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Ingelvac® CircoFLEX™ Symposium

St. Paul, Minnesota
September 15, 2007

1.00 pm	Opening
1.10	Efficacy of Ingelvac® CircoFLEX™ in pigs vaccinated at 3 or 6 weeks of age in a PRRS and *Mycoplasma hyopneumoniae*-negative production system. Drs. G. Cline, V. Wilt and E. Diaz
1.30	Injection site histologic lesions induced by commercial PCV2 piglet vaccines. Drs. J. Kolb and R. Christmas
1.50	Announcements of the three PCVAD Research Awardees. Dr. S. Lange
2.00	Break
2.20	Comparative performance of barns of pigs vaccinated with Ingelvac CircoFLEX or other PCV2 vaccines. Drs. J. Kolb, C. Beard, E. Diaz and R. Edler
2.40	Finishing mortality in a swine production system using different PCV2 vaccination protocols. Dr. F. Cardinal
3.00	Closing

Foreword

This is a critical time for the swine industry. As the porcine circovirus and associated diseases (PCVAD) complex has spread rapidly throughout the North American swine industry, the need for insight and solutions from the research community is great.

At this symposium, we present extensive field experiences with the innovative PCV2 vaccine, Ingelvac® CircoFLEX™. We hope the results of the extensive field trials give swine producers and their animal health professionals a good picture of what they can expect from a novel PCV2 vaccine.

In order to stimulate applied research in the field of PCVAD management, Boehringer Ingelheim Vetmedica sponsors three PCVAD Research Awards for proposals originating from the NAFTA countries. During the symposium the awards, selected by the independent PCVAD Research Award Review Council, will be announced.

Gratitude is expressed to the many individuals who worked to put this research together and to those who have worked to make these proceedings available to the U.S. and international swine industries.

At Boehringer Ingelheim Vetmedica, Inc., we are committed to supporting innovative research and product development to find solutions to emerging threats in swine production. With the help of talented researchers from around the globe, we will continue to make strides benefiting our customers.

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Efficacy of Ingelvac® CircoFLEX™ in pigs vaccinated at 3 or 6 weeks of age in a PRRS and *Mycoplasma hyopneumoniae*-negative production system

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Introduction

The purpose of the study was to assess PCV2 vaccine efficacy (Ingelvac® CircoFLEX™, Boehringer Ingelheim Vetmedica, Inc.) in pigs vaccinated at 3 or 6 weeks of age compared to nonvaccinates in a pork production system which was negative for PRRS and *Mycoplasma hyopneumoniae*.

Materials and Methods

A multiple site, 1250 sow system which was negative for PRRS and *Mycoplasma hyopneumoniae* was used in this study. Two weeks of pig production (n=1106 pigs) were weaned and placed into nursery pens. Prior to placement each pen was randomly assigned to one of three treatment groups. Individual pigs were the experimental unit and were ear tagged and weighed at weaning. Pigs that were designated as vaccinates were vaccinated IM at either 3 or 6 weeks of age with 1mL of the single-dose vaccine. Nonvaccinates received no vaccination. Three randomly selected pigs in each pen were designated as serum collection animals. These 144 pigs (72 per treatment group) were serially bled at 3, 6, 10, 14, 18 and 22 weeks of age. Samples were assayed by PRRS ELISA, PRRS PCR, M. hyo ELISA, *Lawsonia* ELISA, and PCV2 quantitative PCR. All pigs were weighed individually at 3, 10, and 22 weeks of age. Each finisher pig that died or was euthanized for humane reasons during the study was necropsied and a comprehensive set of tissues were submitted to the Iowa State University Veterinary Diagnostic Laboratory for diagnostic testing. Mortality and cull rates were assessed using the Chi-square test (JMP).

Results

No adverse reactions attributable to vaccination were observed. As was the case historically in this system, nonvaccinated control pigs began to show clinical signs of PCVAD in finishing beginning at 11 weeks of age. Gross lesions included enlarged lymph nodes, (particularly the mesenteric), lungs that often failed to collapse normally and in some cases had significant interlobular edema, kidneys that were enlarged and/or had multiple white foci, enteritis suggestive of ileitis, and edema of the colonic mesentery. Nursery mortality rate was not different comparing pigs vaccinated at 3 or 6 weeks to the nonvaccinates (p=0.84). Finishing mortality and cull rates for both the 3 and 6 week vaccinates were significantly reduced compared to nonvaccinated pigs (p<0.0001, table 1). Finishing cull rate was based on pigs that weighed less than 180 pounds at closeout. Pigs vaccinated with Ingelvac® CircoFLEX had fewer pigs diagnosed with PCVAD during the finishing phase.

Conclusions

Ingelvac CircoFLEX was safe and effective in pigs vaccinated at 3 or 6 weeks of age. Both vaccinated groups had significant reductions in finishing mortality, cull, and PCVAD diagnosis rates.

Table 1. Summary of nursery and finishing mortality rates and finishing cull rates by treatment group.

Item	3wkvacc	6wkvacc	Nonvacc	P-value
Number of pigs placed in nursery	374	364	368	-
Nursery mortality rate, %	2.41	2.47	1.90	0.84
Number of pigs placed in finishing	365	355	361	-
Finishing mortality rate, %	1.92	2.25	7.76	<0.0001
Finishing cull rate, %	1.68	0.86	6.31	<0.0001

Injection site histologic lesions induced by commercial PCV2 piglet vaccines

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Introduction and Objectives

Vaccines against PCV2 virus infection have recently been introduced into both the European (2004) and North American (2006) markets. Adjuvants are incorporated into many licensed vaccines to enhance the immune response. Some adjuvants may contain mineral oil or other inflammatory substances which, while stimulating the immune response, may also lead to injection site lesions or anaphylaxis. This study was performed to compare the tissue reactivity at 14 days post-vaccination of three piglet vaccines licensed in the United States.

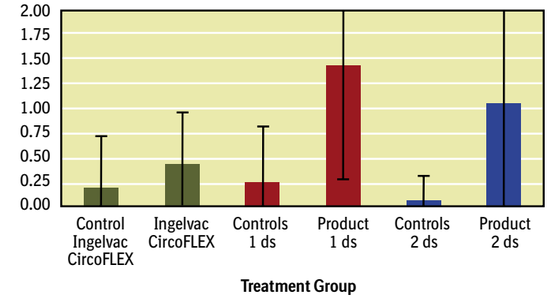
Materials and Methods

Forty-eight weaned feeder pigs, approximately 18 to 21 days of age, were individually identified and randomly allocated to three treatment groups (n=16 per group) in a blinded, internal control study. The three groups included Ingelvac® CircoFLEX™ (Boehringer Ingelheim Vetmedica, Inc, St. Joseph, MO), a one dose vaccine, another one dose commercial vaccine, and a two dose commercial vaccine. Piglets were vaccinated according to manufacturer's instructions. A saline injection of equal volume was made on the opposite side of the neck to serve as an internal control. Piglets were humanely euthanized 14 days following the final injection (first dose for one dose vaccines, second dose for the two dose vaccine). An injection site tissue sample was harvested and placed into 10% buffered neutral formalin and sent to the Iowa State University Veterinary Diagnostic Laboratory. Tissues were processed and blindly scored on a 0-5 scale using the following criteria: score0-no lesion; score1-scattered lymphocytes & macrophages, mild perivascular cuffs; score2-mild scattered moderate nonsuppurative inflammation; score 3-moderate multifocal pyogranulomatous inflammation; score 4-severe diffuse inflammation; score5-massive necrosis or severe pyogranulomatous inflammation.

Results

No significant difference ($p>0.05$, paired t-test) was detected between the internal saline controls (score 0.19) and vaccine injection sites in the Ingelvac CircoFLEX treated pigs (score 0.44). Pigs in the other one dose vaccine group (score 1.06) and the two dose vaccine group (score 1.44) had significantly higher lesion scores than their internal control injection sites ($p<0.01$). Ingelvac CircoFLEX pigs had significantly lower lesion scores than the other vaccine groups ($p=0.02$, ANOVA). The control sites for all three groups were not significantly different from one another (mean score 0.17; Figure 1).

Figure 1 – Injection site lesion scores



Conclusions

The injection sites were examined earlier than labelled withdrawal times, but clearly demonstrated different levels of reaction. Piglets receiving Ingelvac CircoFLEX had significantly lower lesion scores than the other vaccines, and were not significantly different than saline injected internal control sites. The other two vaccines had lesions that were significantly worse than internal control sites and the Ingelvac CircoFLEX group. Injection site lesions may be sustained and warrant extended withdrawal times. Sustained lesions could potentially result in reduced carcass value at harvest or reduced weight gain following vaccination.

Comparative performance of barns of pigs vaccinated with Ingelvac CircoFLEX or other PCV2 vaccines

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Introduction and Objectives

Porcine Circovirus type 2 (PCV2) is the necessary agent of Porcine Circovirus Associated Disease (PCVAD).[1] When combined with other infections, such as PRRS virus (PRRSv) or Swine Influenza Virus (SIV), mortality may exceed 20%. Vaccines against PCV2 have been shown to reduce losses in herds PRRS and *Mycoplasma hyopneumoniae*-negative or positive pigs.[2-4] This paper describes the results of a field evaluation of a novel PCV2 vaccine, Ingelvac® CircoFLEX™ (Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO), and two other commercially available PCV2 vaccines, in a conventional production system positive for PRRSv, *Salmonella typhimurium* and SIV.

Materials and Methods

A commercial production system utilizing conventional nursery and finishing barns implemented vaccination against PCV2 at weaning. Pigs were vaccinated within an 11 day age range, from a minimum of eight days of age to a maximum of 18 days of age. Additionally, pigs were vaccinated against *Mycoplasma hyopneumoniae* after placement into nurseries and again three weeks later.

Barns were placed over a three month period through a single production flow. A total of 51 barns of vaccinated pigs were included in the evaluation, with the following allocation: Intervet PCV2 conditionally licensed vaccine, 19 barns (Intervet, Millsboro, DE), Suvaxyn® PCV2 One Dose™, 15 barns (Ft. Dodge Animal Health, Overland Park, KS), and Ingelvac® CircoFLEX™, 17 barns (Boehringer Ingelheim, St. Joseph, MO). Some barns were housed on sites with all other vaccines (15/51), while others were housed only with barns vaccinated with the same product (36/51). Mortality rate was the parameter of interest in this evaluation. Statistical analysis was made using Chi Square and comparison of proportions using Statistix 8.0 (Analytical Software, Tallahassee, FL).

Results

Chi square data are provided in Table 1. Significant differences were detected among the vaccine treatments, with Suvaxyn PCV2 One Dose having significantly ($p < 0.05$) higher mortality (591 died/16,153 placed = 3.7%) compared to Intervet (392 died/22,321 placed = 1.8%) and CircoFLEX (398 died/19,842 placed = 2.0%). Mortality was not significantly different ($p = 0.71$) between the Intervet and CircoFLEX vaccinated groups.

Table 1 – Frequency data mortality rate

Treatment	Died	Survived
Intervet PCV Vaccine Type 2[a]	392	21,929
Suvaxyn PCV2 One Dose[b]	591	15,562
Ingelvac CircoFLEX[a]	398	19,444

a,b: $P<0.05$

Discussion

In this evaluation, all vaccines reduced the mortality rate in vaccinated barns. Various reports have shown improved results in vaccinated pigs in both acute[2,3] and chronic/endemic situations.[4] The production system in this study suffered acute PCVAD, with losses prior to vaccine implementation more than double the baseline mortality.[5] Following vaccination, some groups had performance meeting or exceeding pre-PCVAD outbreak levels.

A single dose of Ingelvac CircoFLEX provided protection similar to a two dose vaccination program, and significantly better than another one dose vaccine, in this system. It should be kept in mind that not all sites contained equal numbers of barns vaccinated with each product, and assumptions about consistency of management between sites were made. Vaccination against PCV2 virus at or prior to weaning provided long lasting protection against PCVAD challenge through the finishing period.

References
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Finishing mortality in a swine production system using different PCV2 vaccination protocols.

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A severe epizootic of PCVAD struck pig farms in eastern Canada by the end of 2004. During 2006, Circovac® from Merial, Intervet PCV2 vaccine (no trade name) and Ingelvac® CircoFLEX™ from Boehringer Ingelheim became available in Canada. A comparison of the different vaccination protocols was made in a specific swine production system in order to see which protocol was the most effective to reduce mortality in the finisher stage.

Material and Methods

A comparison of mortality in finishing barns related to various PCV2 vaccination protocols was made in a specific swine production system. This 12,000 sow system is located in a high pig density region of Quebec (Canada). Piglets are weaned off-site between 16 and 19 days of age. Nurseries are operated all in – all out by barn and no more than 2 sources of pigs are commingled in each pig flow. Finisher barns are also off-site and operated all in – all out by barn. The system is positive for PRRS virus, *Mycoplasma hyopneumoniae*, *Actinobacillus pleuropneumoniae* serotypes 5 and 7, and swine Influenza H1N1 and H3N2. The level of involvement of these pathogens could vary significantly in the finishing units of the company. Porcine Circovirus Associated Diseases (PCVAD) became a real problem in this system at the beginning of 2005. The onset of mortality was usually observed between 6 and 10 weeks after placement in finishing. What was traditionally referred to as Postweaning Multisystemic Wasting Syndrome (PMWS), respiratory problems and gastric ulcers were the main clinical presentations.

Sows were vaccinated 7 and 4 weeks prefarrowing and gilts twice before breeding. When sow vaccination was begun in a given herd it was not stopped until the end of the studied period. Piglets were vaccinated once or twice, depending on the vaccination protocol, between weeks 3 and 7 after weaning. Vaccination protocols were not used at the same time and in all the pig flows. Sow and piglet vaccinations were used separately and simultaneously for some batches of pigs.

Chi-square test or Two-Samples proportion test were applied when statistical analysis were performed. Bonferroni adjustments were performed in all cases of multiple comparisons. Results were considered significant when the P-value was < 0,05.

Results

The overall mortality results are summarized in Table 1. In this system, sow vaccination did not seem to improve mortality in finishing units in piglets that were either vaccinated or not vaccinated. Both piglet commercial products improved mortality very significantly. The Intervet product administered once gave intermediate results. In order to take into account potential seasonal or pig flow effects on the mortality results, a further comparison between the Intervet PCV2 vaccine and Ingelvac CircoFLEX was performed. Table 2 is showing the mortality results for the 3 month period within which the two protocols were applied simulteaneously. Table 3 is comparing mortality in the 3 pigs flows where the two protocols were applied at some point.

Table 1: Average finishing mortality results for each PCV-2 vaccination protocol

Piglet vaccination	Sow vaccination			
	No		Circovac	
	Mortality (%)	Number of pigs at placement	Mortality (%)	Number of pigs at placement
No	11,6	72,385	12,0	16 164
Intervet PCV-2 vaccine 1 dose	7,5	11 181	nd	nd
Intervet PCV-2 vaccine 2 doses	4,0	23 106	4,9	20 177
Ingelvac CircoFLEX	3,2	7 626	2,9	13 015

[1]Batches placed between March 2006 and March 2007, regardless of the pig flow

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Finishing mortality in a swine production system using different PCV2 vaccination protocols.

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Discussion

This analysis suffers some weaknesses: no real negative control group, possible differences between pig flows using different vaccination regimens or possible changes over time on mortality rates that are not related to vaccination protocol. However, all the data were obtained in only one production system where the genetics of the animals, feeding and management practices were the same. Semen came from the same boars stud and replacement animals came from the same herd for all the sow farms. The health status in all the sow farms is considered very similar if not identical. The large number of batches included in the study also adds value to the results obtained.

In Table 2, mortality is significantly lower in pigs that received Ingelvac CircoFLEX compared to Intervet PCV2 but this is for all the pig flows. In some of the pig flows, Ingelvac CircoFLEX was never used. Table 3 is taking into account only the pig flows that received at some point either Intervet PCV2 or Ingelvac CircoFLEX and shows no statistical difference between the two products.

It can then be concluded that both Intervet PCV2 and Ingelvac CircoFLEX vaccines are reducing mortality very significantly in the finisher barns of this system and that Ingelvac CircoFLEX is at least as effective as Intervet PCV2 administered twice.

Table 2: Average finishing mortality results for vacciinated batches placed between January 2007 and March 2007 [1]

	Mortality (%)	Number of pigs at placement
Intervet PCV-2 vaccine 2 doses	3, 8_a[2]	26,183
Inglevac CircoFLEX	3, 4_b	20,605

[1] Regardless of the pig flow and the sow vaccination status
[2] Different subscripts mean that the results were significantly different (p=0,025)

Table 3: Average finishing mortality results for 3 pig flows within the system [1]

	Mortality (%)	Number of pigs at placement
No	7, 8_a[2]	11,834
Intervet PCV-2 vaccine 2 doses	3, 9_b	12,122
Ingelvac CircoFLEX	3, 7b	10,301

[1] Batches placed between March 2006 and March 2007, regardless of the sow vaccination status
[2] Different subscripts mean that the results were significantly
Non vs Intervet PCV-2 vaccine 2 doses p < 0,001
Non vs Ingelvac CircoFLEX 1 dose p < 0,0001
Ingelvac CircoFLEX 1 dose vs Intervet PCV-2 vaccine 2 doses p = 0,34