

Circumvent® PCV M:

A new tool for combination PCV2 and *Mycoplasma hyopneumoniae* vaccination



TECHNICAL BULLETIN

Introduction

Porcine circovirus type 2 (PCV2) and enzootic pneumonia caused by *Mycoplasma hyopneumoniae* are infectious diseases of swine that continue to challenge the United States pork industry. Both diseases can cause significant production and economic losses in affected herds. Vaccination against both of these diseases has been shown to mitigate the negative effects of infection.¹ Circumvent® PCV M is a newly licensed vaccine from Intervet/Schering-Plough Animal Health that provides producers with a convenient tool for both PCV2 and *Mycoplasma hyopneumoniae* protection. Circumvent PCV M contains the same PCV2 and *Mycoplasma hyopneumoniae* antigens, and the same adjuvant (Microsol Diluvac Forte®), as found in Circumvent PCV and MycoSilencer® ONCE. The following studies demonstrate the efficacy and support the U.S. Department of Agriculture (USDA) licensure of Circumvent PCV M.

Study Design

Study 1: PCV2 challenge

Fifty clinically healthy, crossbred three-week-old pigs were randomly assigned to one of two treatment groups. One group was vaccinated with 2 mL of Circumvent PCV M intramuscularly at three and six weeks of age. The second group was a placebo control group (control), which was given the placebo intramuscularly at three and six weeks of age. Pigs from the two treatment groups were commingled for the duration of the study, fed age-appropriate commercial diets and offered water ad libitum. Pigs were observed daily. Signs of adverse reactions, as well as clinical signs of disease, were recorded.

Fourteen days after the second vaccination, pigs were challenged intranasally as described previously.² Blood samples were collected at the time of both vaccinations. In addition, blood samples, nasal swabs and fecal swabs were collected from pigs on the day of challenge and 4, 8, 12, 16, 20 and 24 days post-challenge. Seven sample collections

from the 25 pigs in each treatment group yielded 175 samples of each type (blood, nasal and fecal swabs) per treatment group.

Serum, nasal swabs and fecal swabs were tested using a polymerase chain reaction test (PCR) for the presence of PCV2. Differences between treatment groups in the frequency as well as the duration of PCR positive tests were evaluated statistically using Fisher's Exact Test. Serum was tested for the presence of PCV2 antibodies using an indirect fluorescent antibody (IFA) assay. An IFA titer of ≥ 20 was considered positive.

Pigs were euthanized 24 days after challenge. Bronchial, mesenteric and inguinal lymph nodes were collected and submitted to the Iowa State University Veterinary Diagnostic Lab and immunohistochemistry (IHC) analysis was used to detect the presence of PCV2 in tissue. Differences in IHC scores between treatment groups were analyzed using Fisher's Exact Test.

Study 2: *Mycoplasma hyopneumoniae* challenge

Fifty commercial pigs, three to four weeks old, were randomly assigned to one of two treatment groups; Circumvent PCV M vaccinated or placebo control (control) as in Study 1. In addition, five pigs were designated as sentinels. Following an acclimation period of one week, pigs in the vaccinated group were vaccinated with 2 mL of Circumvent PCV M intramuscularly (IM). Pigs in the control group were injected with 2 mL of placebo IM. All pigs received a booster dose three weeks later with the same treatment. At six weeks post-initial injection, the five sentinel pigs were euthanized and lungs were evaluated to assess possible prior exposure to *Mycoplasma hyopneumoniae*. No lesions consistent with *Mycoplasma hyopneumoniae* infection were found.

Pigs from both the Circumvent PCV M vaccinated and control groups were challenged intranasally with *Mycoplasma hyopneumoniae* for three consecutive days beginning three weeks after the second vaccination. Pigs



were observed daily throughout the study for general appearance and signs of clinical disease. Four weeks post-challenge, pigs were euthanized and lungs were examined for lesions typical of *Mycoplasma hyopneumoniae* infection. The percent surface area of the lung with lesions was recorded.

Results

Study 1: PCV2 challenge

No injection site or systemic reactions were observed for the duration of the study from either treatment group. Serum IFA titers are shown in Table 1 and Figure 1. IFA titers in the pigs injected with Circumvent PCV M rose above 2000 by the day of challenge and remained high throughout the remainder of the study. In contrast, IFA titers in the control group remained low until 16 days post-challenge then continued to rise on subsequent testing dates.

Figure 1. Geometric mean of PCV2 IFA titer in vaccinated and placebo control pigs

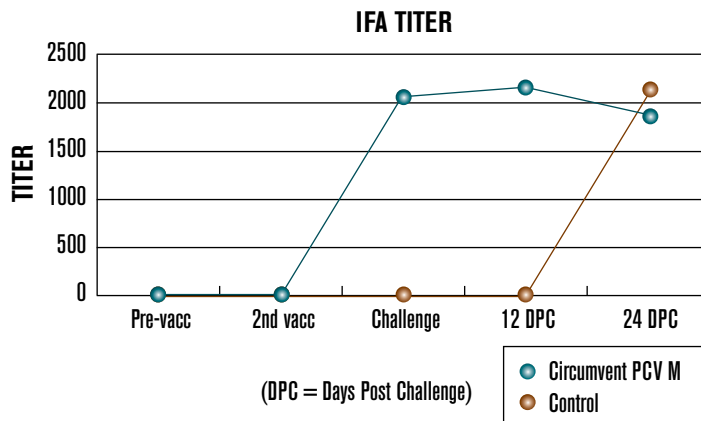


Table 1. Geometric mean of PCV2 IFA titers in vaccinated and placebo control pigs

Treatment	No. Pigs	Pre-vaccination	Day of 2nd vaccination	Day of Challenge	12 Days post-challenge	24 Days post-challenge
Circumvent PCV M	25	22	45	2037	2154	1888
Control	25	22	27	37	19	2168

Serum PCR analysis for PCV2 is presented in Table 2. In Circumvent PCV M vaccinated pigs, 13 of 175 serum samples were PCV2 positive while 73 of 175 samples were positive in the control group ($p < 0.0001$). In the vaccinated group, 5 of 25 pigs tested PCR positive on only two test dates. Whereas in the control group, 24 of 25 pigs tested positive on two or more test dates and of these, 22 pigs tested PCR positive on three or more test dates. Fewer pigs from the Circumvent PCV M vaccinated group developed viremia than in the control group ($p < 0.0001$). In addition, the duration of viremia was reduced in vaccinated pigs versus those injected with placebo ($p < 0.0001$).

Table 2. PCV2 viremia in vaccinated and placebo control pigs.

Treatment	Total No. of samples	Total No. PCR positive samples	No. pigs with ≥ 2 positive test dates	No. pigs with ≥ 3 positive test dates
Circumvent PCV M	175	13 ^a	5/25 ^a	0/25
Control	175	73 ^b	24/25 ^b	22/25

a,b Numbers within a column with different superscripts are different $p < 0.0001$



PCR analysis of nasal swabs for PCV2 is presented in Table 3. In the control group, 23 of 25 pigs had nasal swabs that were positive on two or more test dates during the study, compared to 5 of 25 pigs in the Circumvent PCV M vaccinated group. Seven placebo injected pigs were positive on four or more test dates, whereas none of the vaccinated pigs tested positive on four or more test dates.

Table 3. Nasal shedding of PCV2 in vaccinated and placebo control pigs.

Treatment	Total No. of samples	Total No. PCR positive samples	No. pigs with ≥ 2 positive test dates	No. pigs with ≥ 3 positive test dates	No. pigs with ≥ 4 positive test dates
Circumvent PCV M	175	15 ^a	5/25 ^a	2/25	0/25
Control	175	73 ^b	23/25 ^b	19/25	7/25

a,b Numbers within a column with different superscripts are different $p < 0.0001$

PCR analysis of fecal swabs for PCV2 is presented in Table 4. In the control group, 21 of 25 pigs had fecal swabs that were positive on two or more test dates during the study, compared to 5 of 25 pigs in the Circumvent PCV M group. Four placebo injected pigs were positive on 4 or more test dates, while no vaccinated pigs were positive on 4 or more test dates. Both the number of pigs and their duration of nasal and fecal shedding were reduced in the Circumvent PCV M group versus controls ($p < 0.0001$).

Table 4. Fecal shedding of PCV2 in vaccinated and placebo control pigs.

Treatment	Total No. of samples	Total No. PCR positive samples	No. pigs with ≥ 2 positive test dates	No. pigs with ≥ 3 positive test dates	No. pigs with ≥ 4 positive test dates
Circumvent PCV M	175	18 ^a	5/25 ^a	1/25	0/25
Control	175	61 ^b	21/25 ^b	13/25	4/25

a,b Numbers within a column with different superscripts are different $p < 0.0001$

IHC testing of lymphoid tissues are presented in Table 5. In the control group, 12 pigs had positive IHC tests in all three lymph nodes and 15 pigs had at least one positive lymph node. Only one pig in the Circumvent PCV M group was IHC positive in a single lymph node. The number of IHC positive lymph nodes was significantly lower in vaccinated pigs than in controls ($p < 0.0001$).

Table 5. Occurrence of PCV2 in lymph nodes of vaccinated and placebo control pigs.

Treatment	No. pigs	No. pigs with positive PCV2 IHC tests			
		Bronchial Lymph Node	Mesenteric Lymph Node	Inguinal Lymph Node	Total No. Positive Pigs
Circumvent PCV M	25	1/25 ^a	0/25 ^a	0/25 ^a	1/25 ^a
Control	25	14/25 ^b	13/25 ^b	14/25 ^b	15/25 ^b

a,b Numbers within a column with different superscripts are different $p < 0.0001$

Study 2: *Mycoplasma hyopneumoniae* challenge

One pig in the control group was removed from the study due to enteric disease. The percentage of lung surface with lesions typical of *Mycoplasma hyopneumoniae* for each treatment group is shown in Table 6. Pigs vaccinated with Circumvent PCV M had a significantly lower percentage of lung lesions typical of *Mycoplasma hyopneumoniae* (4.73 percent) than the control group (12.76 percent) ($p = 0.0003$).

Table 6. Percent lung surface lesions in vaccinated and control pigs.

Treatment	No. pigs	Percent lung surface lesions
Circumvent PCV M	25	4.73 ^a
Control	24	12.76 ^b

a,b Numbers within a column with different superscripts are different $p = 0.0003$



Conclusions

These two studies demonstrate that the new, ready-to-use combination vaccine, Circumvent PCV M, is an effective tool for protection against both PCV2 infection and disease caused by *Mycoplasma hyopneumoniae*. These studies supported the U.S. Department of Agriculture (USDA) licensure of Circumvent PCV M with the following claims:

For use in healthy pigs, 3 weeks of age or older:

- As an aid in the prevention of viremia caused by porcine circovirus type 2
- As an aid in the reduction of shedding caused by porcine circovirus type 2
- As an aid in the control of pneumonia caused by *Mycoplasma hyopneumoniae*

References

1. Thacker, B. J., W. D. Wilson, C.J. Francisco, and R. H. Schlueter. Circumvent PCV vaccine: Performance evaluation and serological studies update. 2008. Proceedings of the American Association of Swine Veterinarians Annual Meeting, San Diego, California. pp. 153-6.
2. Francisco, C., Thacker, B. Field performance of a conditionally licensed vaccine: US experience. 2007. Proceedings of the American Association of Swine Veterinarians Annual Meeting, Orlando, Florida. p. 157



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