

# Developing a BVD Vaccine

## FOR NEWBORN CALVES

**PROJECT TITLE** DNA-based, Needle-free Vaccination Methods Against Bovine Viral Diarrhea Virus in Newborn Calves

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### Background

DNA vaccines may help to overcome some of the limitations of traditional killed or modified live BVD vaccines. Using a DNA vaccine does not make the animal transgenic! Instead of an intact but non-pathogenic virus (in a modified live vaccine) or virus particles (in a killed vaccine), a DNA vaccine contains a piece of viral DNA that codes for the E2 protein found on the surface of the BVD virus. When the vaccine is administered to the animal, the DNA is *expressed* to produce the BVD virus E2 antigenic protein. The E2 antigen then causes an immune response that protects against a real BVD infection. DNA vaccines do not contain (or produce) the actual virus, which means that they can stimulate an immune response without any risk of causing the actual disease. DNA vaccines also contain tiny snippets of DNA called “CpG motifs”. These are a telltale sign that the DNA is foreign, so they help to greatly amplify the animal’s immune response to the DNA vaccine.

These researchers have developed an experimental BVDV E2 DNA vaccine. When followed with an E2 protein vaccine booster (formulated with an adjuvant containing the CpG motif), the immune response was excellent and protected nine month old calves from a BVD virus Type 1

challenge. The next steps are to expand the vaccine protection to cover both Type 1 and 2 strains of BVD, and get it to work in young calves using a needle-free injection system.

### Objectives

The overall goal of this research was to develop a needle-free DNA-based vaccination method against BVD virus types 1 and 2 that is effective in newborn and young calves at branding.

### What they did

This team produced BVD virus Type 1 and Type 2 E2 DNA-based vaccines and tested them in the lab, in mice



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and calves. Two approaches were used to make the BVD vaccines. Firstly, the DNA for the Type 1 and Type 2 E2 antigens were connected together in one long, circular DNA molecule called a plasmid. The second approach was to place the BVD Type 1 E2 DNA on one plasmid, the BVD Type 2 E2 DNA on a second plasmid, and mix the two sets of plasmids together.

These two approaches were tested in mice. The second approach (i.e. BVD Type 1 E2 DNA and BVD Type 2 E2 DNA on separate plasmids) produced the strongest immune response, so this vaccine approach was also tested in calves.

Calves were given one of three BVD DNA vaccines (only Type 1 plasmids, only Type 2 plasmids, or a mixture of both Type 1 and Type 2 plasmids). A second DNA vaccination was given three weeks later. A third booster vaccination (using purified BVD Type 1 and Type 2 E2 proteins instead of DNA) was given three weeks after the second vaccination. This is known as a DNA prime – protein boost strategy. Two weeks after the protein booster, calves were challenged with actual Type 1 or Type 2 BVD virus. Immune response, virus shedding, animal temperature and weight gain were measured.

### What they learned

The BVD Type 1 E2 DNA vaccine (followed by the BVD Type 1 E2 protein vaccine booster) provided limited protection against the BVD Type 2 virus. The BVD Type 2 E2 DNA vaccine (followed by the BVD Type 2 E2 protein vaccine booster) provided little or no protection against

the BVD Type 1 virus. However, the vaccine that contained both the Type 1 E2 DNA and the Type 2 E2 DNA on separate plasmids (followed by a booster containing both the BVD Type 1 and Type 2 E2 proteins) protected the calves against both Type 1 and Type 2 BVD viruses.

This research used an initial BVD DNA vaccination, followed by a booster vaccine containing purified BVD E2 protein given eight to 12 weeks later. To be of greatest commercial value, it would be preferable to give the booster vaccination at weaning time. Work is continuing to refine a BVD DNA vaccine protocol that can be given at birth, with a protein booster vaccination at weaning.

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## The experimental vaccine protected the calves against both Type 1 and Type 2 BVD viruses.

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### What it means

Since producing and mixing of DNA plasmids or purified antigen proteins is relatively straightforward, new antigens could be developed and added to these vaccine formulations as BVD strains evolve and change in prevalence.

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