



Efficacy and field safety of Prime Pac® PRRS RR against respiratory disease caused by Porcine Reproductive and Respiratory Syndrome virus

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Introduction

PRRS remains one of the most costly swine diseases in the United States with estimated costs of more than a billion dollars annually (Holtkamp, 2013). In light of the significant impact on production that producers face with PRRSV, it is important for them to have tools, such as modified-live vaccines, that can help mitigate the impact of the disease in their systems. A new tool that can be used in the fight against PRRSV is Prime Pac PRRS RR, which is a modified-live virus vaccine labeled for “the vaccination of healthy swine 3 weeks of age or older against respiratory disease caused by Porcine Reproductive and Respiratory Syndrome (PRRS) virus and for the vaccination of female breeding age swine against reproductive disease caused by PRRS virus.” Licensing study data summarized here demonstrate the protection Prime Pac PRRS RR provides pigs against respiratory disease in the face of a heterologous PRRSV challenge, while also being a safe product under field conditions.

Materials and Method

Efficacy Study

The efficacy study was performed in two locations using the same protocol. At each site, 64 PRRSV negative pigs were enrolled at 3 weeks of age and were randomly assigned to one of two treatment groups with even distribution of treatments within each litter. During the pre-challenge period, treatment groups were housed in separate rooms. One group received 1 mL of Prime Pac PRRS RR intramuscularly at 3 weeks of age while the positive controls received a placebo injection at the same time.

All pigs were challenged intranasally with a heterologous PRRSV strain (NADC 20, kindly supplied by Dr. Lager from the NADC, USDA-ARS) four and a half weeks after vaccination. Pigs were commingled immediately prior to challenge such that each room contained an equal number of pigs from the two treatment groups.

All pigs were necropsied 14 days post-challenge. Gross lung lesion scores, the primary study variable, were assigned by a pathologist that was blinded to treatment. Macroscopic lung lesions were given a score to estimate the percentage of the lung affected by pneumonia (Halbur, 1995). Three tissue sections were collected from each set of lungs for histopathology and immunohistochemistry (IHC) evaluation. Microscopic lesion severity and IHC staining intensity were scored on a 0 to 4 scale (Lesion severity: 0 = no lesions, 1 = mild, 2 = moderate multifocal, 3 = moderate diffuse and 4 = severe; IHC: 0 = no PRRSV antigen positive cells, 1 = 1-10 cells, 2 = 11-30 cells, 3 = 31-100 cells, and 4 = >100 cells per section). The maximum score per animal was used in the analysis.

Individual body weights were recorded one day prior to vaccination, immediately prior to challenge and at necropsy. Blood samples and nasal swabs were collected at enrollment, immediately prior to NADC 20 challenge (0 DPC) and at 3, 7, 10, and 14 days post-challenge and tested by qPCR to determine the level of PRRSV viremia and shedding profiles. Blood samples were also tested by IDEXX PRRSV X3 Ab test to determine serostatus before and after challenge.

Statistical analysis was performed by one way ANOVA on lung lesion scores and average daily weight gains; Kruskal-Wallis non-parametric ANOVA on viremia data; two-sided Cochran-Armitage Trend Test on histopathology and IHC scores; and Fisher’s Exact Test on binary variables. Statistical significance was assigned at $P \leq 0.05$.

Field Safety Study

A field safety evaluation was conducted in three locations (Texas, Iowa, Minnesota) using a total of 677 healthy pigs that were on average 3 weeks of age. Pigs were vaccinated with 1 mL of Prime Pac PRRS RR intramuscularly in the neck. All vaccinated pigs were monitored closely for systemic or local reactions for at least one hour post-vaccination followed by daily observations for the subsequent 14 days. Injection sites were palpated one day after vaccination for evaluating localized reactions. In addition, pigs were observed daily for overall health and all mortalities were necropsied to determine cause of death.

Results

Efficacy Study

Prime Pac PRRS RR vaccinated pigs demonstrated a significant reduction in lung lesions versus controls after the NADC 20 PRRSV challenge (31.8% vs. 9.3%, Combined Average), demonstrating a 71% reduction overall (Figure 1, $P < 0.0001$). More than two-thirds of the controls had lung lesion scores greater than 20% in contrast to markedly fewer vaccinates with scores of that magnitude (Site 1 and 2 – 12.5% and 6.3%). Likewise, on histological examination of lung tissue, the maximum microscopic lesion scores and IHC scores in vaccinates were significantly lower than controls (See Table 1). In both sites, the percentage of control pigs with moderate-diffuse to severe histopathology scores 3 and 4 was greater than the vaccinated pigs (89% vs. 25%). For the IHC results, 88% of controls and 27% of vaccinates had >10 staining cells per section scores 2 to 4.

Figure 1. Average lung lesion scores in Control and Prime Pac PRRS RR vaccinated pigs

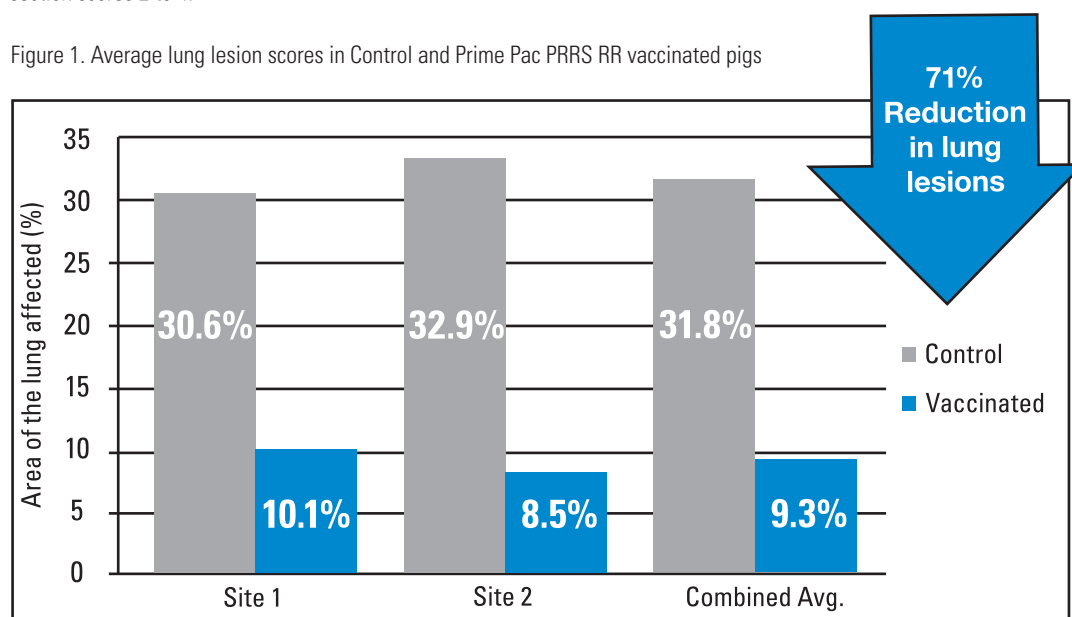
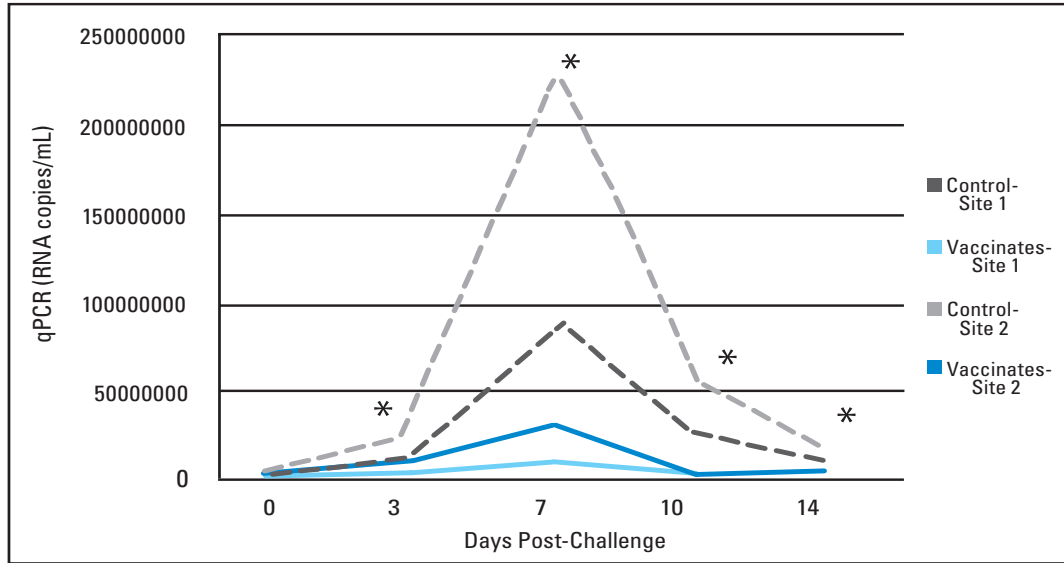


Table 1. Histopathology and IHC Scores from both sites combined

Variable	Treatment Group	Percentage of pigs with scores 0-4				
		0	1	2	3	4
Lung IHC scores	Control	0.0%	12.5%	15.6%	42.2%	29.7%
	Vaccinates	45.3%	28.1%	17.2%	7.8%	1.6%
Lung histopath scores	Control	0.0%	1.6%	9.4%	20.3%	68.8%
	Vaccinates	0.0%	15.6%	59.4%	20.3%	4.7%

All pigs were confirmed PRRSV negative at enrollment via PRRSV PCR and ELISA. At the time of challenge, almost all of the vaccinated pigs were still viremic with presumably vaccine virus while control animals remained negative. Vaccinated pigs seroconverted by the time of challenge while controls remained seronegative until challenge and then seroconverted thereafter. Viremia levels are shown in Figure 2. The groups were 100 percent viremic three days post-challenge with peak viremia occurring at seven days post-challenge. Vaccinates had significantly less virus in serum compared to controls at all sampling points after challenge ($P < 0.01$). There was an overall 77% reduction in peak viremia levels in vaccinated pigs in comparison to the controls. The amount of virus in nasal swabs was much less than in serum at all sampling points. However, at the end of the study there were significantly fewer pigs shedding PRRSV in vaccinated pigs than controls (42% vs. 77%, $P < 0.01$).

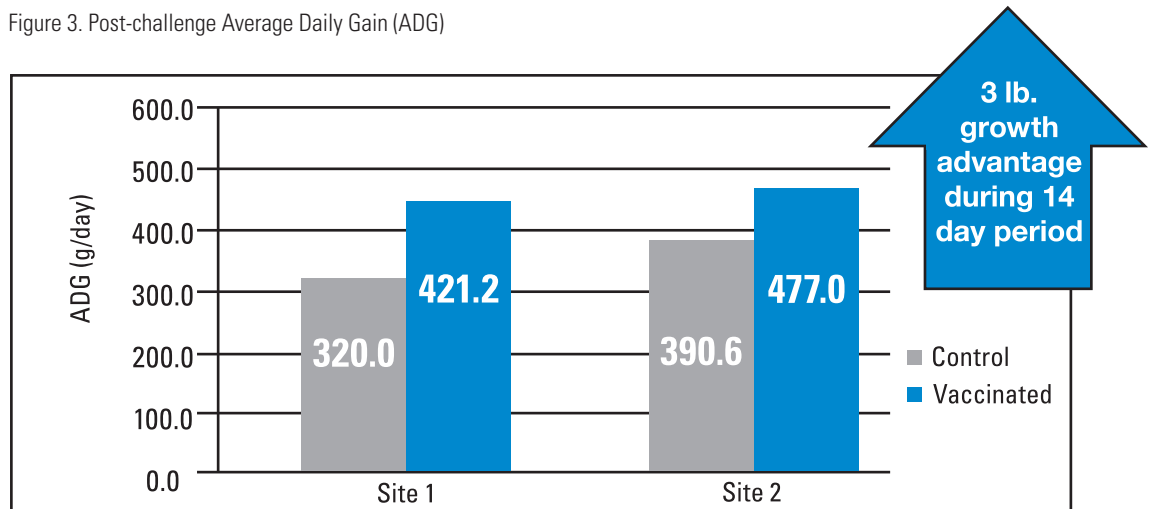
Figure 2. Median levels of PRRSV in serum after challenge with NADC 20



*Vaccinates and Controls statistically differ per site at $P < 0.01$

As shown in Figure 3, Prime Pac PRRS RR vaccinated pigs outperformed the controls on average daily gain (ADG) during the post-challenge period. Prime Pac PRRS RR vaccinated pigs grew on average 95 grams more per day than the unvaccinated controls after challenge with NADC 20, which equates to almost a three pound growth advantage by the end of the 14-day period ($P < 0.0001$).

Figure 3. Post-challenge Average Daily Gain (ADG)



Field Safety Study

There were no injection site or anaphylactic reactions observed following vaccination and no adverse events were attributable to vaccination. Throughout the study, four mortalities occurred, but all were attributed to causes unrelated to vaccination with Prime Pac PRRS RR.

Conclusions

Prime Pac PRRS RR can be an effective management tool shown to reduce the respiratory impact in the face of a heterologous PRRSV challenge. Vaccinated pigs in the efficacy studies showed improved growth performance post-challenge compared to controls. In addition, vaccinated pigs had reduced viral loads during peak viremia. Reduced viral load has been reported to reduce the risk of wild type virus shedding (Zimmerman, 2007). Post-vaccination clinical monitoring indicated that Prime Pac PRRS RR is safe to use in 3-week-old pigs.

Prime Pac PRRS RR is a safe product that can be incorporated into vaccination protocols as a tool to help mitigate the impact of PRRSV introductions in swine herds.

Highlights

- Prime Pac PRRS RR significantly reduces the respiratory effects of PRRSV in pigs in the face of a PRRSV infection.
- Prime Pac PRRS RR is a safe product to include in your vaccination protocols.

Halbur, P.G., et al. Comparison of the Pathogenicity of Two US Porcine Reproductive and Respiratory Syndrome Virus Isolates with that of the Lelystad Virus. *Veterinary Pathology*. 1995. 32:648-660.

Holtkamp, D., et al. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on the United States pork producers. *Journal of Swine Health and Production*. 2013. 72-84.

Zimmerman, J. PRRS virus transmission. American Association of Swine Veterinarians conference proceedings. 2007. 479-484.

Data on file, Merck Animal Health.



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