

Arsenal[®] 4.1

Bovine Rhinotracheitis – Bovine Virus Diarrhea – Parainfluenza 3 – Bovine Respiratory Syncytial Virus Vaccine, Modified Live Virus

For use in healthy, nonpregnant cattle as an aid in the prevention of disease caused by infectious bovine rhinotracheitis (IBR) virus, bovine virus diarrhea (BVD) Type 1 and Type 2 viruses, parainfluenza Type 3 (PI₃) virus and bovine respiratory syncytial virus (BRSV).

Arsenal[®] IBR

Bovine Rhinotracheitis Vaccine, Modified Live Virus

For use in healthy nonpregnant cattle as an aid in the prevention of disease caused by infectious bovine rhinotracheitis (IBR) virus.

Arsenal[®] IBR BVD

Bovine Rhinotracheitis – Bovine Virus Diarrhea Vaccine, Modified Live Virus

For use in healthy, nonpregnant cattle as an aid in the prevention of disease caused by infectious bovine rhinotracheitis (IBR) virus and bovine virus diarrhea (BVD) Type 1 and Type 2 viruses.

CUT LINE

- **Broad-spectrum protection** — Arsenal 4.1 contains a modified live isolate of noncytopathic (NCP) BVD 1b – the biggest BVD challenge facing producers today. It also provides proven respiratory protection against BVD Type 2, IBR, PI₃ and BRSV.
- **Flexibility** — Depending upon the disease challenges of the operation, beef and dairy producers can choose from Arsenal 4.1, Arsenal IBR BVD and Arsenal IBR for targeted protection.
- **Single-dose administration** — Provides proven single-dose protection against all antigens, including the BRSV fraction of Arsenal 4.1. Calves vaccinated at less than six months of age should receive another dose at six months of age or older. Revaccinate annually or as recommended by your veterinarian.
- **Safety** — Field tests showed that Arsenal 4.1 can be used safely in calves as young as two weeks of age. Overall, minimal untoward vaccination reactions (0.2% reaction rate) were noted in commercial dairy calves, veal calves, beef replacement heifers and feedlot cattle.
- **SubQ administration label** — As part of Novartis' ongoing commitment to Beef Quality Assurance efforts, all the products carry a SubQ administration label. Arsenal IBR is also labeled for IN (intranasal) administration.

Product Numbers

Arsenal[™] 4.1

250 - 20 mL - 10 doses
258 - 100 mL - 50 doses

Arsenal[™] IBR

257 - 100 mL - 50 doses

Arsenal[™] IBR BVD

253 - 100 mL - 50 doses



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Technical disease information

Bovine Virus Diarrhea (BVD)

BVD virus is one of the most prevalent and challenging bovine viral pathogens in the world. There are literally hundreds of BVD viral strains, and the number continues to increase due to the mutating nature of the virus. The BVD virus suppresses the immune system, which leads to secondary infections from other pathogens. The virus is associated with:

- Bovine respiratory disease
- Hemorrhagic (bleeding) syndrome
- Reproductive disorders, including infertility, abortion and neonatal defects
- Enteric disorders, such as BVD and mucosal disease in persistently infected (PI) calves
- Bacterial infections, including *Pasteurella multocida* and *Mannheimia (Pasteurella) haemolytica*

BVD viral strains fall into two genotype categories – BVD Type 1 and BVD Type 2. Within BVD Type 1, there are at least two subtypes: BVD Type 1a and BVD Type 1b. Research studies show that BVD Type 1b is the predominant subtype found in respiratory cases involving BVD.¹ See Table 1.

Type 1				Type 2	
Subtype 1a		Subtype 1b		CP	NCP
CP	NCP	CP	NCP		

BVD viral strains are further classified according to whether they are cytopathic (CP) or noncytopathic (NCP). Researchers are determining that NCP BVD is the more prevalent variation. The major isolate in clinical BVD, NCP BVD accounts for 90 to 95 percent of all clinical outbreaks.² NCP also is the cause of all PI calves, and a major cause of BVD-induced abortions.

While percentages vary among different geographic regions, neutralizing antibodies for this pestivirus have been detected in 60 to 85 percent of U.S. cattle, and 1 to 2 percent are persistently infected.³ See Tables 2 and 3 for BVD post-challenge results.

Infectious Bovine Rhinotracheitis (IBR)

IBR is caused by bovine herpesvirus 1, which also is responsible for the disease syndrome known as infectious pustular vulvovaginitis and balanoposthitis (IPV-IPB). IPV was the primary form of the disease until animals were concentrated into high population units, such as beef feedlots and large dairy herds. The IBR virus is associated with:

- Upper respiratory tract infections
- Bovine respiratory disease (BRD)
- Conjunctivitis
- Reproductive disorders, such as IPV, abortion and neonatal death

See Table 4 for IBR efficacy data.

Bovine Respiratory Syncytial Virus (BRSV)

BRSV was first isolated in the U.S. in 1974 and has been identified as a major contributing agent in the BRD syndrome. It was named BRSV because this pneumovirus invades the cell lining of the trachea and lungs and because it promotes the formation of large multinucleated cells called syncytial cells in the epithelium and interstitial spaces of the lung. BRSV appears to be widespread across the United States. Nationwide studies have shown that BRSV is present in 38 to 76 percent of beef and dairy herds.⁴

An initial exposure to the virus usually produces a mild subclinical infection, which occurs approximately five days after stress and exposure. Within two to 10 days after recovery from this primary infection, some animals will exhibit a severe clinical form of the disease, which if untreated will last 12 to 14 days and result in a high percentage of deaths. At any of these stages, the course and severity of the disease can be aggravated by invasion of the weakened animals by other viral and bacterial pathogens. See Figure 1 for BRSV post-challenge results.

Parainfluenza 3 (PI₃)

Parainfluenza 3 is a paramyxovirus in the same family as bovine respiratory syncytial virus (BRSV). PI₃ virus has been isolated, identified and studied in relation to bovine respiratory disease syndrome. PI₃ virus is commonly isolated from animals suffering from BRD, although it appears to be more of a contributing agent rather than a primary pathogen. By itself, PI₃ virus usually produces a rather benign infection of the lungs. It most commonly invades the lungs, causing a fibrinous pleuritis and pneumonia. See Table 5 for PI₃ efficacy data.

	Total Average Clinical Score**/Group
Vaccinate	2.80
Control	6.27
P Value*	0.0056

Arsenal 4.1 significantly protected against PI₃ in challenge trials, as evidenced by significant differences in total clinical scores and virus shedding between vaccinated and control calves.

* A P value ≤0.05 is considered statistically significant.

** The clinical scoring system included nasal discharge, respiratory signs, ocular signs and anorexia.

References:

1. Fulton RW, et al. Bovine viral diarrhea virus (BVDV) 1b: predominant BVDV subtype in calves with respiratory disease. *Can J Vet Res.* 2002;66:181-190.
2. Chase CL. Department of Veterinary Science, South Dakota State University, Brookings, SD.
3. Houe H. Epidemiological features and economical importance of bovine virus diarrhea virus (BVDV) infections. *Vet Microbiol.* 1999;64:89-107.
4. Richey EJ. Extension Veterinarian, College of Veterinary Medicine, Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL.

TABLE 2. BVD Type 1 Post-Challenge Results

Number of Animals/Total				
	Temp (≥103.5° F)	Clinical Signs	Leukopenia (Drop in white blood cells)	Virus Shedding
Vaccinate	0/20	0/20	0/20	0/20
Control	4/5	3/5	4/5	5/5
P Value*	0.0004	0.0043	0.0004	<0.0001

Challenge trial data prove that Arsenal 4.1 provides protection against BVD NCP 1b, the BVD viral strain that's most likely to cause respiratory outbreaks.

* A P value ≤0.05 is considered statistically significant.

Protocol:

- 20 vaccinates and 5 nonvaccinated controls
- 750- to 1,000-pound yearlings
- 4-mL dose of virulent BVD Type 1 USDA-approved challenge administered intranasally at 21 days post-vaccination
- Animals observed two days prior through 14 days post-challenge

TABLE 3. BVD Type 2 Post-Challenge Results

Number of Animals/Total					
	Temp (≥103.5° F)	Clinical Signs	Mortality	Leukopenia (Drop in white blood cells)	Virus Shedding
Vaccinate	0/20	0/20	0/20	1/20	0/20
Control	9/12	12/12	3/12	10/12	7/12
P Value*	<0.0001	<0.0001	0.0444	<0.0001	0.0002

Arsenal 4.1 provides proven respiratory protection in tough challenge models against BVD Type 2

* A P value ≤0.05 is considered statistically significant.

Protocol:

- 20 vaccinates and 12 nonvaccinated controls
- 750- to 1,000-pound yearlings
- 4-mL dose of virulent BVD Type 2 USDA-approved challenge administered intranasally at 21 days post-vaccination
- Animals observed two days prior through 14 days post-challenge

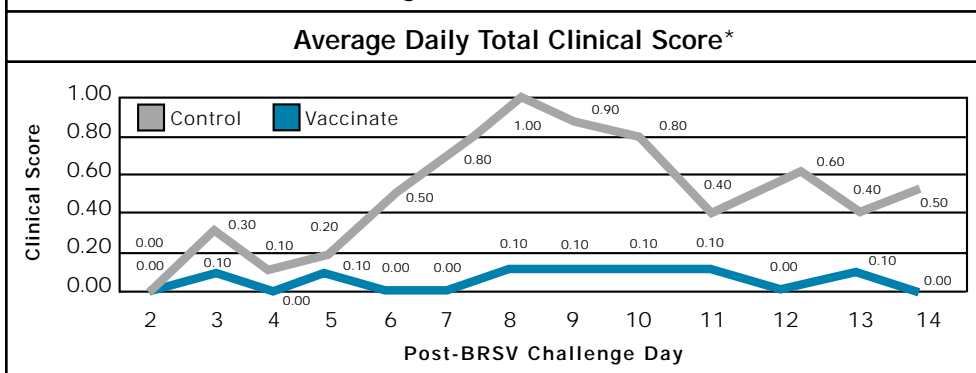
TABLE 4. IBR Efficacy Data

	Total Average Clinical Score**	Temp (≥103.5° F) No. of Animals/Total	Virus Shedding No. of Animals/Total
Vaccinate	0.05	0/20	1/20
Control	30.67	18/18	18/18
P Value*	<0.0001	<0.0001	<0.0001

Arsenal 4.1 significantly protects against IBR, as proven by this demonstration of significant differences in temperature responses, clinical scores and virus shedding between vaccinated and control calves.

* A P value ≤0.05 is considered statistically significant.

** The clinical scoring system included nasal discharge, respiratory signs, ocular signs and anorexia.

FIGURE 1. BRSV Post-Challenge Results


Even with one SubQ dose, Arsenal 4.1 was able to significantly control the clinical signs associated with BRSV.

* The clinical scoring system included nasal discharge, respiratory signs and ocular signs.

Protocol:

- 22 vaccinates and 12 nonvaccinated controls
- Aged 18 to 36 weeks old
- 4-mL dose of virulent USDA-approved BRSV challenge administered intranasally at 21 days post-vaccination
- Animals observed two days prior through 14 days post-challenge

Arsenal® 4.1

DIRECTIONS: Aseptically rehydrate the freeze-dried vaccine with the diluent supplied. Shake well before using. Administer 2 mL subcutaneously. In accordance with Beef Quality Assurance guidelines, this product should be administered subcutaneously (under the skin) in the neck. Calves vaccinated prior to six months of age should be revaccinated after six months of age. Revaccinate annually or as recommended by your veterinarian.

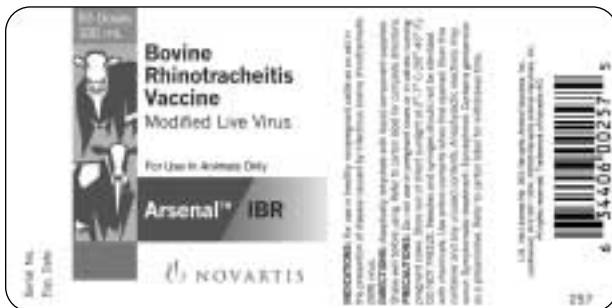


PRECAUTIONS: Do not use in pregnant cows or in calves nursing pregnant cows. Store out of direct sunlight at 2°-7° C (35°-45° F). DO NOT FREEZE. Needles and syringes should not be sterilized with chemicals. Use entire contents when first opened. Do not vaccinate within 21 days prior to slaughter. Burn containers and any unused contents. Anaphylactic reactions may occur. Symptomatic treatment: Epinephrine. Contains gentamicin as a preservative.

PACKAGING: 20 mL/10 dose and 100 mL/50 dose bottles.

Arsenal® IBR

DIRECTIONS: Aseptically rehydrate the freeze-dried vaccine with the diluent supplied. Shake well before using. Administer 2 mL intranasally or subcutaneously. In accordance with Beef Quality Assurance guidelines, when this product is administered subcutaneously, it should be under the skin in the neck. Calves vaccinated prior to six months of age should be revaccinated after six months of age. Revaccinate annually or as recommended by your veterinarian.

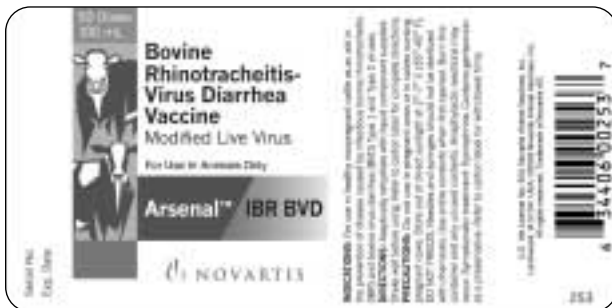


PRECAUTIONS: Do not use in pregnant cows or in calves nursing pregnant cows. Store out of direct sunlight at 2°-7° C (35°-45° F). DO NOT FREEZE. Needles and syringes should not be sterilized with chemicals. Use entire contents when first opened. Do not vaccinate within 21 days prior to slaughter. Burn containers and any unused contents. Anaphylactic reactions may occur. Symptomatic treatment: Epinephrine. Contains gentamicin as a preservative.

PACKAGING: 100 mL/50 dose bottles.

Arsenal® IBR BVD

DIRECTIONS: Aseptically rehydrate the freeze-dried vaccine with the diluent supplied. Shake well before using. Administer 2 mL subcutaneously. In accordance with Beef Quality Assurance guidelines, this product should be administered subcutaneously (under the skin) in the neck. Calves vaccinated prior to six months of age should be revaccinated after six months of age. Revaccinate annually or as recommended by your veterinarian.



PRECAUTIONS: Do not use in pregnant cows or in calves nursing pregnant cows. Store out of direct sunlight at 2°-7° C (35°-45° F). DO NOT FREEZE. Needles and syringes should not be sterilized with chemicals. Use entire contents when first opened. Do not vaccinate within 21 days prior to slaughter. Burn containers and any unused contents. Anaphylactic reactions may occur. Symptomatic treatment: Epinephrine. Contains gentamicin as a preservative.

PACKAGING: 100 mL/50 dose bottles.

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