

Arsenal® 4.1

Bovine Rhinotracheitis – Virus Diarrhea – Parainfluenza 3 – 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), bovine virus diarrhea (BVD Type 1 and Type 2), parainfluenza Type 3 (PI₃) and bovine respiratory syncytial (BRSV) viruses. When administered to cows and heifers 30 days prior to breeding, this product aids in the reduction of persistently infected calves caused by BVD Type 1. This product contains noncytopathic BVD Type 1 attenuated virus.

Product Numbers

Arsenal® 4.1

250 - 20 mL

258 - 100 mL



- **Broad-spectrum protection** — Arsenal 4.1 is a modified live vaccine that provides proven protection against BVD Types 1 and 2, IBR, PI₃ and BRSV.
- **Real-world strains** — Arsenal 4.1 responds to today's emerging BVD challenge – noncytopathic (NCP) BVD. Most respiratory outbreaks involving BVD are caused by NCP strains. In addition, NCP BVD is **always** the cause of persistently infected (PI) calves.
- **Protects against persistent infection.** University research has demonstrated protection against both Type 1 and Type 2 BVD persistent infections.
- **Smooth** — Research shows that Arsenal 4.1 doesn't contribute to post-vaccination fever in calves.
- **Little effect on milk production** — Arsenal 4.1 has a minimal effect on milk production post-vaccination.
- **Single-dose administration** — Provides proven single-dose protection against all antigens, including the BRSV fraction. 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 show that Arsenal 4.1 can be used safely in calves as young as two weeks of age. Minimal adverse reactions (0.2% reaction rate) were noted in commercial dairy calves, veal calves, beef replacement heifers and feedlot cattle.

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Technical disease information

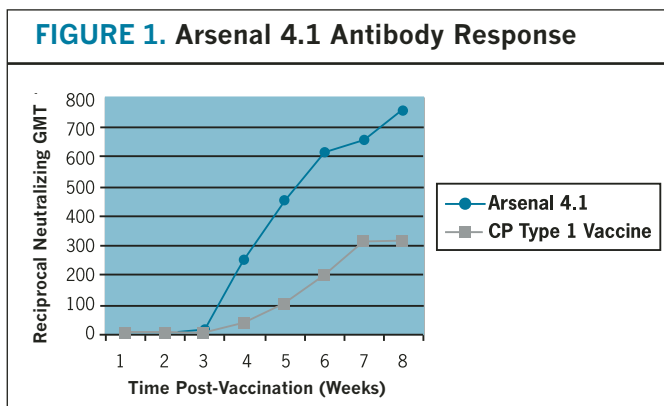
Bovine Virus Diarrhea (BVD)

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
- Persistently infected (PI) calves that shed enormous amounts of infective virus throughout their lives
- Gastrointestinal disorders
- Mucosal disease in PI calves

BVD viral strains fall into two genotype categories – BVD Type 1 and BVD Type 2. **See Table 1 and Table 2 for BVD Type 1 and Type 2 post-challenge results.**

BVD viral strains are further classified according to whether they are cytopathic (CP) or noncytopathic (NCP). Researchers have determined 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.¹ With Arsenal 4.1, NCP is in the bottle for a significantly higher antibody response.^{2,3} **See Figure 1.**



This study shows larger, faster antibody response with Arsenal 4.1 vs. a vaccine containing only cytopathic (CP) BVD Type 1.

NCP also is the cause of all PI calves, and a major cause of BVD-induced abortions. University-conducted research demonstrated that Arsenal 4.1 reduced the occurrence of PI calves when pregnant heifers were challenged with BVD 1 and BVD 2 viruses.⁴

Infectious Bovine Rhinotracheitis (IBR)

IBR, sometimes referred to as “red nose,” is caused by

Bovine Herpesvirus 1. Prior to the advent of large feedlots and dairy complexes, the primary manifestation of IBR was in a reproductive form called IPV (infectious pustular vulvovaginitis). Today, the IBR virus is associated with:

- Upper respiratory tract infections
- Bovine respiratory disease
- Eye disorders like conjunctivitis
- Reproductive disorders, such as IPV, abortion and neonatal death

See Table 3 for IBR post-challenge results.

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 promotes the formation of large multinucleated cells called syncytial cells. BRSV is widespread across the United States, with studies showing BRSV present in 38 to 76 percent of beef and dairy herds.⁵

An initial exposure to the virus usually produces a mild subclinical infection occurring 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 2 for BRSV post-challenge results.**

Parainfluenza 3 (PI₃)

Parainfluenza 3 is in the same family as bovine respiratory syncytial virus (BRSV) and 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 an inflammation of the membranes around the lungs, which may result in pneumonia.

References:

1. Chase CL. Department of Veterinary Science, South Dakota State University, Brookings, SD.
2. Lambot et al. Characterization of the immune response of cattle against noncytopathic and cytopathic biotypes of bovine viral diarrhea virus. *J Gen Virol.* 1997;78:1041-1047.
3. Data on file, Novartis Animal Health US, Inc.
4. Brock K, et al. Protection against Fetal Infection with Either Bovine Viral Diarrhea Virus Type 1 or Type 2 Using a Noncytopathic Type 1 Modified-Live Virus Vaccine. *Vet Ther.* 2006;27-34.
5. Richey EJ. Extension Veterinarian, College of Veterinary Medicine, Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL.
6. Data on file, Novartis Animal Health US, Inc.
7. Data on file, Novartis Animal health US, Inc.
8. Garrett EF. Effect of Two Commercially Available Multivalent Modified Live Viral Vaccines on Milk Production of Holstein Dairy Cows. AABP Proceedings. 2005.

Pre-licensing efficacy studies⁶

TABLE 1. 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*	<0.01	<0.01	<0.01	<0.01

Challenge trial data prove that the BVD component in Arsenal 4.1 provides protection against BVD Type 1, 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 2. 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*	<0.01	<0.01	<0.05	<0.01	<0.01

The BVD component in 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 3. IBR Efficacy Data

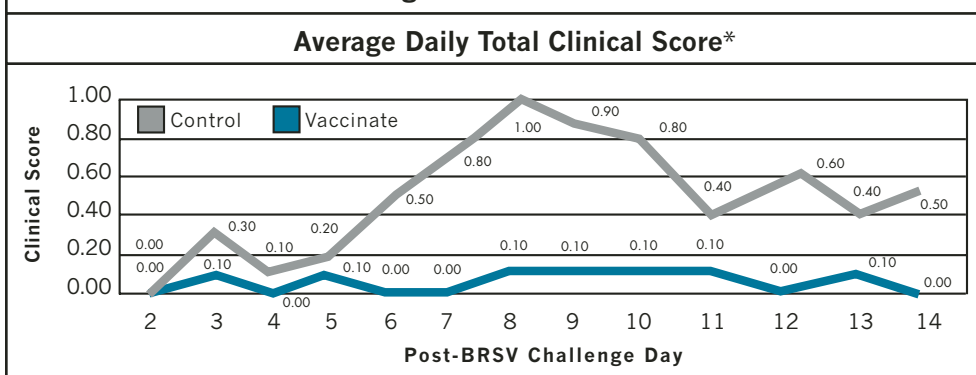
	Total Average Clinical Score**	Temp (≥103.5° F) No. of Animals/Total	Virus Shedding No. of Animals/Total
Vaccinate	0.05	0/20	1/20
Control	30.67	18/18	18/18
P Value*	<0.01	<0.01	<0.01

The IBR component in 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 2. BRSV Post-Challenge Results



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

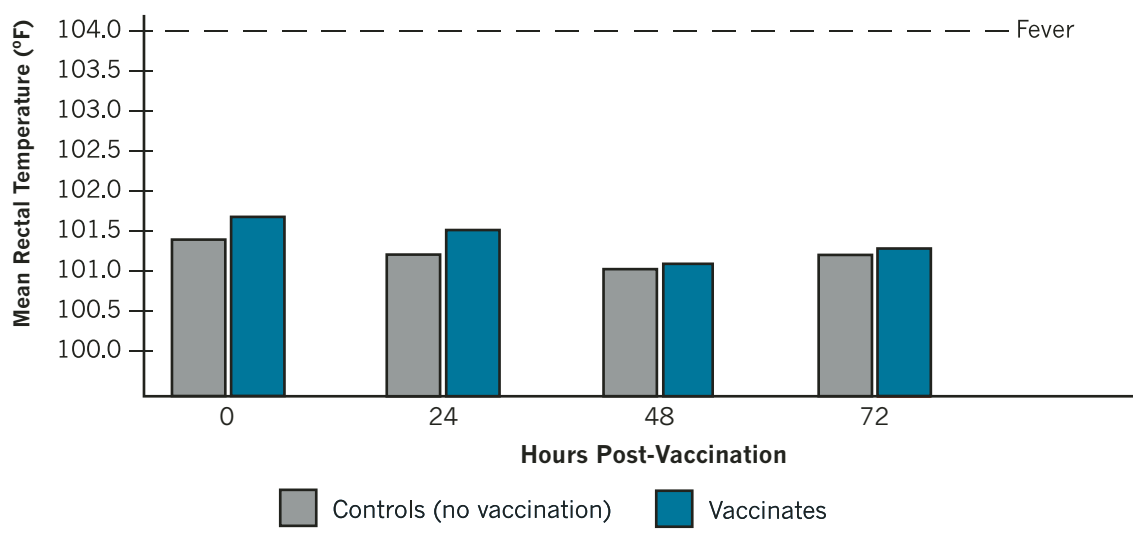
* The clinical scoring system included nasal discharge, respiratory signs and ocular signs.

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

Safety information

FIGURE 3. Average Temperature Response After Vaccination with Arsenal 4.1

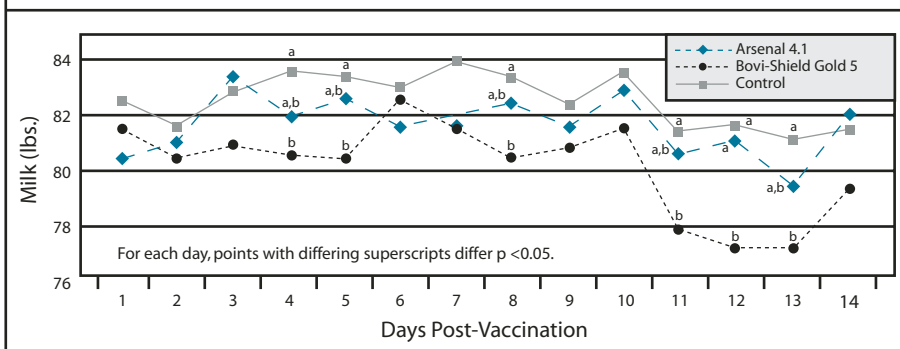


Smooth – won't contribute to fevers or set back animals.

Research shows Arsenal 4.1 won't cause sweats in calves. A study on 40 Holstein steers and heifers – ranging in age from six to eight months and weighing about 500 pounds each – showed no significant difference in body temperature between vaccinated and control animals.⁷

Calves did not develop fevers within 72 hours after vaccination with Arsenal 4.1.

FIGURE 4. Least Squares Means Daily Milk Production Post-Vaccination



A field trial compared the effect of sterile water and two commercially available modified live virus vaccines – Arsenal 4.1 and Bovi-Shield® Gold™ 5 – on milk production⁸.

Protocol:

- 259 Holstein cows vaccinated according to label directions
- 86 in Arsenal 4.1 group, 87 in Bovi-Shield Gold 5 group, 86 in control group (2-mL sterile saline SubQ)
- Animals were open, 40 to 357 days in milk and in good health
- Daily milk production recorded for each animal, five days prior to vaccination through 14 days after vaccination

Results: No significant drop was observed in the Arsenal 4.1-vaccinated group when compared to control animal milk production. Conversely, Bovi-Shield Gold 5 significantly reduced milk production days when compared to controls on post-vaccination days 4, 5, 8, 11, 12 and 13.

Arsenal® 4.1

DIRECTIONS: Aseptically rehydrate with liquid component 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. Proven safe in calves 2 weeks of age or older. 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 this container and any unused contents. Anaphylactic reactions may occur. Symptomatic treatment: Epinephrine. Contains amphotericin B and gentamicin as preservatives.

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



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