



Efficacy trial data for Circumvent® PCV G2¹

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Introduction

The durable nature and widespread distribution of porcine circovirus type 2 (PCV2) ensures its presence in nearly all swine operations. While vaccination has been effective in most situations, it does not eliminate shedding, so the virus continues to persist in the environment. Therefore, effective control requires continual vaccination.

Development of an effective PCV2 vaccine involves a number of steps that are critical to determine the right formulation. To evaluate whether a vaccine formulation will work, vaccinated pigs are challenged with the pathogen under experimental conditions. However, the challenge model should be designed to help predict how well the vaccine will perform in the field. Merck Animal Health researchers used a PCV2 and porcine reproductive and respiratory syndrome virus (PRRSv) co-infection challenge model to test the ability of the new Circumvent® PCV G2 to protect under real-world conditions. PCV2 infection by itself is not very infectious. The PRRSv co-challenge stimulates the immune system resulting in more susceptible immune cells, which in turn results in a more intense PCV2 infection and subsequent development of PCV2 disease.

Within this challenge model, the main measurement is the presence of PCV2 in the blood, which is called viremia. Following exposure to PCV2, viremia starts building in the blood and is the initial step in the development of PCV2 disease in the pig. Controlling PCV2 disease by controlling viremia is a highly effective approach as the damage caused by the infection is limited or essentially eliminated.

Merck Animal Health's current PCV2 vaccines – Circumvent PCV and Circumvent PCV M – are highly effective at preventing or greatly reducing the level of viremia. The new vaccine, Circumvent PCV G2, will replace the monovalent Circumvent PCV and provides the same level of efficacy and protection against viremia, but now also includes long-lasting, 5-month duration of immunity (DOI). Plus, with its new convenient dosing options, it's the only PCV2 vaccine approved for use in pigs as early as 3 days of age (two-dose option).

Materials and Methods

Development: The same antigen and adjuvant used to make current Merck Animal Health PCV2 vaccines were used in formulating Circumvent PCV G2. Alterations were made to facilitate the single-dose and lower-volume, two-dose option. In the two studies reported here, the vaccine was administered through a single, 2-mL injection in pigs 3 weeks of age (one-dose option study) or as two, 1-mL injections with the first injection at 3 days of age and the second injection at 3 weeks of age (two-dose option study). Each study was conducted independent of the other.

Animals: Crossbred pigs from a herd free of *Mycoplasma hyopneumoniae* and PRRSv were used in the studies. Piglets had low levels of PCV2 maternal antibody and were negative for PCV2 by PCR on serum at enrollment.

Experimental design: Pigs were co-challenged with PCV2 and PRRSv at 10 weeks of age. Prior to challenge, pigs were bled periodically to assess serum antibody levels. Following challenge, blood was collected weekly for 5 weeks to test for PCV2 viremia by polymerase chain reaction (PCR) and to assess serum antibody levels. In addition, nasal and fecal swabs were collected weekly post-challenge to evaluate PCV2 virus shedding. Tissues were collected at necropsy 5 weeks post-challenge to evaluate the level of PCV2 infection and PCV2 specific lesions. In this study, vaccinated and control pigs were co-mingled. This resulted in a continuous challenge for the vaccinated pigs, as the control pigs will start shedding large amounts of virus about 2 weeks post-challenge.

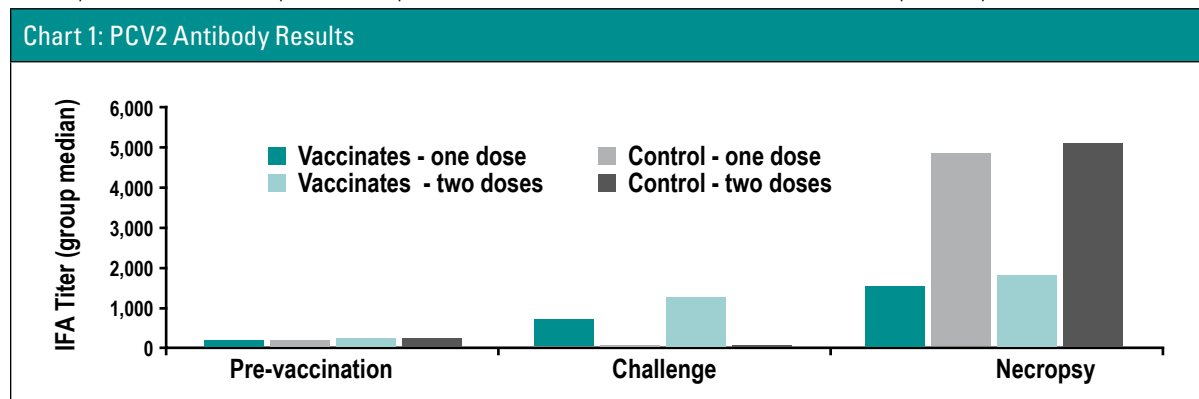
Laboratory testing: Serum antibody testing by indirect immunofluorescence assay (IFA) and virus detection by quantitative PCR were performed by Merck Animal Health Research and Development. Virus detection by immunohistochemistry (IHC) and by histopathology were performed at the Iowa State University Veterinary Diagnostic Laboratory.

Statistical analysis: Data were analyzed by Merck Animal Health Research and Development using procedures required by USDA Center for Veterinary Biologics (CVB) for license approval. The data and statistical analysis were approved by CVB resulting in the claims presented on the product label.

Results

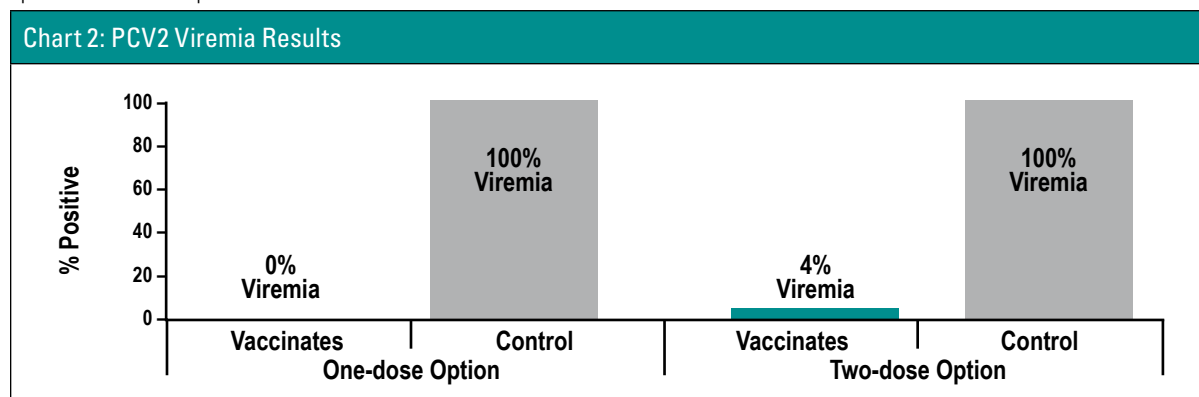
Induced PCV2 antibody titers

Chart 1 presents PCV2 antibody data. Both options – one dose or two doses – induced a PCV2 antibody titer response.



Helped prevent or significantly reduce PCV2 viremia

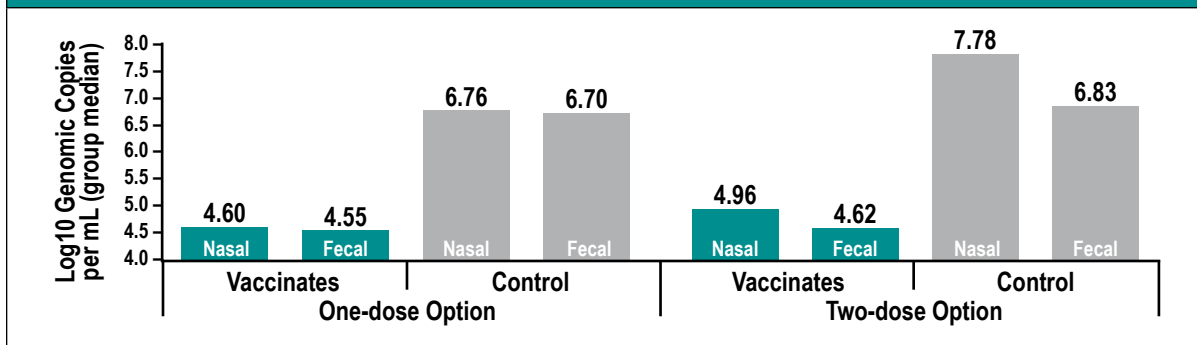
Chart 2 presents the percentage of pigs that were found to be viremic during the entire post-challenge monitoring period where vaccinates and controls were co-mingled resulting in continuous challenge for the vaccinated pigs. Both vaccination options show that vaccinated pigs had no viremia or a minimal level of viremia compared to controls. Accordingly, the label claim for either vaccination option is to aid in the prevention of PCV2 viremia.



Reduced virus shedding by more than 100-fold

Chart 3 presents nasal and fecal virus shedding data. The data represents the group median value for the cumulative amount of PCV2 virus measured in each pig over the 5-week, post-challenge evaluation period where vaccinates and controls were co-mingled resulting in continuous challenge for the vaccinated pigs. Vaccination with either option reduced the level of virus shedding by more than 100-fold. Accordingly, the Circumvent PCV G2 label claim is to aid in the reduction of virus shedding.

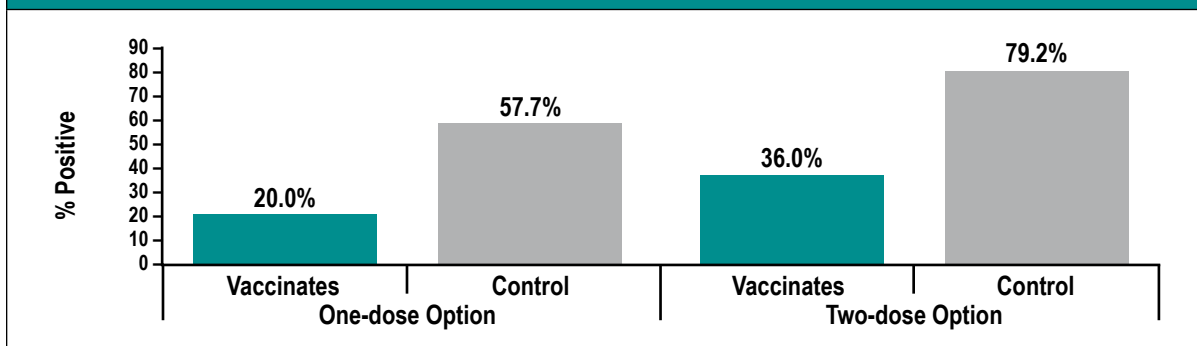
Chart 3: Virus Shedding Results - Nasal and Fecal



Reduced the level of PCV2 infection in lymphoid tissues

Chart 4 presents the percentage of lymphoid tissues that were infected with PCV2 as measured by IHC. With both vaccination options, the level of PCV2 infection in lymphoid tissues was significantly reduced in vaccinated pigs compared to controls. The label claim aids in the reduction of PCV2 lymphoid infection.

Chart 4: Lymphoid Tissue Infection Results



Discussion

PCV2 remains a costly disease for swine producers worldwide. Producers who fail to immunize their pigs, either by plan or mistake, can attest to the ability of PCV2 to cause devastating disease. Economic losses in unprotected pigs can be up to \$20 per pig.²

PCV2 vaccination helps control viremia, which is the initial step in developing disease following virus exposure. Because PCV2 infects cells of the pig's immune system, the impact of the disease goes beyond the direct infection, as PCV2 can potentiate the impact of other pathogens, including PRRSV, *Mycoplasma hyopneumoniae* and swine influenza virus (SIV). Likewise, PRRSV and *Mycoplasma hyopneumoniae* also suppress the immune system, making PCV2 infections more severe. The bottom line is that PCV2 vaccination serves as the foundation for controlling other diseases like PRRSV, mycoplasmal pneumonia and SIV.

PCV2 vaccines developed by Merck Animal Health have played a large role in controlling PCV2 infection and disease worldwide. In the United States, Merck Animal Health markets two PCV2 vaccines, the monovalent Circumvent PCV and the bivalent Circumvent PCV M, which also controls pneumonia caused by *Mycoplasma hyopneumoniae*.

In continuing to investigate better approaches for PCV2 vaccination, Merck Animal Health has developed a second generation of the circovirus protection you've come to expect – new Circumvent PCV G2, which will replace the original monovalent.

Circumvent PCV G2:

- Is the only PCV2 vaccine that is approved for use in pigs as early as 3 days of age
- Offers convenient dosing options – one dose or two lower-volume doses
- Provides long-lasting, 5-month DOI

Circumvent PCV G2 can be administered through two options:

- Option 1 is a single, 2-mL injection in pigs 3 weeks of age or older
- Option 2, is two, 1-mL injections with the first injection as early as 3 days of age and the second injection approximately 3 weeks later.

Through research and development, Merck Animal Health is committed to continual product improvement in order to add value to and better serve customers' evolving needs. As the efficacy data reflects, both options of Circumvent PCV G2:

- Induced protective levels of PCV2 antibody titers
- Helped prevent or significantly reduce PCV2 viremia
- Reduced virus shedding by more than 100-fold
- Reduced the level of PCV2 infection in lymphoid tissues

1. Data on file.

2. Gillespie, J., Opriessnig, T., Meng, X.J., Pelzer, K. and Buechner-Maxwell, V. Porcine circovirus type 2 and porcine circovirus-associated disease. *J. Vet. Intern. Med.* 2009. Vol. 23, 1151-1163.

Merck Animal Health

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