



November 14, 2011

VETERINARY SERVICES MEMORANDUM NO. 800.212

**United States
Department of
Agriculture**

Animal and Plant
Health Inspection
Service

Veterinary Services

Washington, DC
20250

TO: VS Management Team (VSMT)
Directors, Center for Veterinary Biologics
Biologics Licensees, Permittees, and Applicants

FROM: John R. Clifford /s/ *John R. Clifford*
Deputy Administrator

SUBJECT: Licensing Considerations: Vaccine Claims for Protection of the Fetus
Against Bovine Virus Diarrhea Virus

I. PURPOSE

This memo provides guidance to licensees, permittees, and applicants concerning vaccine claims for protection against the reproductive effects of Bovine Virus Diarrhea Virus (BVDV). Historically, BVDV vaccines have been licensed based on respiratory challenge, as described in title 9, *Code of Federal Regulations* (9 CFR), sections 113.215 and 113.311. As knowledge of BVDV pathogenesis has increased, interest in obtaining label claims to include the reproductive effects of the disease has also increased. Infection with BVDV can cause a wide array of reproductive sequelae, including abortion, persistently infected calves, unthrifty or stunted calves, and congenital anomalies. The Center for Veterinary Biologics (CVB) allows label claims for the reproductive effects of BVDV. Additional studies must be performed, however, to support label claims regarding the reproductive effects of BVDV. As per 9 CFR, section 112.1(b), no label shall include statements that are false or misleading. Similarly, as per 9 CFR, section 102.4(b)(3), biologics shall not be advertised as to mislead or deceive the purchaser, and packages or containers in which biologics are marketed shall not bear any statement, design, or device which is false or misleading. This memo clarifies the type of data that is needed to support various label claims and promotional materials against the reproductive effects of BVDV.

II. BACKGROUND

Licensing Considerations provide guidance to licensees, permittees, and applicants concerning the submission of documents to support licensure and label claims. This guidance assists CVB Policy, Evaluation, and Licensing with maintaining uniformity and consistency in the review of license applications and associated label claims. It also provides guidance for conducting studies to support label claims against the reproductive effects of BVDV. Conducting these studies supports label claims and supports associated promotional materials regarding the reproductive effects of BVDV. The complexity of



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the disease, including the effect of persistently infected calves on herd health, requires certain clarifications to be included on the labeling.

III. POLICY

- A. Types of Claims. Label claims for BVDV reproductive effects are divided into claims for fetal protection and claims for abortion (which may be due to maternal, as well as fetal, causes). The claims are type-specific (i.e., BVDV Type 1 or Type 2). Each claim must be directly supported by acceptable data that have been approved by and filed with CVB. Three categories have been identified:
1. *Abortion*. Claims for efficacy against abortion due to BVDV must be supported by studies in which abortions occur in an acceptable proportion of the nonvaccinated control cattle. Since many strains of BVDV do not routinely cause abortion, appropriate challenge strains must be used. Alternatively, acceptable field studies, using natural exposure to BVDV, may be performed.
 2. *Persistently infected calves*. Claims for efficacy against the development of persistently infected calves may be supported by challenging pregnant cattle at 50 to 100 days of gestation and performing virus isolation procedures on tissues from all fetuses on or after 150 days of gestation. Those fetuses from which BVDV is isolated are considered to be persistently infected.
 3. *Fetal infection*. Claims for efficacy against fetal infection by BVDV (e.g., “*aids in the prevention of fetal infection*” or “*aids in the prevention of fetal infection, including persistently infected calves*”) may be supported by generating data to support a claim for persistently infected calves AND challenging a separate group of pregnant cattle at approximately 180 days of gestation, and evaluating the fetuses (or calves) at or after ≥ 220 days of gestation. Serology and virus isolation procedures must be performed. Fetuses (or calves) are considered to be protected from infection if they are seronegative for BVDV antibodies, and negative for BVDV using virus isolation techniques.

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B. Labels and Promotional Materials

1. Product labels should not be more specific than what can be supported by the filed data (e.g., should not make a specific label claim for congenital anomalies if the efficacy study did not produce calves with congenital anomalies in the nonvaccinated control group).
2. Labeling for products that have label claims for BVDV reproductive effects should include a description of the efficacy study results. Promotional materials for BVDV products with reproductive claims should be appropriate for the label claim. Products with claims for persistently infected calves or fetal infection should not be promoted as being effective against abortion or fetal loss. Promotional materials for products with claims for fetal infection may discuss the possible sequelae of fetal infection (e.g., congenital anomalies, unthrifty calves), but should not imply that protection against these conditions has been directly proven unless supported by acceptable data.
3. Promotional materials for BVDV products with reproductive claims should be appropriate for the label claim. Products with claims for persistently infected calves or fetal infection should not be promoted as being effective against abortion or fetal loss. Promotional materials for products with claims for fetal infection may discuss the possible sequelae of fetal infection (e.g., congenital anomalies, unthrifty calves), but should not imply that protection against these conditions has been directly proven unless supported by acceptable data.

V. IMPLEMENTATION/APPLICABILITY

This change is effective immediately. This policy applies to BVDV products with reproductive claims.