Discussion

PCV2 remains a costly disease for swine producers worldwide. Because the virus and disease threat persists in the environment, continual vaccination is critical for maintaining a healthy herd and avoiding devastating economic losses.

These studies clearly show the ability of Circumvent PCV G2 to control PCV2 infection even when pigs are first challenged 20 weeks after vaccination. In addition, the co-mingling of controls and vaccinates creates a situation where the level of PCV2 exposure of the vaccinated pigs is increased, because the controls start shedding large quantities of virus at 2 weeks post-challenge. That said, viremia reduction was achieved in the vaccinated pigs over the 5-week post-challenge period.

An effective PCV2 vaccination protocol helps control viremia, which is the initial step in developing disease following virus exposure. However, the virus can linger for as long as 4 to 5 months after a pig is infected, which greatly increases the chance of shedding the disease and infecting other pigs, along with making the pig more susceptible to other diseases. Protecting pigs early and ensuring extended protection through a long DOI (5 months) not only helps keep pigs healthy through the growing stages, but also can reduce costly late-stage mortality as the pig approaches its market value.

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 is 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.

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DOI trial data for Circumvent® PCV G2[1]

Brad Thacker, DVM, PhD, MBA, DABVP
Merck Animal Health, De Soto, KS

Porcine circovirus Type 2 (PCV2) is a ubiquitous and durable virus that persists in the growing pig's environment. It not only negatively affects production performance, such as daily gain, feed efficiency and mortality, but PCV2 also opens the door to other economically impactful swine diseases, such as *Mycoplasma hyopneumoniae*, porcine reproductive and respiratory syndrome virus (PRRSv) and swine influenza (SIV). Co-infections and late-stage production losses can hit a producer's bottom line particularly hard, which makes extended PCV2 protection important.

Key to the progression of PCV2 is viremia – or the presence of the virus in the blood. Following exposure to PCV2, the virus starts circulating in the blood, which is the initial step in PCV2 disease developing in the pig. Controlling viremia is critical because the virus can linger for as long as 4 to 5 months after a pig is infected, which increases the chance of shedding the virus and infecting other pigs in the group. Therefore, early protection along with extended protection – or a vaccine's duration of immunity (DOI) – is important in controlling PCV2 in commercial production settings.

To replicate real-world challenges, Merck Animal Health researchers used a PCV2 and PRRSv co-challenge model to test the protective efficacy of new Circumvent® PCV G2 and to determine its DOI. The data demonstrated that the vaccine is efficacious for at least 20 weeks after vaccination with either convenient dosing option:

- One-dose option – One 2-mL dose administered to pigs at 3 weeks of age or older
- Two-dose option – Initial 1-mL dose can be given to pigs as early as 3 days of age, with the second dose three weeks later

Circumvent PCV G2 has a long-lasting, 5-month DOI. Plus, it's the only PCV2 vaccine with a dosage option approved for use in pigs as early as 3 days of age.

Materials and Methods

Vaccine 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 option and the 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 3 weeks later (two-dose option study). Each study was conducted independent of the other.

Animals: Crossbred pigs from a herd free of *M. hyopneumoniae* and PRRSv were used in the studies. Piglets had low levels of PCV2 maternal antibody and were negative for PCV2 by polymerase chain reaction (PCR) on serum at enrollment and remained negative until challenge at 23 weeks of age.

Experimental design: Twenty weeks following the completed vaccination protocol (at 3 weeks of age) for both the one-dose and two-dose options, the pigs were co-challenged with PCV2 and PRRSv. Prior to challenge, the pigs were bled periodically to assess serum antibody levels. Following challenge, blood was collected weekly for 5 weeks to test for PCV2 viremia by quantitative PCR and to assess serum antibody levels. In addition, nasal and fecal swabs were collected weekly for 5 weeks post-challenge to evaluate the level of PCV2 virus shedding. Tissues were collected at necropsy 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 immunoflorescence assay (IFA) and virus detection by quantitative PCR were performed by Merck Animal Health Research and Development. Virus detection by immunohistochemistry (IHC) and lesion development 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 the 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.

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Results

PCV2 antibody titer responses: Post-vaccination and post-challenge

Chart 1 presents PCV2 antibody data for the one-dose option. The antibody response following vaccination was significantly elevated by 4 weeks, peaked at 8 weeks and declined to low levels at the time of challenge. After challenge, the controls mounted a vigorous but ineffective antibody response based on their high level of viremia (See Chart 1). The PCV2 antibody response following challenge in the vaccinated pigs showed only a slight increase, and along with the low level of viremia post-challenge, indicates that the vaccine provided a high level of protection.

Chart 1: One-dose Option – PCV2 Antibody Results

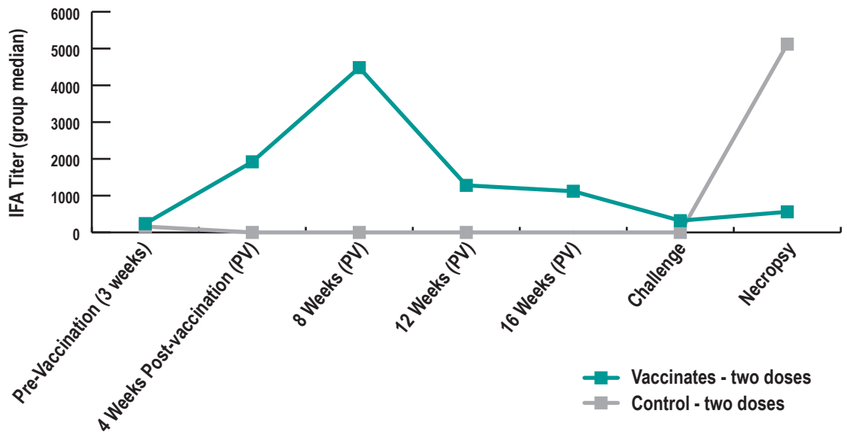
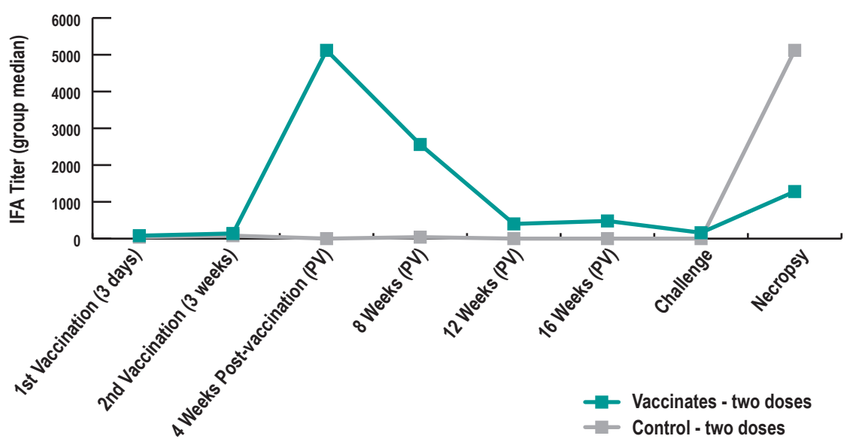


Chart 2 presents PCV2 antibody data for the two-dose option. Antibody titers in vaccinated pigs peaked at 4 weeks after the second vaccination and then declined to low levels at the time of challenge. As in the one-dose study, the controls mounted a vigorous but ineffective response and the vaccinated pigs showed only a slight increase, again indicating a high level of protection.

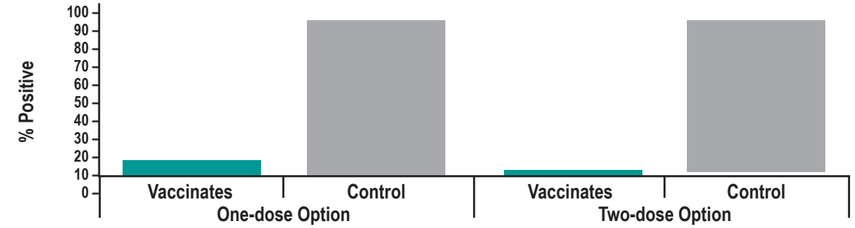
Chart 2: Two-dose Option: PCV2 Antibody Results



Prevented or significantly reduced PCV2 viremia

Chart 3 presents the percentage of pigs that were found to be viremic following challenge 20 weeks after the single, one-dose vaccination or after the second dose of the two-dose vaccination. 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.

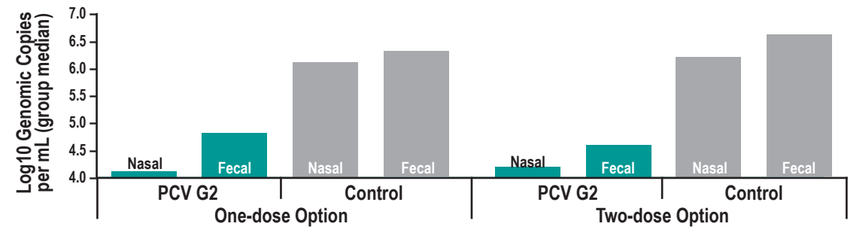
Chart 3: PCV2 Viremia Results



Reduced virus shedding by more than 100-fold

Chart 4 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 following challenge at 20 weeks post-vaccination. Vaccination with either dosing option reduced the level of virus shedding by more than 100-fold compared to controls. Accordingly, the Circumvent PCV G2 label claim is to aid in the reduction of virus shedding.

Chart 4: Virus Shedding Results – Nasal and Fecal



Reduced level of PCV2 infection in lymphoid tissues

Chart 5 presents the percentage of lymphoid tissues, collected at necropsy 5 weeks post-challenge and 25 weeks after vaccination, 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. Accordingly, the label claim for both dosing options aids in the reduction of lymphoid infection.

Chart 5: Lymphoid Tissue Infection Results