD Type 1 or 2 viruses when fetal ages ranged from approximately 73–98 days. Results of these studies are summarized in the following table.

<b>Group</b>	<b>Challenge</b>	<b>No. of Heifers Challenged</b>	<b>Viremia Heifers<sup>3</sup></b>	<b>No. of Calves Evaluated</b>	<b>Calves BVD Positive<sup>4</sup></b>
Vaccinates <sup>1</sup>	BVD1	19	0/19 (0.0%)	19	0/19 (0.0%)
Vaccinates <sup>2</sup>	BVD1	19	0/19 (0.0%)	19	1/19 (5.3%)
Controls	BVD1	10	9/10 (90.0%)	10	7/10 (70.0%)
Vaccinates <sup>1</sup>	BVD2	20	1/20 (5.0%)	18	6/18 (33.3%)
Vaccinates <sup>2</sup>	BVD2	20	1/20 (5.0%)	19	7/19 (36.8%)
Controls	BVD2	10	9/10 (90.0%)	10	9/10 (90.0%)

<sup>1</sup> Vaccination with a single dose 1 month prior to breeding. Seronegative heifers with no history of vaccination with any product containing IBR or BVD vaccine viruses were selected for use in the efficacy studies.

<sup>2</sup> Vaccination with 2 doses at 5 months and 1 month prior to breeding.

<sup>3</sup> Virus isolations performed on whole blood samples collected on days 0, 2, 4, 6, 8, 10, and 14 postchallenge of heifers.

<sup>4</sup> Whole blood collected from calves on the day of calving and prior to nursing (pre-colostral) was tested for BVD virus. Full-thickness ear notch and skin sample biopsies were tested by immunocytochemistry evaluation for the presence of BVD virus. If any sample was determined to be positive, the fetus was considered persistently infected with BVD virus.

**DIRECTIONS:**

1. *General Directions:* Vaccination of healthy cattle is recommended. Aseptically rehydrate the freeze-dried vaccine (Bovi-Shield FP 4) with the liquid bacterin provided (Leptoferm-5+A), 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.
2. *Primary Vaccination:* Administer a single 2-mL dose to healthy cattle, followed by a single dose of Bovi-Shield BRSV 3–4 weeks later. As an aid in preventing IBR-induced abortion and BVD persistently infected calves, administer a 2-mL dose approximately 1 month prior to breeding.
3. *Revaccination:* Annual revaccination with a single dose of Bovi-Shield FP 4+L5 is recommended.
4. Good animal husbandry and herd health management practices should be employed.

**PRECAUTIONS:**

1. Do not use in pregnant cows (abortions can result) unless they were vaccinated, according to label directions, with Bovi-Shield FP 4+L5, Bovi-Shield FP 4+VL5 or PregGuard FP 9 prior to breeding. Do not use in calves nursing pregnant cows unless their dams were vaccinated, according to label directions, with Bovi-Shield FP 4+L5, Bovi-Shield FP 4+VL5 or PregGuard FP 9 prior to breeding.
2. Store at 2°–7°C. Prolonged exposure to higher temperatures and/or direct sunlight may adversely affect potency. Do not freeze.
3. Use entire contents when first opened.
4. Sterilized syringes and needles should be used to administer this vaccine. Do not sterilize with chemicals because traces of disinfectant may inactivate the vaccine.
5. Burn containers and all unused contents.
6. Do not vaccinate within 21 days before slaughter.
7. Contains gentamicin as preservative.
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 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.

Technical inquiries should be directed to Pfizer Animal Health Veterinary Services,  
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75-4168-04