Content

page 5  PCVD - Historical perspective and successful control  
John C. S. Harding, University of Saskatchewan, Canada

page 13  PCVAD control in Canada using different vaccination protocols  
François Cardinal, Les Consultants Avi-Porc, Canada

page 19  Vaccination benefits beyond clinical protection in a US finishing unit  
Thomas G. Gillespie, Rensselaer Swine Services, USA

page 27  Benefits of controlling subclinical PCVAD in a large US operation  
Doug King, Cargill Pork, USA

page 35  Experiences with Ingelvac CircoFLEX® in severe PCVD in the UK  
Nigel Woolfenden, Bishopton Veterinary Group, United Kingdom

page 41  Efficacy of Ingelvac CircoFLEX® in PCVAD affected farrow to finish farms in Korea  
Young S. Lyoo, Konkuk University, Seoul, Korea

page 47  Ingelvac CircoFLEX®- The “bleeding” edge of innovation toward the control of complex disease syndromes  
Mike Roof, Boehringer Ingelheim Vetmedica Inc., USA
John C. S. Harding

PCVD - Historical perspective and successful control
Postweaning multisystemic wasting syndrome (PMWS) was first described by Harding and Clark at the Western Canadian Association of Swine Practitioners’ (WCASP) conference in 1996, and later at the American Association of Swine Veterinarians’ (AASV) meeting in Quebec City in 1997. These conference presentations described a novel, devastating disease affecting nursery and grower pigs in a select number of biosecure high health herds characterized by wasting, respiratory disease, enteritis, enlarged lymph nodes, pallor and jaundice. These affected herds were located in the Canadian prairie provinces of Alberta and Saskatchewan, and included the widely publicized Saskatchewan 600 sow farrow to finish farm that experienced a 16-20 month epizootic as well as a cluster of 15 unrelated herds in Alberta. The fact that this 600 sow farm was a closed, high health status farm, confirmed negative for porcine reproductive and respiratory syndrome (PRRS) virus, and virtually all other swine respiratory and enteric pathogens, strongly suggested the epizootic was possibly associated with a new pathogen.

Retrospectively, the first known outbreak of PMWS in western Canada occurred in 1991 on a 40 sow farrow to (25 kg) feeder pig operation located in a remote region of northeastern Saskatchewan. The farm was depopulated and was restocked with high health breeding stock in January 1990. One year later, the farm experienced nursery mortality of 12-15% associated with sudden death, ill thrift and icterus. Clinical signs consisted of jaundice (caused by diffuse liver necrosis), diarrhea (caused by a focal necrotizing enteritis), and pneumonia (caused by granulomatous interstitial pneumonia and Pneumocystosis). Evidence of immunosuppression (lymphoid depletion) was observed microscopically. Multiple diagnostic submissions had failed to identify known pathogens. Serum antibody levels were consistently 1/3 to 1/4 of normal values. While the etiology was never confirmed, liver toxins were suspected and the problem subsided within 12 months. Several years later, and after to the original reporting of PMWS in 1996\(^1\), \(^2\), a retrospective examination of archived paraffin embedded tissues was undertaken, and disease caused by porcine circovirus type 2 (PCV2) was confirmed.
Unbeknownst to us, a similar disease characterized by depression, muscle wasting, diarrhea and/or respiratory distress affecting 8 - 13 week old piglets was observed beginning in 1995 in approximately 100 herds in Brittany, France. Within several years of these initial reports in Canada and France, circoviral disease had been reported in virtually all other hog rearing countries in the world. Because PCV2 was easily frequently identified in both healthy and unhealthy pigs, Sorden proposed a PMWS case definition which simplified diagnosis by requiring the demonstration of characteristic clinical signs, microscopic lesions and antigen in typical lesions. This case definition provided pathologists and field veterinarians critical diagnostic guidelines for individual animals.

Porcine circovirus was first identified as a non-pathogenic contaminant of PK-15 cells in 1974. However, a retrospective study using archived formalin-fixed paraffin-embedded tissues, identified PCV2 DNA in pig tissues dating back to 1962. The oldest archived tissues in which PCV2 DNA has been identified in characteristic lesions (lymphatic depletion, granulomatous inflammation, cytoplasmic inclusion bodies, multinucleate giant cells, interstitial pneumonia, hemorrhagic dermatitis and exudative glomerulonephritis lesions) fulfilling the diagnostic criteria for PMWS, date back to 1985.

PCV2 is now considered globally ubiquitous and a major threat to the pig industry. It has caused devastating disease and mortality in numerous hog-dense countries. Annual financial losses are estimated to be as high as 600 million EUR for Europe, and 200 million CAD for Canada. Faced with a mounting number of herd epizootics in 2005/06, the American Association of Swine Veterinarians developed a case definition in an attempt to distinguish farms with epizootic disease, from those experiencing only sporadic losses. Until then, segments of the North American industry had been reluctant to acknowledge PCV2 as a significant swine pathogen, and were more concerned about the unstoppable spread of virulent PRRSV. In fact, as far back as 1997 when the role in PCV2 in PMWS was first proposed, the disease and virus were hotly debated in North America. Editorials in widely-read publications such as the Journal of Swine Health and Production and International Pigletter contested the emergence of a new syndrome. Ironically, this debate abruptly ceased after the successful introduction of PCV2 vaccines in N.A. in 2006.

Concomitantly with the North American epizootic, the widespread use of the term “PMWS” was discontinued in favour of porcine circovirus associated disease (PCVAD), due to the potentially negative connotations the word “wasting” would potentially have on consumer purchasing habits, and because PCV2-affected pigs do not always demonstrate weight loss. Alternatively, the term porcine circovirus diseases (PCVD) is also widely used to describe the syndrome, and was first proposed in 2004 by the European research consortium studying the control of PCVDs (www.pcvd.org). PCVD and PCVAD are synonymous terms for multisystemic disease associated with PCV2 infection. Clinical signs may include weight loss and emaciation, enlarged lymph nodes, respiratory distress, diarrhea, pallor, nephropathy, thymic atrophy, jaundice, reproductive failure and pre-natal myocarditis. In addition to PMWS, PCV2 infection has been associated with PRDC (Porcine Respiratory Disease Complex), PNP (Proliferative & Necrotizing Pneumonia), enteritis (clinically...
resembling ileitis), and PDNS (Porcine Dermatitis and Nephropathy Syndrome).

Fulfillment of the AASV case definition requires a doubling of mortality without the introduction of known pathogen(s), whereas the EU consortium case definition states that increases in mortality, if recorded, should be either statistically significant (determined using the Chi square test), or be higher than the historical mean mortality by 1.66 times the standard deviation (SD). The EU case definition goes on to state that if no mortality records are available for a herd, the increase in mortality should exceed the national or regional level by 50%.

In reality, many epizootically affected herds experience mortality levels in excess of these criteria. In fact, the 600 sow farrow-finish index herd experienced a four-fold increase in post-weaning mortality (2% to 8%), in spite of being a high health free of virtually all major swine pathogens including PRRS, Mycoplasma hyopneumoniae, swine influenza virus, Actinobacillus pleuropneumoniae, TGE, porcine respiratory coronavirus, and Brachyspira hyodysenteriae. Conventional health status farms may experience mortality approaching 50% in some batches of grow-finisher pigs.

Prior to the release of PCV2 vaccines, PCVD control focused on the implementation of good production practices, and the control of concurrent disease. At the time of writing, there are four PCV2 vaccines licensed in North America (one sow vaccine and three piglet vaccines), and two in Europe (the sow vaccine and a one-shot piglet vaccine). North America in particular, is very fortunate in that PCV2 vaccine became widely available in the midst of the PCVD epizootic.

In contrast, many other countries devastated by PCVD between 1995 and 2004, did not have these valuable tools in their arsenal and thus experienced prolonged periods of devastation. So, here is the key question of this presentation. *Is PCV2 vaccine a silver bullet, or simply a tool to be used concurrently with other non-immunoprophylactic control strategies?*

Time will tell, but PCV2 piglet vaccination is clearly very efficacious when used according to the manufacturer’s instructions. In many cases vaccination surpassed expectations by bringing mortality rates down to a level below the historical level before the PCVD. This, and the fact that the growth rates of subclinically infected pigs improve following vaccination, suggest that PCV2 vaccination might have a beneficial effect in herds even in the absence of typical clinical signs.

Where vaccination is not efficacious, producers and their veterinarians are obliged to seek technical guidance from the manufacturer. All vaccines have limitations, and the risk of vaccine failure increases when used in an extra-label manner. Additionally, PCV2 vaccines are specific and although vaccination against PCV2 might help pigs cope with co-infections, it cannot replace immune prophylaxis against other major pathogens, like PRRS, M hyo, Lawsonia. Non-immunoprophylactic control strategies in my opinion, are equally important for the control of PCVD, and other concurrent diseases on farms, and may in fact reduce the development of emerging pathogens or antimicrobial resistance trends. The PCV2 experience of the past decade should therefore stand as a reminder that there will most likely be another novel disease or syndrome sometime in the future. This is a great opportunity to get things done right on farms, and
avoid the pitfalls of the “silver bullet” mentality. In the end, our job is to enhance disease control using all the available tools and make a long term positive contribution to the global swine industry.

References

7. Krüger L. Retrospective study on porcine circovirus type 2 infection in pigs from the Institute of Pathology of the University of Veterinary Medicine, Hannover, by in situ-hybridization. Hannover, DE., 2005.
After graduating from the Ontario Veterinary College at the University of Guelph in 1988, Dr. Harding worked in a mixed animal practice in Humboldt, Saskatchewan. He has specialized in swine since 1991, and in 1997 established Harding Swine Veterinary Service Inc. In 1997 he also completed a Master of Science degree in Veterinary Medicine, at the University of Minnesota. Dr. Harding has consulted for both small family and large corporate swine operations in Western Canada. In August 2004, he became an Associate Professor, Swine Production Medicine, at the Western College of Veterinary Medicine, University of Saskatchewan, assuming teaching, research, clinical and service responsibilities. His research interests are in the area of prenatal immune programming and porcine circovirus. Dr. Harding is a frequent speaker at both domestic and international swine veterinary meetings and was 1999 recipient of the A.D. Leman Science in Practice Award. He was the founding President of the Canadian Association of Swine Veterinarians from 2004-2005, and is the program chair of the Western Canadian Association of Swine Veterinarians (WCASV), and Vice-President/Secretary of the IPVS 2010 organizing committee. He has reviewed manuscripts for the Canadian Veterinary Journal, Canadian Journal of Veterinary Research, Journal of Swine Health and Production, Journal of the American Association of Laboratory Animal Scientists.

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PCVAD control in Canada using different vaccination protocols
A severe epizootic of PCVAD struck pig farms in eastern Canada by the end of 2004. During 2006, Circovac® from Merial, Circumvent™ PCV from Intervet and Ingelvac CircoFLEX® from Boehringer Ingelheim became available in Canada. The first one is to be used in gilts and sows, the second one is a two dose vaccine for pigs and the third is a one dose vaccine for pigs. Initially, there was a huge demand for PCV2 vaccines and for a period of time, pharmaceutical companies were not able to meet such a demand. Since the availability of each product was limited, not all the pigs within a specific production system could be vaccinated with only one product. This allowed a comparison of the different vaccination protocols that were used within a short period of time to find the most effective protocol 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 were weaned off-site between 16 and 19 days of age. Nurseries were operated all in - all out by barn and no more than 2 sources of pigs were commingled in each pig flow. Finisher barns were also off-site and operated all in - all out by barn. The system was 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 (17-21 weeks of age). 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 with either, Circovac® or Circumvent™ PCV. 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 analyses were performed. Results were considered significant when the P-value was under 0.05. Where multiple Chi-square or Proportions tests were run on sub-groups of data, the Bonferroni correction of the overall test alpha-probability was used.

**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 the one dose and two dose products for use in pigs, given according to manufacturer’s recommendations, improved the mortality very significantly. Circumvent™ PCV administered once did improve mortality, but not as much as with the one dose vaccine, or the two dose vaccine given according to the manufacturer’s recommendations.

In order to take into account potential seasonal or pig flow effects on mortality results, other comparisons between the Circumvent™ PCV and Ingelvac CircoFLEX® vaccines were performed. To limit the potential impact of differences in the time period when the vaccines were used, Table 2 is showing the mortality results for a 3 month period during which the two protocols were applied simultaneously, but in different pig flows. To reduce the impact that vaccination of different pig flows could have, Table 3 is comparing mortality in 3 pig flows where both vaccines were used, but at different points in time.

**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 the vaccination protocol. However, all data were obtained in only one production system where genetics of the animals, feeding and management practices were the same. Semen came from the same boar stud and replacement animals came from the same herd for all sow farms. The health status in all 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 Circumvent™ PCV but this is for all the pig flows. In some pig flows, Ingelvac CircoFLEX® was never used. Table 3 is taking into account only pig flows that received at some point either Circumvent™ PCV or Ingelvac CircoFLEX® and shows no statistical difference between the two products.

It can then be concluded that both Circumvent™ PCV and Ingelvac CircoFLEX® vaccines, given according to manufacturer’s recommendations, are reducing mortality very significantly in the finisher barns of this system and that Ingelvac CircoFLEX® is at least as effective as Circumvent™ PCV administered twice.
### Table 1: Average finishing mortality results for each PCV2 vaccination protocol (1)

<table>
<thead>
<tr>
<th>Piglet vaccination</th>
<th>Sow vaccination</th>
<th>Mortality (%)</th>
<th>Number of pigs at placement</th>
<th>Mortality (%)</th>
<th>Number of pigs at placement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No</td>
<td></td>
<td>No 10.4</td>
<td>10.7</td>
<td>18 101(2)</td>
</tr>
<tr>
<td></td>
<td>Circumvent™ PCV</td>
<td>7.0</td>
<td>12 023</td>
<td>nd</td>
<td>nd</td>
</tr>
<tr>
<td></td>
<td>1 injection</td>
<td></td>
<td>24 041</td>
<td>3.8</td>
<td>26 415(3)</td>
</tr>
<tr>
<td></td>
<td>Circumvent™ PCV</td>
<td>3.9</td>
<td>7 872</td>
<td>3.4</td>
<td>14 226(4)</td>
</tr>
<tr>
<td></td>
<td>2 injections</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ingelvac CircoFLEX®</td>
<td>3.1</td>
<td>7 872</td>
<td>3.4</td>
<td>14 226(4)</td>
</tr>
</tbody>
</table>

(1) Batches placed between March 2006 and March 2007, regardless of the pig flow
(2) All pigs born from sows vaccinated with Circovac
(3) 72% pigs born from sows vaccinated with Circovac
(4) 89% pigs born from sows vaccinated with Circovac

### Table 2: Average finishing mortality results for vaccinated batches placed between January 2007 and March 2007 (1)

<table>
<thead>
<tr>
<th></th>
<th>Mortality (%)</th>
<th>Number of pigs at placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circumvent™ PCV</td>
<td>3.9</td>
<td>12 122</td>
</tr>
<tr>
<td>2 injections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingelvac CircoFLEX®</td>
<td>3.4</td>
<td>10 301</td>
</tr>
<tr>
<td>1 injection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(1) Regardless of the pig flow and sow vaccination status
(2) Different subscripts mean that the results were significantly different

### Table 3: Average finishing mortality results for 3 pig flows within the system where both vaccines were used (1)

<table>
<thead>
<tr>
<th></th>
<th>Mortality (%)</th>
<th>Number of pigs at placement</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>7.8</td>
<td>11 834</td>
</tr>
<tr>
<td>Circumvent™ PCV</td>
<td>3.9</td>
<td>12 122</td>
</tr>
<tr>
<td>2 injections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ingelvac CircoFLEX®</td>
<td>3.7</td>
<td>10 301</td>
</tr>
<tr>
<td>1 injection</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(1) Batches placed between March 2006 and March 2007, regardless of the sow vaccination status
(2) Different subscripts mean that the results were significantly different
Dr. François Cardinal is a practicing veterinarian. He is working with Les Consultants Avi-Porc, a veterinary clinic based in Drummondville (Quebec, Canada) and specialized in avian and swine medicine.

He got his DVM from the University of Montreal in 1999 and worked exclusively in swine since then. In 2003, he completed a Master Degree on the epidemiology of postweaning E.coli diarrhea at the University of Montreal. He has been chairman of the PCVAD committee of the Quebec association of swine veterinarians, and is also a member of the PCV2 Task Team of the American Association of Swine Veterinarians (AASV).

More recently, he worked for the Quebec swine industry council to develop a strategic plan to improve swine health in the province. He is also a member of the board of directors of the Canadian Swine Health Board.
Vaccination benefits beyond clinical protection in a US finishing unit
Vaccination benefits beyond clinical protection in a US finishing unit

Introduction

Since the emergence of a disease causing severe wasting, ill-thrift and elevated mortality in nursery pigs was first described in western Canada in 1997 by Drs. John Harding and Ted Clark, Postweaning Multisystemic Wasting Syndrome (PMWS), as it was initially called, has been identified in most swine-producing countries worldwide. The clinical problems associated with PCV2 were noted only sporadically in North America for many years. However, since about 2004 porcine circovirus associated diseases (PCVAD) exploded across the continent in severe epidemics in various regions of Canada and USA. The clinical appearances vary, although the most severe economic presentation was in the grower/finisher stage with growth retardation, mortality and unthrifty animals that lead to under weight animals of little to no market value.1

Within a few months a rapidly growing number of units were experiencing PCVAD. The mortality rate easily reached 8 to 12% range and more. The mortality rate often peaked in the range of 20 to 35% and much higher depending on the presence of co-factors. The list of infectious co-factors includes but is not limited to PRRS virus, mycoplasma, swine influenza virus and secondary bacteria. In a few cases other viral pathogens were found and complicated the diagnostic findings. Retroviridae and Pestiviridae (predominately BVD-like virus) have been isolated in cases with extreme high mortality rates and suggested as potential co-infection with PCV2. Clinical signs varied significantly between farms and included conditions associated with PCV2 like porcine respiratory disease complex (PRDC), porcine dermatitis and nephropathy syndrome (PDNS), proliferative necrotizing pneumonia and reproductive problems.

Pathologists, veterinarians and researchers debated if the causative agent was PCV2. Evidence of PCV2 was easy to find and isolate in the tissues and samples submitted. The discussion deliberated around if PCV2 was the “real” or causative agent for the clinical signs since the virus was universally found. The devastation continued with growth retardation of 8 to 45% of the pigs in a group creating under weight animals at market. The severe economic wreckage of dealing with high mortality rates, little response to therapies and shrinking cash flow from under valued animals drove the emotional aspects of this disease to breaking points for individuals and organizations.

Pharmaceutical companies were already developing PCV2 vaccines due to the damaging disease epidemics in other parts of the world, primarily Europe. The North American swine industry was very fortunate to receive the first vaccines that became available around 2006. Although the first doses were limited in available quantities, news about miraculous post vaccin-
tion results spread rapidly throughout the swine industry.

PCVAD is considered a multifactorial disease of pigs that involves infection with PCV2 and the influence of infectious and/or non-infectious risk factors.2, 3 The debate quickly moved into the arena of why the sudden change of clinical signs and devastation if PCV2 had not changed. To add to the mystification and debate, the naming of the most common isolate of PCV2 that was found in most of the severe cases occurred. The strain of PCV2 in the outbreaks was first identified by restriction fragment length polymorphism (RFLP) analysis as PCV2-321. The recent terminology for this strain is PCV2b.4 The raging debate on PCV2 as the cause of PCVAD evaporated as more producers and veterinarians used the commercially available vaccines with outstanding results. Vaccination quickly became a “no brainer” in the majority of US pig farms. Vaccinations significantly reduce mortality rates and clinical signs associated with PCVAD problems. However, additional benefits beyond clinical protection were found in a few flows when grow finish records were closely examined. This paper describes the effects of vaccination against PCV2 on mortality rate, growth performance and carcass parameters.

Materials and Methods

A production system utilizing four off-site conventional finishing barns housing all barrows by barn (all-in/all-out) was used in this evaluation. PCVAD was first diagnosed in late 2005. Average finishing mortality rate increased from 2-3% pre-PCVAD to over 8% after PCVAD became established. Twelve barns of approximately 830 pigs/group were vaccinated at weaning (approximately 3 weeks of age) with a one-shot PCV2 vaccine and were compared to 12 non-vaccinated barns of pigs. A total of almost 20,000 pigs were included in the evaluation. The experimental unit was the barn; however, some variables were legitimately calculated back for the individual animal as the numbers of the individual animals were exactly known for each barn (number in – number out). Efficacy parameters included mortality rate, cull rate, average daily gain (ADG), feed conversion rate (FCR), average daily feed intake (ADFI), back fat depth, loin muscle depth and lean meat yield. In most of the groups (10/12 non-vaccinated, 8/12 vaccinated) pigs were fed ractopamine during the late finishing period. Data were analysed using analysis of (co)variance procedures (ANCOVA) with treatment (vaccine/control) as main effects and ractopamine treatment as covariate, where appropriate (SAS, Cary, North Carolina, version 8e). Results were considered significant if \( p \leq 0.05 \). A Statistical Process Control (SPC) Chart was prepared to evaluate the effect of vaccination on predictability of the production process, displaying the non-adjusted FCR means.

Economic benefit of vaccination was calculated based on sales of pigs produced (standard marketed and culls) minus costs involved (feed costs and piglet price). Assumptions made for both groups: 1.10 US$/kg live weight, 0.78 US$/kg cull live weight, 180 US$/1,000 kg feed, 42 US$ per 25 kg pig. Improvement in carcass parameters and vaccination costs were not included in the calculation.
Results

Compared to non-vaccinates, vaccinated pigs had significantly decreased mortality rate and back fat depth while achieving increased ADG, percentage lean meat yield and increased percentage of pigs marketed (Table 1). Culls were markedly decreased in vaccinated groups, though not statistically significant due to large variation among individual groups. FCR was not significantly different between the two groups. However, FCR was numerically lower in vaccinated groups and appeared to be less variable in the vaccinated groups (Fig. 1). The total gross benefit of vaccination was calculated to be approximately US$10 per vaccinated animal. The positive return was based on income minus costs. Income was generated from revenues of market and cull animals and costs coming from standardizing a value on the pigs placed, FCR and standardized feed price.

However, this calculation does not take into account the costs for the vaccine and labor. Additional benefits were also not calculated which include improved carcass parameters, reduced use of antibiotics and a higher number of each group being sold as full market value animals, i.e. less cull or light weight animals at market time. The improved emotional outlook by the employees is priceless. The employees look forward to taking care of healthy, fast growing animals rather then animals that do not respond to therapies and often die even with timely treatments.

Discussion

Vaccination at weaning with a one-shot PCV2 vaccine not only significantly reduced mortality rate, but improved performance and carcass parameters as well. Significant effects on ADG, back fat and lean meat were demonstrated. In this field setting, vaccination against PCV2 clearly had positive effects on health status and relevant economic parameters.

Reference

Table 1: Performance differences of 12 barns of PCV2-vaccinated pigs versus 12 barns of non-vaccinated pigs.

<table>
<thead>
<tr>
<th>LS Means</th>
<th>Vaccinates</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality (%)</td>
<td>2.28</td>
<td>9.08</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Culls (%)</td>
<td>4.84</td>
<td>7.69</td>
<td>0.3046</td>
</tr>
<tr>
<td>ADG (g/day)</td>
<td>814</td>
<td>728</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>FCR</td>
<td>2.95</td>
<td>3.03</td>
<td>0.55</td>
</tr>
<tr>
<td>ADFI (kg)</td>
<td>2.4</td>
<td>2.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Back fat (mm)</td>
<td>19.7</td>
<td>22.0</td>
<td>0.0003</td>
</tr>
<tr>
<td>Loin depth (mm)</td>
<td>54.4</td>
<td>54.1</td>
<td>0.8324</td>
</tr>
<tr>
<td>Lean meat (%)</td>
<td>53.77</td>
<td>52.65</td>
<td>0.0014</td>
</tr>
</tbody>
</table>

Figure 1: Feed conversion ratio of non-vaccinated versus PCV2-vaccinated groups of pigs (non-adjusted means).
Tom is the owner and founder of Rensselaer Swine Services. He graduated from Purdue University with a DVM degree in 1979 and initially entered into a mixed animal practice in Illinois before moving to a mixed animal practice in Rensselaer in 1981. After several years of focusing on swine production medicine, he started Rensselaer Swine Services, P.C. in 1991. He obtained diplomate status with the American Board of Veterinary Practitioners in Swine Health and Management Specialty in 1989 and successfully was recently recertified for another term. Tom consults with swine operations worldwide and has been very involved in the swine industry since his 4-H years on a hog and grain farm. Professional involvement includes membership in the American Association of Swine Veterinarians, American Veterinary Medical Association and Indiana Veterinary Medical Association. Tom is the past president of American Association of Swine Veterinarians (AASV) and since 2006 he is the chairperson of the AASV Task Force on PCVAD.

He has several papers on different topics and pathogens in the literature. Tom has lectured in most hog producing states in the United States and Canada and several countries in SE Asia and Europe. Tom and his wife, Denise, live in Rensselaer and have three kids: Kevin graduated from Purdue with a degree in Ag Systems Management and is plant manager of Remington Hybrids, a seed corn company in Francesville, IN; Matthew graduated with a degree in Ag Systems Management from Purdue University and is working for ADM; and Kendra is a senior at Rensselaer Central High School. Tom’s hobbies include gardening (especially growing roses), spending time with his family, shooting sports, camping and fishing.
Doug King

Benefits of controlling subclinical PCVAD in a large US operation
Introduction

The financial benefits using a PCV2 vaccine in farms affected clinically by porcine circovirus associated diseases (PCVAD) are obvious. However, on many farms pigs do not show the typical clinical signs though the herd is infected with PCV2 and histological lesions characteristic for PCVAD are present. The objective of this trial was to evaluate the benefits of vaccinating piglets at 3 weeks of age with Ingelvac CircoFLEX® in a production system with a so-called subclinical presentation of PCVAD.

Materials and Methods

The 3-site production system was negative for PRRS and positive for Mycoplasma hyopneumoniae and PCV2. Peak PCV2 viremia occurred around 10 weeks of age without clinical expression of PCVAD. Pigs weaned at approximately 21 days of age from multiple sow herds were commingled at the nursery. A total of 1200 pigs were placed on test (600 vaccinates and 600 controls). Like pens of pigs (same sex, same size) with either 25 or 50 pigs per pen were designated as study pens. Within the study pens, every other pig was vaccinated or injected with placebo, and individually weighed. Vaccinates and controls were commingled within study pens contained in barns where the rest of the pigs (non-study pigs) were not vaccinated. Vaccinates received a single 1 mL IM dose of Ingelvac CircoFLEX®. Controls received a single 1 mL IM injection of sterile water placebo. Pigs were individually weighed on the day of vaccination (day 0), day 41 prior to being moved to a finishing barn, and again on day 131 at the end of the study. Blood samples were collected at 6, 9, 13, 17 and 21 weeks of age for quantitative PCR (qPCR) testing. Finally, 509 vac-
cinated and 474 control pigs were evaluated at the slaughter plant for various carcass measures. Necropsies and tissue diagnostics were performed on a subset of mortalities. The experimental unit was the individual pig and performance data were analyzed using ANCOVA (JMP) with starting weight used as a covariate. One-way ANOVA was used to analyze the PCV2 qPCR geometric values. Comparisons in both models were made to the non-vaccinated controls using Student’s t-test. An arbitrary cut-off weight of 82 kg on day 131 was utilized to reflect cull rates. Carcass data were analyzed using ANOVA having treatment and date of marketing as main effects. Comparisons were made using Student’s t-test. Economic benefits were calculated based primarily upon the total live weight delivered to slaughter and the relative market value of pig weight classes. Pigs exceeding 116 kg live weight were valued at US$1.12 per kg while lighter pigs were valued at US$0.68 per kg.

Results

Pig groups were considered clinically normal throughout the evaluation even though PCVAD was confirmed histologically in individual pigs in the study, thereby confirming the presence of subclinical PCVAD. No adverse local or systemic side effects attributable to vaccination were observed. Vaccinated pigs had significantly reduced PCV2 qPCR viral loads at 13, 17 and 21 weeks of age ($p<0.0001$; Figure 1).

Figure 1: Viral load in vaccinated and non-vaccinated groups
There were no differences between the two treatment groups for day 0-41 ADG during the nursery phase ($p=0.94$, Table 1). Pigs vaccinated with Ingelvac CircoFLEX® had improved day 41-131 ADG and day 0-131 ADG compared to non-vaccinated controls ($p<0.0001$, Table 1).

### Table 1: Growth rates of vaccinated and non-vaccinated pigs.

<table>
<thead>
<tr>
<th>Item</th>
<th>Ingelvac CircoFLEX®</th>
<th>Control</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>d0 starting weights, kg</td>
<td>5.30</td>
<td>5.35</td>
<td>0.48</td>
</tr>
<tr>
<td>d0-41 ADG, g/day (3-9 weeks of age)</td>
<td>363</td>
<td>363</td>
<td>0.94</td>
</tr>
<tr>
<td>d41-131 ADG, g/day (9-22 weeks of age)</td>
<td>872</td>
<td>840</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td>d0-131 ADG, g/day (3-22 weeks of age)</td>
<td>719</td>
<td>690</td>
<td>$&lt;0.0001$</td>
</tr>
</tbody>
</table>

There were no significant differences between the two treatment groups for either nursery (p=0.54) or finishing (p=0.27) mortality rates (Table 2). Vaccinated pigs had a significant reduction in cull rate compared to non-vaccinates (p=0.001, Table 2).

### Table 2: Mortality and cull rates for vaccinated and non-vaccinated pigs.

<table>
<thead>
<tr>
<th>Item</th>
<th>Ingelvac CircoFLEX*</th>
<th>Control</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pigs placed</td>
<td>600</td>
<td>600</td>
<td>-</td>
</tr>
<tr>
<td>Nursery mortality rate, %</td>
<td>3.17</td>
<td>4.00</td>
<td>0.54</td>
</tr>
<tr>
<td>Finishing mortality rate, %</td>
<td>2.07</td>
<td>3.16</td>
<td>0.27</td>
</tr>
<tr>
<td>Combined nursery and finishing mortality rate, %</td>
<td>5.18</td>
<td>7.07</td>
<td>0.19</td>
</tr>
<tr>
<td>Cull rate, %*</td>
<td>5.16</td>
<td>10.24</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Pigs less than 82 kg on day 131*
Pigs vaccinated with Ingelvac CircoFLEX® had heavier hot carcass weights ($p=0.01$) and a more muscular carcass with greater depth of loin muscle ($p=0.003$, Table 3). Vaccinate ($n=509$) hot carcass weights averaged 88.3 kg while control ($n=474$ head) hot carcass weight averaged 86.7 kg. In terms of total live weight delivered for slaughter (including culls), vaccinates produced 2,639 kg more than controls (63,993 kg vs 61,354 kg, respectively). The total market value (including culls) of vaccinates and controls was determined factoring in additional revenue based on the packer market grid matrix with vaccinates earning about a 1% premium in value relative to the controls. From those total values, one can conservatively estimate a US$4.38 return on investment (ROI) for every dollar invested in Ingelvac CircoFLEX® vaccine in this study.

<table>
<thead>
<tr>
<th>Item</th>
<th>Ingelvac CircoFLEX®</th>
<th>Control</th>
<th>$p$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of pigs</td>
<td>509</td>
<td>474</td>
<td>-</td>
</tr>
<tr>
<td>Hot carcass weight, kg</td>
<td>88.3</td>
<td>86.7</td>
<td>0.01</td>
</tr>
<tr>
<td>Loin muscle depth, mm</td>
<td>58.36</td>
<td>56.79</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Table 3: Least square means for pig carcass measures.

Conclusions

The presence of PCV2 infection in growing pigs seems to have a negative impact on performance even when we do not observe clinical manifestations of the disease. Consistent with a herd diagnosis of subclinical PCVAD, mortality rate was not different between vaccinates and controls, nor were clinical signs of PCVAD evident even though PCVAD was confirmed histologically in individual pigs. The vaccinated group had significant increases in key productivity parameters which were associated with reductions in PCV2 viral load. Significant biologic and economical improvements were achieved by controlling the subclinical impact of PCVAD by vaccination resulting in an excellent ROI. Because of that each pig produced by Cargill is now vaccinated with Ingelvac CircoFLEX® independent of the clinical signs expressed on a specific farm.

References

EDUCATION
Doctor of Veterinary Medicine with distinction, 1983,
Iowa State University Ames, Iowa
Executive Veterinary Program (Swine), with completion
in 2000, University of Illinois Champaign, IL

VETERINARY PRACTICE
Cargill Pork LLC Wichita, KS
8/2000 to present. Staff Veterinarian Otley, IA.
Overseeing health of commercial farrow-to-wean,
wean-to-finish, and finishing production in Iowa,
Missouri, and Illinois.

Walcott Veterinary Clinic Walcott, Iowa

West Point Veterinary Clinic West Point, Iowa
6/84 to 2/85. Associate in mixed practice.

Pines Meadow Veterinary Clinic Oregon, Illinois
6/83-5/84. Associate in mixed practice.

PROFESSIONAL MEMBERSHIPS & LICENSES
Licensed to practice in Iowa, Missouri, Illinois,
and Minnesota
Member AASV, AVMA, IVMA, MOVMA
Nigel Woolfenden

Experiences with Ingelvac CircoFLEX®
in severe PCVD in the UK
Experiences with Ingelvac CircoFLEX® in severe PCVD in the UK

The production unit selected for the study consisted of two sites, one containing 1100 breeding sows farrowed on a three weekly batch system with piglets being transferred at weaning to the second site, 100km away, which was a combined nursery and finishing unit taking piglets from approximately 7kgs to a slaughter weight of 105kgs. The breeding herd was of typical UK commercial genetics with the female being a Landrace cross Large White (Yorkshire) hybrid artificially inseminated with Pietrain cross Large White terminal sire semen. The farm had changed to two site and batch production in the preceding two years to deal with the impact of PMWS on production since these changes allowed better ‘all-in all-out’ management and improved hygiene. The breeding herd had also undergone a medicated partial depopulation programme in 2004 which had been successful in eliminating enzootic pneumonia and PRRS (EU) and, whilst growth rates and mortality had improved above the UK average for a PMWS affected unit, both mortality and daily liveweight gain was still felt to be considerably affected by PCV2 infection and the secondary problems associated with PCV2-related immunosuppression.

Prior to and during the trial the health status remained Mycoplasma hyopneumoniae negative, PRRS negative and Streptococcus suis serotype 2 positive. Newly weaned pigs up to seven weeks of age had a history of suffering from colibacillosis (E.coli Abbotstown strain) with Salmonella Typhimurium occasionally also isolated from episodes of post-weaning diarrhoea. Problems with PCV2 began to be seen from 6-7 weeks of age with typical PMWS symptoms of anaemia and weight loss occurring, often complicated by secondary diarrhoea, coughing episodes and Glässer’s disease. Mortality varied from batch to batch between 8% and 18% with an average mortality of 12% for the six months prior to the trial. Active euthanasia accounted for half this mortality since chronically PMWS stunted animals were not economically saleable. Sudden death mortality and PDNS continued to affect older pigs approaching slaughter weight which was believed associated with ongoing PCV2 effects.

The vaccine study was randomised, double blinded and placebo controlled. Two consecutive farrowing house batches of approximately 770 suckling piglets at around three weeks of age were selected for inclusion based on their achieving a minimum body weight, age and their having a lack of clinical disease symptoms. Piglets were randomised within their own litter based on body weight and allocated to either treatment or control group. Each piglet was individually ear tagged, blood sampled for serology to determine maternally derived PCV2 antibody levels, weighed and then injected with
either a single 1ml dose of vaccine or placebo by intramuscular injection in the neck. Post treatment the animals were co-mingled and returned back to their own sow as a complete litter, and weaning took place some seven days later with immediate transport to the second farm at this time. Vaccinated and control animals were further co-mingled at weaning with both groups being present in the same pens, at normal stocking densities and fed usual commercial diets.

All animals were clinically examined daily by the farmer and weekly by the veterinary surgeon from inclusion onwards, with any signs of general ill health being noted including lethargy, dyspnoea, cough, diarrhoea, lameness, skin discolouration including jaundice and weight loss. Records of any deaths of trial animals from inclusion onwards were maintained and post mortem examination of each animal took was performed at the Veterinary Laboratories Agency with histological examination as necessary. Twenty percent of the trial animals were blood sampled each week up to week 12 after inclusion and thereafter every second week until week 20 of the trial. Samples were tested by quantitative PCR for PCV2 DNA and by ELISA for PCV2 antibodies. All animals were weighed at inclusion, seven weeks after treatment and again at weeks 12, 17 and 20 post-inclusion.

Until around four weeks after inclusion no differences between the study and control groups in terms of clinical disease incidence could be detected but by week 12 and continuing into weeks 17 and 20 a significant difference in animals showing ill thrift was shown with vaccinated animals being much less likely to show signs of PMWS.

Mortality prior to the onset of PCV-2 viraemia at four weeks post-inclusion (7 weeks of age) was similar in the two groups at 1.3%. However a significant difference in mortality from all causes developed from four weeks post-inclusion to the end of the trial at 20 weeks post inclusion with mortality for the control groups totalling 14.3% overall versus 4.6% for the vaccinated group. As it was possible through post mortem examination and associated histopathology to confirm causes of death, this difference represented an 89% reduction in PCV-2 associated mortality.

Of the surviving animals, bodyweight differences were apparent at the first weighing by seven weeks post-inclusion with a difference of 30g per day daily liveweight gain in favour of the vaccinated animals. Vaccinated animals continued on average to gain weight by some 92g per day above the controls during the period of peak viraemia from study week 7 to 12, and showed a 62g per day growth improvement against a control from weeks 12-17 of the study. By the end of the trial at week 20 this translated into 6.8kg difference in the mean bodyweight of the vaccinated animals versus the controls. This significant difference in mean weight was partly achieved through a notable reduction in the incidence of poorly grown “wasted” animals in the vaccinated group.

Recent experience following the routine use of Ingelvac CircoFLEX® on all piglets on the trial farm since Autumn 2007 has shown consistent reductions in total post weaning mortality to below 5%, and improvements in overall daily liveweight gain of over 40 g per day. No deaths attributed to PDNS have been reported.
Qualified with honours from Liverpool University in 1986. Worked in mixed large animal practice before specialising in pig medicine 10 years ago. Currently a partner with Bishopton Veterinary Group, a 12 vet team based in Yorkshire in the North of England, working full time with commercial pig herds. I have specific interests in preventive medicine, training pig farmers and managing health to optimise growth.

Past President of the Yorkshire Veterinary Society and past member of the Pig Veterinary Society Executive Committee. Director of Vetscore Ltd responsible for gathering abattoir surveillance data on behalf of the British Pig Health Scheme.
Young S. Lyoo

Efficacy of Ingelvac CircoFLEX® in PCVAD affected farrow-to-finish farms in Korea
Efficacy of Ingelvac CircoFLEX® in PCVAD affected farrow-to-finish farms in Korea

Porcine Circovirus Associated Disease (PCVAD) including PMWS is now recognised as a global epidemic disease that causes significant economic losses to pig farmers throughout the world. Since its first occurrence in Korea in 1999, it has been reported extensively in the field. Estimated losses due to PCVAD in Korea are running over KRW 456 billion (326 million EUR) per year (Korean Swine Association, 2006). In Korea PCVAD is reported to affect mainly pigs between 5 to 12 weeks of age. Pigs affected with PCVAD show a variety of clinical signs, including growth retardation, dyspnoea, cough and diarrhoea (Roh, 2005). Clinical symptoms in herds varies dramatically in severity of the disease and mortality. Co-infections also vary significantly between farms. Major co-infections reported include PRRSV, PPV, Haemophilus parasuis and Pasteurella multocida (Kim, 2002, Roh, 2005). In co-infected herds post-weaning mortality can easily reach 30% or higher.

Materials and Methods

This trial was performed to determine the efficacy of Ingelvac CircoFLEX® under Korean field conditions. Three farms A, B, C (Table 1) with different disease expression were selected and PCV2 infection confirmed by necropsy, histopathology, PCR and IHC. Serological testing was carried out to determine co-infections present. All three farms were positive for PRRSV, Mycoplasma hyopneumoniae and Salmonella.

<table>
<thead>
<tr>
<th>Farm</th>
<th>No. of sows</th>
<th>Post-weaning mortality (historical)</th>
<th>Clinical disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>300</td>
<td>~ 30%</td>
<td>PMWS since 2000, high mortality, severe pneumonia (Glasser’s) and mild diarrhea (E.coli &amp; Salmonella)</td>
</tr>
<tr>
<td>B</td>
<td>250</td>
<td>~ 15%</td>
<td>PMWS since 2002, mild mortality and pneumonia</td>
</tr>
<tr>
<td>C</td>
<td>330</td>
<td>~ 25%</td>
<td>PMWS since 2003, pneumonia and diarrhea (Salmonella)</td>
</tr>
</tbody>
</table>

Table 1: Farm size and disease history.
In total 532 pigs were included in the trial consisting of 272 in the vaccinated group (VG) and 260 in the non-vaccinated group (NVG). Pigs of VG received 1ml of vaccine via intramuscular route and non-vaccinated control pigs were given PBS (Phosphate buffered saline pH 7.2) in the same manner. All pigs were individually weighed at 3, 10, 16, 22 weeks of age. Mortality and clinical signs were recorded. The clinical observation included fever, depression, dyspnea, cough, diarrhea, behavior and skin lesions. Distribution and amount of PCV2 antigen in various fresh tissue and fixed tissues of dead pigs (VG; n=20, NVG; n=73) were evaluated by PCR and IHC (immunohistochemistry). Tissue samples for PCR were taken from lymph node, tonsil and lung and for IHC from tonsils, lungs, lymph nodes, livers, spleens, intestines and kidneys. The amount of viral load in tissues by IHC was scored 0, 1, 2, 3, respectively. On farm A blood samples were collected from 20 animals of each group at 3, 7, 10, 13, 16 weeks of age to measure white blood cell population. Lymphoid cell depletion which is a typical sign of PCV2 infection was evaluated by routine histopathology and white blood cell differential counting (WBC).

Results

The mortality rate was reduced significantly on all farms by up to 82% in VG compared to NVG, overall it was reduced by 74% from 28% to 7% (Table 2), respectively. Clinical signs were drastically reduced in the vaccinated group and typical clinical signs of PCVAD were only observed in non-vaccinated groups from 7 to 8 weeks of age onwards, including severe diarrhea, increased breathing, fever and PDNS. The average final body weight at 22 weeks of age and weight gain from 3 to 22 weeks of age was significantly increased in VG on farms A and B. On farm C the difference was not statistical significant. However, it needs to be taken into account that at the final weighing date already 8 of the heaviest pigs in the VG had been sold, compared to only two in the NVG. The mean of body weight in 22-week-old pigs was 86.4 kg (farm A), 97.36 kg (farm B), 94.29 kg (farm C) in VG and 70.1 kg (farm A), 83.26 kg (farm B), 92.55 kg (farm C) in NVG.

<table>
<thead>
<tr>
<th>Farm</th>
<th>NVG</th>
<th>VG</th>
<th>ChiSquare</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>48% (28/58)</td>
<td>8% (5/59)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>B</td>
<td>24% (13/54)</td>
<td>6% (3/54)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>C</td>
<td>22% (32/148)</td>
<td>8% (12/159)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Total</td>
<td>28% (73/260)</td>
<td>7% (20/272)</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Table 2: Mortality rate from 3 - 22 weeks of age.
Conclusion

Single dose vaccination against PCV2 at 3 weeks of age increased weight gain and reduced mortality and clinical signs compared to the control groups. The efficacy of the vaccine to reduce virus replication in target tissues and lymphoid depletion by PCV2-infection was confirmed, as well. In addition to that, the WBC of the vaccinated pigs remained in the normal range, in contrast to the decreased values in the non-vaccinating pigs, suggesting that vaccination protects against the negative effects of PCV2 infection on the immune system. Therefore, we have concluded that under the conditions of Korean pig production Ingelvac CircoFLEX® is very effective in the control of PCVAD and highly recommendable to farms suffering from the disease to minimize losses and to increases resistance against PCVAD. However, the remaining non-PCVAD related clinical signs in the vaccinated groups underline the need to address all major pathogens on a farm.

References


Roh, IS (2005): Prevalence and Pathogenesis of Postweaning Multisystemic Wasting Syndrome by Porcine Circovirus 2 in Korea, Kangwon University, Chuncheon, Korea

D.V.M., Konkuk University, Seoul Korea 1983
Ph.D. Iowa State University Ames IA USA 1995
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2003~2004  Associate professor, University of
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Konkuk University, Seoul Korea

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Mike Roof

Ingelvac CircoFLEX® -
The bleeding edge of innovation toward the control of complex disease syndromes
The global swine industry has undergone incredible change and development over the past decade. Changes in herd size, management practices, and emerging diseases have all re-shaped the industry. Associated with these changes, animal health companies also need to change and adapt to insure they provide tools that meet the current industry needs as well as those of the future.

Historically, animal health companies focused on vaccine registration with goals related to addressing a single clinical issue. However, with the emergence PRDC (Porcine Respiratory Disease Complex) and PCVAD (Porcine Circovirus Associated Diseases) we have moved away from dealing with clinical disease associated with a single etiological agent and move into complex disease syndromes involving multiple pathogens that interact in a complex fashion and wreak economic havoc for swine producers.

In the late 1990’s Boehringer Ingelheim Vetmedica recognized that Porcine Circovirus type II (PCV 2) was an important and emerging disease. Because of our commitment to the swine industry we made this pathogen a priority in our R&D efforts. However we quickly determined that control of PCV 2 alone would provide some value to the industry, but that long term we needed to develop FLEXIBLE tools, tools that worked globally, tools that took into account regional needs, and tools that addressed complex syndromes. The cornerstone of our effort was built and designed around our Ingelvac CircoFLEX® vaccine, containing the unique combination of Purified Circovirus Antigen (PCA™) and the highly effective aqueous polymer adjuvant ImpranFLEX™.

In starting this project, we worked with Boehringer Ingelheim scientists, veterinarians, and global disease experts. We felt in order to develop a world class vaccine, we needed to know and understand the following key issues:

1. Where does PCVAD disease most commonly manifest itself within the global swine population?
2. If a vaccine were available, when/where would it be used to be most effective?
3. What would be the properties of a world class vaccine that would provide the most benefit to swine producers across the globe?
4. How to best match customer demands for efficacy, safety and convenience all at the same time?

When we looked at herds across the globe we routinely found that almost all pigs and pig herds were PCV 2 positive for antibody and antigen and yet not all herds had clinical disease. When we focused only on herds that had clinical disease we consistently noted that the timing of the disease was almost exclusively in the grower and finisher (> 6 weeks of age). This suggested that pigs in their first week of life, although exposed to the PCV 2 virus were likely protected by maternal immunity. Disease was then observed after maternal decay.

Based on this assessment, sow vaccination and inducing additional maternal immunity didn’t make sense or seem to add value to a control program. Sows were already positive and maternal immunity already appeared to be present and yet pigs were experiencing PCVAD. Vaccination of a sow seemed like it would have little benefit and may only push the disease into older and more valuable finisher animals. This was the basis for our focus on a pig vaccine and not on a sow vaccine. In hindsight this was a great decision!

Numerous studies and reports have been done looking at PCVAD and investigating the presence of swine pathogens. In general almost all reports, no matter on the method or geographical region, consistently list some combination of PCV 2, PRRSV, and M. hyopneumoniae as the most commonly detected agents in this disease syndrome. Therefore, we concluded that ultimately, not only would we need to develop a tool to control PCV 2, but it must be compatible with other vaccines based on the regional needs and disease agents. It needed to be FLEXIBLE to the herd and customer.

So at this point, we knew we had a disease that was found in the grower and finisher. We knew we needed to vaccinate pigs and induce immunity in the pig. We needed a vaccine that could be used with other respiratory vaccines. So the next step was to consider WHEN to vaccinate a pig for optimal protection. Because there were many reports of clinical disease in the grower (> 6 weeks of age), we knew that an effective vaccine had to placed and used prior to this time and yet be given enough time to induce protective immunity PRIOR to the clinical disease. So we worked backwards.

<table>
<thead>
<tr>
<th>≥ 6 weeks of age</th>
<th>Clinical Disease Observed</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-4 weeks</td>
<td>General time to induce a maximum immune response</td>
</tr>
<tr>
<td>2-3 weeks of age</td>
<td>Optimal time to vaccinate pigs and insure disease control!!</td>
</tr>
</tbody>
</table>

We knew that ORF 2 was a neutralizing epitope and so this would be the basis of a quality PCV 2 vaccine. Vaccination at 2-3 weeks of age would mean that a 2 dose vaccine would not be of value and potentially induce immunity too late. We didn’t have time to get 2 doses into pigs before disease started and would leave herds susceptible during early infections and maternal decay.
Traditional grow it, kill it, 2 dose vaccine technology is easy and commonly used in autogenous vaccines and older commercial products that are used in naïve animals. However development of 1 dose vaccine technology and vaccines that work in the face of maternal antibodies requires:

- A high quality, purified, stable, neutralizing antigen, at the proper dosage – PCATM (Purified Circovirus Antigen). The PCA\textsuperscript{TM} is forming a hollow PCV-2 virus, so live virus like antigen is presented to the immune system.
- A world class adjuvant that induces rapid onset of immunity, has good duration of immunity, and induces the proper immune response – ImpranFLEXTM. ImpranFLEX\textsuperscript{TM} is a buffered solution containing an aqueous polymer. It has an excellent safety profile as it does not contain mineral oil.
- A high quality scientific team
- A little dose of LUCK!

The conclusion of 7 years of research and development by the BIVI R&D team was the US launch of Ingelvac CircoFLEX\textsuperscript{®} in 2006 and the European launch in 2008. Ingelvac CircoFLEX\textsuperscript{®} is a one-shot vaccine, 1ml per dose, with an outstanding safety profile. It has been proven to override maternal immunity in pigs from 2 weeks of age onwards. The vaccine provides a rapid onset of immunity as early as two weeks after vaccination and has proven to deliver protective immunity through to slaughter in close to 100 million pigs. The product has taken the market by storm and consistently exceeded expectations in PCV 2 and PCVAD disease control. In former times this would have been enough and the end of the story...

However, as was stated earlier we no longer work in a world where control of a single etiological agent is enough. We need to provide solutions that meet complex disease syndromes. For this reason we have developed the Ingelvac CircoFLEX\textsuperscript{®} in parallel to another new vaccine Ingelvac MycoFLEX\textsuperscript{®}. This new vaccine was launched in the US in 2008 and registration in other countries is in progress. This will be the second phase of our delivery of the FLEX concept to the swine industry.

1. Ingelvac CircoFLEX\textsuperscript{®} vaccine – 1 ml/1 dose
2. Ingelvac MycoFLEX\textsuperscript{®} vaccine – 1 ml/1 dose
3. Formulated with a compatible adjuvant that allows mixing.
4. Ingelvac MycoFLEX\textsuperscript{®} and Ingelvac CircoFLEX\textsuperscript{®} can be mixed and allows the use of a 2 ml/1 DOSE vaccine to control 2 key components of PRDC
   * Highly effective in controlling both Mycoplasma lung lesions and PCVAD at the same time.
   * Convenient dose size (1+1=2 ml)
   * Convenient and cost effective 1 dose program
   * Very safe with no systemic and injection site reactions
5. This allows producers the chance to have both monovalent vaccines on hand and then use those relevant ONLY to their farm and mix if their disease situation changes. The data demonstrating efficacy of the FLEX combination was presented at the AASV meeting in San Diego in March 2008.
We are truly excited about these innovative developments and hope that Boehringer Ingelheim give you the power to FLEX your muscle and control these economically significant disease complexes, raise healthy pigs, and maximize your economic returns.

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Number of Animals</th>
<th>Average lung lesion score (% of lung)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingelvac MycoFLEX*</td>
<td>18</td>
<td>5.5\textsuperscript{a}</td>
</tr>
<tr>
<td>MycoFLEX* mixed with CircoFLEX*</td>
<td>19</td>
<td>3.9\textsuperscript{a}</td>
</tr>
<tr>
<td>Challenge Controls</td>
<td>19</td>
<td>14.3\textsuperscript{b}</td>
</tr>
<tr>
<td>Strict Controls</td>
<td>6</td>
<td>0.0</td>
</tr>
</tbody>
</table>

\textsuperscript{a,b}: Values with different superscripts differ significantly (\(p < 0.0001\))

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Number of Animals</th>
<th>Lymphoid depletion (%)</th>
<th>Lymphoid inflammation (%)</th>
<th>Lymphoid IHC (% affected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingelvac MycoFLEX* mixed with Ingelvac CircoFLEX*</td>
<td>24 CDCD pigs</td>
<td>0\textsuperscript{a}</td>
<td>4.2\textsuperscript{a}</td>
<td>8.3\textsuperscript{a}</td>
</tr>
<tr>
<td>Non-Vaccinated Controls</td>
<td>24 CDCD pigs</td>
<td>83.3\textsuperscript{b}</td>
<td>87.5\textsuperscript{b}</td>
<td>91.7\textsuperscript{b}</td>
</tr>
</tbody>
</table>

\textsuperscript{a,b}: Values with different superscripts differ significantly (\(p < 0.0001\))
EXPERIENCE
Boehringer Ingelheim Vetmedica Inc. (1995 – Present) – Executive Director of Bio-R&D. Responsible for Biological R&D with emphasis on global cattle and swine vaccines and investigations of new technology. Key registrations completed include PRRS ATP, Lawsonia FF, Lawsonia LF, Mycoplasma, and Porcine Circovirus.


Iowa State University (1987-1991) – Veterinary School Diagnostic teaching clinic and Salmonella Research Laboratory.

PUBLICATIONS
Thirty-three peer reviewed scientific publications describing research efforts in Porcine Reproductive and Respiratory Syndrome Virus (11 publications), Lawsonia intracellularis (9 publications), and Salmonella (13 publications).

EDUCATION
Doctor of Philosophy/Co-major: Immunobiology and Veterinary Microbiology, Iowa State University, 1991.

Master of Science/Major: Veterinary Microbiology, Iowa State University, 1989.

Bachelor of Science/Major: Microbiology, Iowa State University, September 1983 to May 1987.

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