



PROFESSIONAL SERVICES

Boehringer Ingelheim Vetmedica, Inc.

TECHNICAL BULLETIN

Express® FP Vaccines Unsurpassed Protection against BVD Persistent Infection

Introduction

Five fetal protection efficacy studies have been completed with the Express® FP (formerly Breed-Back® FP) family of vaccines. Two studies have involved challenge with BVDV Type 1 strains and three studies have involved challenge with BVDV Type 2 strains. The objective of each study was to provide proof that the vaccine protects the fetus against persistent infection with the challenge strain of BVD virus.

BVDV Type 1 Fetal Protection Studies

DESIGN		
	Study #1	Study #2
Vaccinates	11	18
Controls	8	10
Vaccination (days prior to breeding)	-45 days	-53 days
Challenge (day of gestation)	Day 75 (+/-15)	Day 75 (+/-7)
Fetal Harvest (day of gestation)	Day 150 (+/-15)	Day 200 (+/-7)
BVDV Challenge Strain (intranasal challenge)	KE9 – Type 1b non-cytopathic	BJ – Type 1a non-cytopathic
Test used to detect virus in fetus	rt-PCR	VI and rt-PCR

RESULTS				
	Treatment	# of Heifer Deaths and Abortions	# of PI positives/total	Percent Protected
Study #1	Vaccinates	0	1 of 11	91%
	Controls	0	8 of 8	0%
Study #2	Vaccinates	0	0 of 18	100%
	Controls	0	10 of 10	0%

BVDV Type 2 Fetal Protection Studies

DESIGN			
	Study #1	Study #2	Study #3
Vaccinates	10	19	17
Controls	7	8	14
Vaccination (days prior to breeding)	-53 days	-53 days	-31 days
Challenge (day of gestation)	Day 75 (+/-7)	Day 75 (+/-7)	Day 77
Fetal Harvest (day of gestation)	Day 200 (+/-7)	Day 200 (+/-7)	Day 155 & 156
BVDV Challenge Strain (intranasal challenge)	NY93 – Type 2 non-cytopathic	PA131 – Type 2 non-cytopathic	PA131 – Type 2 non-cytopathic
Test used to detect virus in fetus	rt-PCR	VI and rt-PCR	VI and re-PCR

RESULTS				
	Treatment	# of Heifer Deaths and Abortions	# of PI positives/total	Percent Protected
Study #1	Vaccinates	0	0 of 10	100%
	Controls	6 (3 of 3)	7 of 7	0%
Study #2	Vaccinates	0	1 of 19	95%
	Controls	0	8 of 8	0%
Study #3	Vaccinates	0	1 of 17	94%
	Controls	3 (2 and 1)	14 of 14	0%

SUMMARY OF ALL TRIALS			
Challenge	Treatment	# Positive/Total	Percent Protected
BVDV Type 1 (2 studies)	Vaccinates	1 of 29	96%
	Controls	18 of 18	0%
BVDV Type 2 (3 studies)	Vaccinates	2 of 46	96%
	Controls	29 of 29	0%

Conclusion

These results show that after challenge with four different non-cytopathic BVD strains, a Type 1a, Type 1b, and two Type 2, Express® FP successfully prevented BVD persistent infection in the offspring of vaccinated cattle. In each of the studies, **100% of the unvaccinated control heifers had persistently infected offspring**; however, the vaccine consistently held against the severe BVDV challenge.

Implications

Due to the strength of the data, and the level of protection demonstrated by Express FP, APHIS has granted a **“Prevention of persistently infected calves caused by BVD Types 1 and 2”** label claim for Express FP vaccines.

References:

1. F. Kovacs, T. Magyar, C. Rinehart, et al. *The live attenuated bovine viral diarrhea virus components of a multi-valent vaccine confer protection against fetal infection*. Veterinary Microbiology 96 (2003) 117-131.
2. K. Fairbanks, C. Rinehart, W. Ohnesorge, et al. *Evaluation of fetal protection against experimental infection with type 1 and type 2 bovine viral diarrhea virus after vaccination of the dam with a bivalent modified-live virus vaccine*. JAVMA, Vol. 225, No. 12, Dec. 2004.
3. C. Rinehart, W. Ohnesorge, C. Chase, et al. *BVDV fetal protection vaccine proof of efficacy studies: Requirements include both consistency and diversity*. Poster presentation at the BVDV: The Future is Now Conference; Denver, CO, Jan. 2006.

Level of Protection Label Claims What are they and what do they mean?

There has been a lot of talk recently concerning label claims for vaccines, especially label claims as they relate to protection against BVD virus. The label claims for a product must be supported with data that accurately reflects the expected performance by the product. Depending on the strength of the data, USDA-APHIS may grant a vaccine one of label claims listed below.



A claim that the product is intended to **prevent infection** may be made only for products able to prevent all colonization or replication of the challenge organism in vaccinated and challenged animals. If such a conclusion is supported with a very high degree of confidence by convincing data, a label statement such as “for the prevention of infection with [specific microorganism]” may be used.

A claim that the product is intended to **prevent disease** may be made only for products shown to be highly effective in preventing clinical disease in vaccinated and challenged animals. The entire 95% interval estimate of efficacy must be at least 80%. If so, a label statement such as “for the prevention of disease due to [specific microorganism]” may be used.

A claim that the product is intended to **aid in disease prevention** may be made for products shown to prevent disease in vaccinated and challenged animals by a clinically significant amount which may be less than that required to support a claim of disease prevention (see above). If so, a label statement such as “an aid in the prevention of disease due to [specific microorganism]” may be used.

A claim that the product is intended to **aid in disease control** may be made for products which have been shown to alleviate disease severity, reduce disease duration, or delay disease onset. If so, a label statement such as “an aid in the control of disease due to [specific microorganism]” or a similar one stating the products particular action may be used.

Other Label Claims

Products with beneficial effects other than direct disease control, such as the control of infectiousness through the reduction of pathogen shedding, may make such claims if the size of the effect is clinically significant and well supported by data.

Information taken from Veterinary Services Memorandum No. 800.202, June 14, 2002

Vaccine Claims for Protection of the Fetus against Bovine Virus Diarrhea Virus

Bovine virus diarrhea virus (BVDV) can result in a multitude of reproductive problems in cattle including abortion, stillbirths, congenital anomalies, persistently infected calves, and unthrifty, stunted calves. The Center for Veterinary Biologics has published a notice that clarifies the type of data required to support various label claims against the reproductive effects of BVDV.

Label claims for BVDV reproductive effects have been divided into claims for fetal protection and claims for abortion (due to maternal or fetal causes). The claims must be type-specific (BVDV Type 1 or Type 2) and must be supported by acceptable data as outlined in Veterinary Services Memorandum 800.202.

Categories of Claims for BVDV Reproductive Effects¹

1. **“Aids in the prevention of abortion”:**
 - a. Supported by studies in which abortions occur in an acceptable proportion of the non-vaccinated control cattle
 - b. Must utilize challenge strains that routinely cause abortion
 - c. Field studies, using natural exposure to BVDV, may be performed

2. **“Aids in the prevention of persistently infected calves”:**
 - a. Challenge pregnant cattle at 75-90 days of gestation
 - b. Perform virus isolation procedures on tissues from all fetuses on, or after, 150 days of gestation
 - c. Fetuses from which BVDV is isolated are considered to be persistently infected

3. **“Aids in the prevention of fetal infection” or “Aids in the prevention of fetal infection, including persistently infected calves”:**
 - a. May be supported by data to support the claim for “aids in the prevention of persistently infected calves” AND,
 - b. Must challenge a separate group of pregnant cattle at ~180 days of gestation and evaluate the fetuses (or calves) at, or after, ≥ 220 days of gestation.
 - c. Serology and virus isolation procedures must be performed.
 - d. Fetuses (or calves) are considered to be protected from infection if they are BVDV negative and seronegative for BVDV antibodies.

¹Information taken from Center for Veterinary Biologics Notice No. 02-19, Sept. 5, 2002