

# Bovine Viral Diarrhea FAQs



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# Classification

- BVDV is an RNA virus. It is a member of the *Pestivirus* genus, belonging to the family *Flaviviridae* <sup>1</sup>
- Two BVDV genotypes are recognized, based on the nucleotide sequence of the 5'untranslated (UTR) region; BVDV-1 and BVDV-2. BVDV-1 isolates have been grouped into 16 subtypes (a -p) and BVDV-2 has currently been grouped into 3 subtypes (a - c) <sup>2</sup>
- BVDV strains can be further divided into distinct biotypes (cytopathic or non-cytopathic) according to their effects on tissue cell culture <sup>13</sup>
  - cytopathic (cp) biotypes, formed via mutation of non-cytopathic (ncp) biotypes, induce apoptosis in cultured cells
  - Non-cytopathic (ncp) viruses can induce persistent infection in cells and have an intact NS2/3 protein. In cp viruses the NS2/3 protein is either cleaved to NS2 and NS3 or there is a duplication of viral RNA containing an additional NS3 region.
- Recently a new strain (BVDV 3, HoBi-like or atypical pestivirus) has been isolated from FBS from Brazil and is causing concern. It is currently thought that this strain is a problem across Brazil. <sup>3</sup>



# Epidemiology

- BVDV is considered one of the most significant infectious diseases in the livestock industry worldwide due to its high prevalence, persistence and clinical consequences. <sup>15</sup>
- BVDV is considered one of the most significant infectious diseases in Cell Culture due to its ability to reproduce in cells and the effect on cells
- BVDV crosses the placental barrier in cattle. Thus the fetus is exposed to the virus from the dam's exposure.
  - If a fetus is exposed prior to the development of their independent immune system (between 80 and 150 days of gestation) the fetus becomes "persistently infected". This will result in the animal being infected throughout their life with no ability to produce an immune response.



# Epidemiology – continued

- Transmission of BVDV occurs both horizontally and vertically <sup>13</sup>
  - Virus is transmitted via direct contact, bodily secretions and contaminated fomites, with the virus being able to persist in the environment for more than two weeks.
  - Persistently infected animals are the most important source of the virus, continuously excreting a viral load one thousand times that shed by acutely infected animals.
- BVDV is considered one of the most significant infectious diseases in the livestock industry worldwide due to its high prevalence, persistence and clinical consequences. <sup>8</sup>



# Pathogenesis

- Following viral entry and contact with the mucosal lining of the mouth or nose, replication occurs in epithelial cells
- BVDV infection of the dam prior to conception, and during the first 18 days of gestation, results in delayed conception and an increased calving to conception interval. If the embryo is attached, infection during days 29–41 can result in embryonic infection and resultant embryonic death.
- Infection of the dam from approximately day 30 of gestation until day 120 can result in immunotolerance and the birth of calves “persistently infected” with the virus
- BVDV antibodies do not pass the placental barrier between the dam and the fetus.
- Persistently infected dams always produce persistently infected fetus and calves. <sup>7</sup>



# Clinical Signs

- BVDV infection has a wide manifestation of clinical signs including fertility issues, milk drop, pyrexia, diarrhea and fetal infection. Occasionally, a severe acute form of BVD may occur. These outbreaks are characterized by thrombocytopenia with high morbidity and mortality. However, clinical signs are frequently mild and infection insidious. <sup>11</sup>
- In “persistently infected (PIs)” animals the virus remains present in a high percentage of the animal’s body cells throughout its life and is continuously shed. PIs often fail to thrive and are smaller than their peers, however they can appear normal.



# Incidence

- BVDV occurs in herds world-wide.
- Incidence appears to be fairly consistent world-wide. It is impacted by cattle density and less so by seasons.
- Persistently infected (PIs) cattle range from 1 to 2% in a herd
- Serum Incidence follows basic principles of statistical binomial probability
  - If a pool of 1000 animals is used at 1% incidence then the pool will be positive 100% of the time
  - If a pool of 100 animals is used at 1% incidence then the pool will be positive 60% of the time (87% negative at 2% incidence)
  - If a pool of 20 animals is used at 1% incidence then the pool will be positive 20% of the time (33% positive at 2% incidence)
- Hence it is possible but expensive to reduce the BVDV burden



# Eradication and Control

- The mainstay of eradication is the identification and removal of persistently infected animals. Re-infection is then prevented by vaccination and high levels of biosecurity, supported by continuing surveillance.
- Leading the way in BVDV eradication, almost 20 years ago, were the Scandinavian countries. It took all countries approximately 10 years to reach their final stages. This program requires continual monitoring of the entire herd on an ongoing basis. <sup>4,5</sup>
- While challenge studies indicate that killed, as well as live, vaccines prevent fetal infection under experimental conditions, the efficacy of vaccines under field conditions has been questioned. The birth of PI calves into vaccinated herds suggests that killed vaccines do not stand up to the challenge presented by the viral load excreted by a PI in the field. <sup>6</sup>



# Gamma Irradiation

- BVDV is very susceptible to gamma irradiation
  - Almost 6 log reduction at 30kGy



# Testing

There are numerous tests for BVDV but the most common are: <sup>9,10</sup>

- BVDV Virus Isolation - Virus isolation has been the "gold standard" for BVDV detection. This involves the incubation of specific cells in the presence of a sample and the subsequent analysis of the cells for BVD.
- BVDV PCR Detection - Samples are treated to extract RNA which is then converted to DNA. The DNA is replicated up to 50 times (thus  $2^{50}$  is  $10^{15}$  replications) and quantified.
- BVDV Antibody Detection - Antibody (Ig) ELISAs are used to detect historical BVDV infection; these tests have been validated in serum, milk and bulk milk samples. Ig ELISAs do not diagnose active infection but detect the presence of antibodies produced by the animal in response to viral infection.



# Testing - BVDV Virus Isolation

- **Strengths**
  - Required by many regulatory agencies
  - Can be developed to be extremely sensitive through selection of BVDV sensitive cells and viral concentration. Such tests are often developed by independent testing labs
- **Weakness**
  - Can be adjusted to provide desired result. For example, use of cells less sensitive to BVDV will provide a false negative result.
  - BVDV Antibody can block the ability of cells to replicate BVDV
  - Requires weeks of incubation



# Testing - BVDV PCR Detection

- **Strengths**

- Extremely sensitive, on the same level as very sensitive BVD Isolation tests
- Measures both active and inactive virus
- Relatively quick

- **Weaknesses**

- Measures both active and inactive virus



# Testing - BVDV Antibody Detection

- **Strengths**
  - Easy and inexpensive
  - Does not detect presence of the Virus
- **Weaknesses**
  - Quantitative but not sensitive



# Summary

- **Regulations**

BVDV regulated by governments and pharmaceutical agencies

- BVDV risk to cattle herds is over regulated because BVDV is a world wide disease with little differences in incidence rates between countries anywhere in the world.
- BVDV testing for pharmaceutical use requires greater definitions of testing and additional testing. Although common practice is to use very sensitive BVD Isolation Assays to protect cell lines
- BVDV Testing for “research use” is usually designed to provide a negative result.

- **BVDV Free Serum**

- The gold standard for BVDV activity is BVDV Isolation but there is no standard of sensitivity
- Serum screened in small batches can be pooled to pass to provide BVDV free serum
- Raw Serum can be gamma irradiated to pass BVD Virus Isolation Test
- Raw serum can be treated with BVDV antibody to provide a negative BVDV Isolation test
- Using all three tests can determine the status of serum and the means by which the serum is BVDV free.



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