Vaccination of Sows and Gilts against PCV2 Diseases: Field Experiences in Europe

F. Joisel [1], C. Charreyre [1], L. Coulombe [2], J.C. Noël [2] and S Longo[3]

[1]Merial SAS, 29 Avenue Tony Garnier, Lyon, 69007 France; [2]Merial Ltd, Montreal, QC; [3]BPC, Labruguière, France; ***Email***: Francois.JOISEL@Merial.com

■ Introduction

Porcine circovirus type 2 (PCV2) has been associated with a number of disease syndromes in pigs, including post-weaning multisystemic wasting syndrome (PMWS), proliferating and necrotizing pneumonia, porcine respiratory disease complex (PRDC), abortion and reproductive problems (Allan & Ellis, 2000). Porcine dermatitis and nephropathy syndrome (PDNS) and a new ear necrosis syndrome have also been associated with PCV2 but today, there is not definitive evidence that PCV2 is the major cause of these syndromes. Since the end of 2004, CIRCOVAC® (Merial), a PCV2 vaccine dedicated to sows and gilts to control PCVD in the whole herd, has been used in several parts of the world. The goal of this paper is to review the large-scale studies of PCV2 vaccination in Europe.

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■ Rationale of PCV2 Vaccination

PCV2 is a very small, stable and resistant virus. It is ubiquitous in the pig-rearing environment. In PMWS affected herds, piglets are exposed to PCV2 very early in their life. An early uncontrolled PCV2 load can be found within the Dendritic Cells (DC), a particular type of immunological cell responsible for antigen presentation to lymphocytes. In DC, PCV2 is able to escape in-cell lysis and to stay unprocessed in large quantities for a long period of time (Vincent et al., 2005). Furthermore, PCV2 will block the DC ability to initiate the immune cascade, not only necessary to fight against PCV2 itself, but also to protect the piglets from numerous other pathogens (Vincent et al., 2003). Such “immuno-compromised” status will result in the pig being susceptible to

infectious diseases including PMWS/PCVD and other bacterial and viral infections for the rest of its life (McCullough et al., 2007).

Maternally derived immunity has been demonstrated to be protective (Reynaud et al., 2001). Numerous case-control studies have repeatedly identified poor colostrum intake as a risk factor for the clinical expression of PMWS (Rose et al., 2003; de Jong et al., 2003). Thus, high quality maternal immunity transferred to piglets will cover the right period at the early phase of the piglet's life. Colostrum not only contains antibodies but also immuno-competent cells. In species having an epithelio-chorial placenta, like swine, it has been often demonstrated that colostrum from vaccinated mothers contains antigen-specific maternal immunoglobulins which have an important role in the passive protection of newborn animals. Colostrum also contains T and B lymphocytes. Recent functional experiments (McCullough et al., 2007) in SPF sows, clearly showed that colostrum from sows vaccinated with CIRCOVAC® contained IFN producing PCV2-specific $CD8^+$ T cells, whereas no IFNγ production could be detected in the colostrum of non-vaccinated sows. These data, together with previous reports, demonstrating that leukocytes isolated from colostrum can pass through the intestinal barrier of newborn piglets, strongly suggest that maternal antigen-specific leukocytes may be transferred to the piglets via the colostrum and constitute another line of active defense against infections in neonates or newborn piglets.

The early exposure of piglets to PCV2 needs to be under control. This is the role of an efficient maternally derived immunity which is protective over the right period of the piglet's early life. In addition, a strong and adapted immunity against PCV2 in sows will reduce the PCV2 load in the farrowing crates by reducing fecal excretion both by sows and by the young piglets (Charreyre et al., 2006a, b). Provided the piglets can get a sufficient amount of colostrum from their biological mother, maternal immunity enables the pig to properly build its own immune response that will be protective for the rest of its life span.

In emergency situations, and where an appropriate transfer of a maternal immunity of good quality could not be ascertained, vaccination of the piglets has also been used successfully. An adapted vaccination scheme with CIRCOVAC® has been used in experimental or emergency situations in several countries to vaccinate piglets and the results have shown very good safety and efficacy (data not shown). Although both maternal immunity and early immuno-compromission due to uncontrolled PCV2 exposure will hinder somewhat the efficacy of piglet vaccination, satisfactory results can be obtained because the vaccine will draw on remaining immune cells.

▪ Field Experiences of Sow and Gilt Vaccination against PCV2 with CIRCOVAC®

Field results in France

Two large studies were conducted in France using the records of the national data program "*Gestion Technico-Economique*" (GTE) focussing on production data and "*Gestion Technique des Troupeaux de Truies*" (GTTT or G3T) focussing on reproduction parameters.

The first study (Hérin et al., 2007) included 24 of the very first herds to begin using sow PCV2 vaccination. Included in this study were herds for which GTE results were available for at least a 1-year period from pigs born to non-vaccinated sows and at least for a 6-month period in which results were entirely attributable to pigs born from vaccinated sows. The herds were diversely affected with other pathogens such as PRRSV, M hyo, APP, SIV, etc. but all had a clinical and post mortem diagnosis of PCVD, recently confirmed by laboratory examination in 40% of the cases. The study included 7750 sows (mean = 310 per herd). Vaccination with CIRCOVAC® took place from December 2004 to February 2005. Significant improvements were found in:

- post-weaning mortality rate: from 3.6% to 2.2% (-1.4 points)
- fattening mortality rate: from 7.2% to 5.1% (-2.2 points)
- weaning-to-slaughter mortality rate: from 10.6% to 7.1% (-3.5 points)
- standardized feed efficiency: 2.75 to 2.64 (-0.11 kg feed per kg of pig meat)

A financial analysis of the benefits resulting from the improvement in these parameters showed significant differences between "before" and "after" PCV2 vaccination (**Table 1**). The added values per point/unit of improvement used in this calculation were based upon data from the Institute of Pig (ITP/IFIP) standard figures, base 2005. The use of CIRCOVAC® was calculated to produce an average benefit of € 101 per inventoried sow per year.

The second study gathered the GTE and G3T results of 36 vaccinated herds and compared those obtained in a similar 20-herd non-vaccinated control population. Vaccination occurred from January 2004 to February 2006. Types of herds are summarized in **Table 2**.

Table 1. Estimated economic benefit per inventoried sow per year following vaccination with CIRCOVAC® in the "GTE" study

	For the improvement unit of:	Average added value (source: IFIP/ITP, France)
Additional benefit of a decrease of the mortality rate in the nursery by	1%	€14
Additional benefit of a decreased mortality rate in the finishing barn by	1%	€19
Increase of the feed efficiency	0.1 unit	€36
Results	**Statistically significant improvement**	**Added value or benefit for the considered index**
Additional benefit for nursery	1.4%	1.4x14 = €19.6
Additional benefit for finishing	2.2%	2.2x19 = €41.8
Increase in feed efficiency 8-105kg	0.11 unit	0.11x36 = €39.6
Average benefit per sow* per year	TOTAL	€101

Table 2. Types of herd in a recent GTE and G3T CIRCOVAC efficacy study.

	Vaccinated	Non-vaccinated
Number of herds		
Farrow-to-finish	21	10
Farrowing	9	3
Finishing	6	7
Total number of sows	8719	3030
Average # of sows	291	379
Monitoring		
GTE	14	17
G3T	28	9

Table 3a. Second French GTE study, results in the vaccinated herds. Not all data were available for every herd.

CIRCOVAC® vaccinated herds	n	Before ± SD*	After ± SD*	Difference
Average weight at weaning, kg	13	7.08 ± 0.77[a]	7.18 ± 0.84[a]	+0.1
Average weight at slaughter, kg	13	116.91 ± 6.42[a]	119.37 ± 7.35[a]	+2.5
Weaning-to-slaughter mortality rate	13	7.09 ± 2.51[a]	5.98 ± 2.71[a]	-1.1
FCR 8-115, kg/kg	13	2.60 ± 0.17[a]	2.53 ± 0.12[a]	-0.07
ADG 8-115, g/d	13	685 ± 39.18[a]	723 ± 31.43[b]	+38
Age at 115 kg, days	6	180 ± 4.59[a]	174 ± 5.5[c]	-6
Days to market	13	165 ± 10.44[a]	160 ± 9.44[b]	-5

Table 3b. Second French GTE study, results in the non-vaccinated herds. Not all data were available for every herd.

Non-vaccinated herds	n	Before ± SD*	After ± SD*	Difference
Average weight at weaning, kg	14	7.66 ± 0.74[a]	7.61 ± 0.83[a]	-0.05
Average weight at slaughter, kg	14	117.04 ± 6.68[a]	116.43 ± 7.35[a]	-0.6
Weaning-to-slaughter mortality rate	15	5.98 ± 2.80[a]	5.78 ± 3.23[a]	-0.2
FCR 8-115, kg/kg	14	2.68± 0.16[a]	2.61 ± 0.23[a]	-0,07
ADG 8-115, g/d	15	686 ± 50.07[a]	679 ± 61.29[a]	-7
Age at 115 kg, days	10	188 ± 12.97[a]	192 ± 19.17[a]	+4
Days to market	14	161 ± 10.61[a]	162 ± 10.72[a]	+1

*Standard Deviation
[a, b]: significant difference on the same line ($p < 0.05$)
[a, c]: significant difference on the same line ($p < 0.10$)

After validation of the GTE and G3T data herd by herd, an analysis of the changes in production in both populations was performed and the main results are shown in **Tables 3a, b and 4a, b**. Not all data were available for each herd. No improvement, nor any significant difference, was found in the control population. In vaccinated herds, although initial mortality was already lower than the national average, indicating both a relatively good health status and a rather sub-clinical PCV2 impact, weaning-to-slaughter mortality rate decreased by 1.1% (NS) from around 7 to 6% (**Tables 3a, b**). Despite the rather low number of herds in which data were usable, this study clearly shows the dramatic improvement in growth with 38g/day increase of the weaning-to-slaughter ADG and a reduction in days to market for vaccinated pigs in the barns. Comparison of the G3T results showed significant positive effects of vaccination on reproduction (**Tables 4a and b**).

Table 4a. G3T results in vaccinated herds

		n	Mean	SD*	Difference	p value
Live born piglets per litter	Before	28	11.83	0.86	+0.44	Tendency p=0.109
	After		12.27	0.75		
Weaning-to-service[a] interval, days	Before	27	10.62	4.8	-1.35	Tendency p=0.146
	After		9.27	2.24		
Farrowing rate, %	Before	14	85.96	5.09	-1.9	NS p=0.396
	After		84.06	3.5		

Table 4b. G3T results in non-vaccinated herds

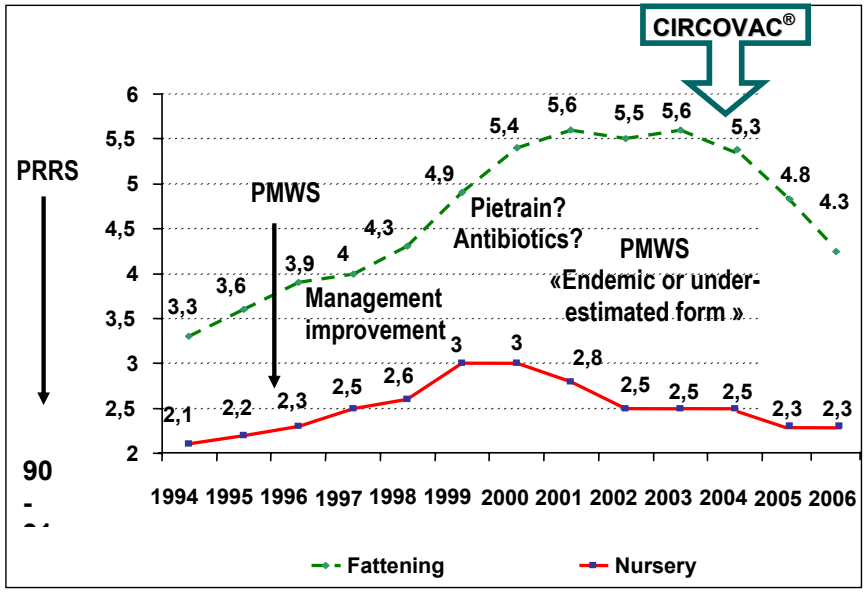
		n	Mean	SD*	Difference	Statistical difference
Live born piglets per litter	Before	8	12.34	0.69	+0.09	NS
	After		12.43	0.75		
Weaning-to-service[a] interval, days	Before	9	8.27	2.24	+0.89	NS
	After		9.16	4.43		
Farrowing rate, %	Before	7	82.63	10	+0.31	NS
	After		82.94	10.08		

*Standard deviation; NS: non statistically significant
[a]Weaning to successful breeding, includes return to service

Financial analysis of the benefits resulting from the improvement in production parameters showed significant differences or a strong tendency between "before" and "after" CIRCOVAC® vaccination was performed. The econimic values per point/unit of improvement used in this calculation were based upon data from the Institute of Pig (ITP/IFIP) standard figures, base 2005. The economic benefit resulting from sow vaccination with CIRCOVAC® was calculated to be on average €74.24 and €73.60 per inventoried sow per year for the GTE (production) and the G3T (reproduction) parts, respectively.

In addition to these study results, the GTE national/regional programs deliver on a yearly basis consolidated information regarding all the different criteria. **Figure 1** shows average mortality rates in post-weaning and fattening over the last twelve years, in relation to the major events concerning the last emerging diseases i.e. PRRS and PMWS. Around 3-3.5% additional mortality may be attributed to PCVD and despite many different attempts to control mortality, the rates had not evolved much. Weaning-to-slaughter mortality was almost steady around 8% for 2001 to 2004. Vaccination started at the end of 2004 and today, 28 to 30% of the sows are routinely vaccinated with CIRCOVAC®. Since the fall 2004, although other factors may have helped to improve the situation, sow PCV2 vaccination appears to have had a prominent effect.

Figure 1. Average postweaning and fattening mortality in Brittany. Source: IFIP/ITP, Paris and EDE, Chambre d'Agriculture de Bretagne, May 2007



Field results in Germany

In order to comply with the requirements of the exceptional licenses granted by the German authorities in August 2004, efficacy data had to be collected in all herds using the vaccine and forwarded to the drug agency. A PMWS diagnosis by different methods had to be performed before vaccination. Depending on the individual situation, these commercial herds used were affected with current pathogens, i.e. PRRSV, *M. hyopneumoniae*, APP, *S. suis*, *H. parasuis,* etc. Depending on the herd, vaccination with CIRCOVAC® started from the last quarter of 2004. A standard questionnaire was designed and filled by the veterinarians and the stockpersons for each of the herds where CIRCOVAC® was used. Results were communicated to the German authorities and synthetic analysis was also presented. By the end of 2006, completed questionnaires had been received from veterinarians for 233 herds located in all parts of Germany. Mortality rates, average daily weight gains (ADG) and frequencies of medication and antibiotic use before or during vaccination, i.e. 1 year before and 6 months to 1 year after, were compared in the suckling, post-weaning and finishing age groups, using the appropriate statistical techniques (Joisel et al., 2007a, b).

Table 5. Mortality rates before and during vaccination in the German study (233 herds)

		n	Mean (%)	SD*	Decrease: "Delta %"
Suckling piglets	Before vacc.	198	13.9	5.6	2.9±4.9
	During vac.	198	11.0	3.8	(P<0.05)
Post-weaned pigs	Before vacc.	198	8.0	6.9	4.8±5.8
	During vacc.	198	3.1	2.3	(P<0.05)
Fattening pigs	Before vacc.	109	5.7	4.1	2.6±3.9
	During vacc.	109	3.0	1.7	(P<0.05)

*Standard Deviation

T**able 6. Average daily weight gain per age group before and during vaccination in herds in the German study** (233 herds)

		Number of herds n=233	Mean	STD*	Difference in ADG, g/day
Suckling piglets	Before	91	172.0	121.4	+7.6
	During	91	179.6	126.0	(P<0.05)
Post-weaned pigs	Before	116	345.3	143.1	+25.9
	During	116	371.2	151.3	(P<0.05)
Fattening pigs	Before	77	715.9	92.0	+33.2
	During	77	749.0	91.8	(P<0.05)

*Standard Deviation
ADG – average daily gain

Comparison of before vs. during vaccination for mortality rates, average daily weight gains and treatments are shown in **Table 5, 6 and 7**, respectively. Mortality (**Table 5**) significantly decreased in the three age groups: 2.9%, 4.8% and 2.6% of mortality in the suckling, post weaning and finishing phases, respectively. The most striking and consistent finding was that mortality rates occurring after a period of vaccination were close to what would be the recommended optimal targets for achievement in the standard hand books in pig production (Muirhead & Alexander, 2002), indicating that what was achieved after the period of vaccination represented the recovery of a "close-to-optimal" health situation. These findings show that pigs born from vaccinated sows were protected against the deleterious impact of PCV2 during their whole life span.

Table 6 summarizes the results of the average daily weight gain (ADG) before and after vaccination in the herds where the data were available for both periods (N=91, 116 and 77 in suckling piglets, in post-weaning and finishing barns, respectively). A significant (P<0.05) ADG improvement of 7.6, 25.9 and 33.2 g/day were reported in suckling, post-weaning and fattening groups after vaccination, respectively.

Although all medications appeared to be used less after vaccination in all age groups -3.2%, -8.4% and -5.6% in suckling piglets, post-weaning and fattening, respectively (**Table 7**), a significant difference was only observed in the post-weaning areas (decrease=8.4%, P=0.006). However, a stronger

effect was observed on the use of antibiotics after vaccination, with a significant difference in the post-weaning (7.9%; p=0.035) and strong trend in fattening pigs (10.4%; at the limit of the significance p=0.096).

Table 7. Percentage reduction in medication recorded in the different groups of pigs from herds that gave information before and after vaccination in the German study (233 herds)

	Suckling Piglets		Post-weaned Pigs		Fattening Pigs	
	#	%	#	%	#	%
Participating Herds:	186	79.8	202	86.7	125	53.7
Use of Medication:						
Before	161	86.6	189	93.6	65	52.0
During	155	83.3	172	85.1	58	46.4
Decrease, %		3.2		8.8		5.6
P value	0.384		0.006		0.376	
Use of Antibiotics:						
Before	124	66.7	175	86.6	59	47.2
During	126	67.7	159	78.7	46	36.8
Decrease		-1.1		7.9		10.4
P value	0.825		0.035		0.096	

Under conditions of this very large study, with results from 233 herds, about 66,700 sows and some 2,000,000 pigs, vaccination of the sow herds with CIRCOVAC® resulted in a marked improvement of the health and economic status of the herds. There was a decrease in both mortality and the use of medications, especially antibiotics, and a significant increase of ADG at all stages of the pig's production cycle. Decrease in mortality rates and improvements in performances and health status in post-weaning and finishing were expected because these age groups are those well known as being hit by PCVD. Such a clear improvement in the early stage of life is very striking, indicating that PCV2 has a subclinical effect as early as in the very

first weeks of the life and that sow vaccination is able to dramatically change this situation.

Field results in other European countries

Other countries using CIRCOVAC® have been reporting similar results. In Denmark, mortality was already at low levels when CIRCOVAC® was introduced in the field. Besides better growth and homogeneity of pigs, the first effect noticed by the veterinarians and stockpersons was a quick and clear improvement in the reproduction parametrers. Today, between 15 and 20% of the Danish sows are vaccinated with CIRCOVAC®.

In the UK, the vaccine was introduced in the beginning of 2007 with special herd-specific import permits. The first herd receiving the permit to import and use the vaccine was a 2800-sow herd in 4 separate units. In an attempt to test how PCV2 sow vaccination was working, sows were vaccinated in a first unit of 520 sows. In this unit, the first PMWS sign occurred in March 2006 in the finishing barns. Quickly, mortality spread in the post weaning parts and mortality peaked as high as 20%, with a 17% average. The clinical signs were usually seen around 8 to13 weeks of age, which included both PMWS and PDNS. Vaccination of the sows with CIRCOVAC® was started batch after batch from early January 2007. The stockperson and the veterinarian reported from the first vaccinated sows, the following effects:

- healthier and more lively baby pigs from birth
- the first 3 batches slaughtered had weaning-to-slaughter mortality down to 3%
- Weaning weight: increased to 8.4 kg versus 8.2 kg prior to vaccination
- 1 or 2 runts per batch (The stockperson believes that number of runts was reduced following vaccination.)
- No PDNS any more
- Late abortions stopped
- Piglets born alive per litter 14.7 versus 11.8 prior to vaccination (a record…)

The most encouraging comment was that now, the 2800 sows are vaccinated.

■ Conclusion

PMWS/PCVD are still major causes of impaired economic performance in all parts of the world. Vaccination of the sows with CIRCOVAC® has now extensively, and in various geographic areas, been shown to prevent PMWS mortality and to decrease total mortality in piglets as well as to improve growth

and performance of the piglets. The vaccinated herds previously suffering from PCVD were able to recover and to return to a “close-to-normal” performance (even sometimes better than before the PCVD outbreak), due to an almost total reduction of the increase in mortality above the basic non-PCV2-related mortality. In addition, the recent studies presented here confirm the largely reported beneficial effects of CIRCOVAC® in the field on reproduction as well as on the very early period of the piglet’s life. The data regarding reproduction are in contradiction with other recently presented observations in the United States, using the PigCHAMP system (Nerem, 2007), that did not show PCV2 vaccination in 18,000 sows to improve reproduction results, although the tool used is quite similar to the GTE data analysis system. This may have several explanations including a different health status of the herds/sows, a difference in the time frame of the study or a difference in the vaccine used.

Vaccination of the sows and gilts with CIRCOVAC® induced major improvements in reproduction parameters, in the piglet performance during the suckling phase as well as impressive improvements in pig heath status and growth for their life span.

References

Allan GM and Ellis JA (2000), Porcine circovirus: a review, J Vet Diagn Invest 12 : 3-14

Charreyre C., Bésème S., Brun A., Bublot M., Lapostolle B., Sierra P., Vaganay A.: (2006a) Virological protection of piglets against a PCV2 experimental challenge by vaccinating gilts with an inactivated adjuvanted PCV2 vaccine. Proceedings of the 19th IPVS Congress, Copenhagen, Abstract O.30-03, 1:177

Charreyre C., Bésème S., Brun A., Bublot M., Lapostolle B., Sierra P., Vaganay A.: (2006b) PMWS protection of pigs born to sows vaccinated with an inactivated adjuvanted PCV2 vaccine under field condition. Proceedings of the 19th IPVS Congress, Copenhagen, abstract P.07-08, 2:107

de Jong MF, Elbers A and Wellenberg GJ (2003) Factors associated with PMWS and PDNS: a case control study. 4th International Symposium on Emerging and Re-emerging Pig Diseases: Rome Italy pp: 215

Hérin JB, Fily B, Longo S and Joisel F (2007) Field results of the use of CIRCOVAC® a sow PCV2 vaccine in France under provisional registration. 5th International Symposium on Emerging and Re-emerging Pig Diseases: Krakow, Poland, June 24-27th, pp. 125

Joisel F, Brune A, Schade A , Longo S and Charreyre C (2007a) Results of the vaccination against PCV2 diseases with CIRCOVAC® in 233 German sow herds: decrease in mortality. 5th International

Symposium on Emerging and Re-emerging Pig Diseases: Krakow, Poland, June 24-27th, pp. 126

Joisel F, Brune A, Schade A, Longo S and Charreyre C (2007b) Results of the vaccination against PCV2 diseases with CIRCOVAC® in 233 German sow herds: improvement of pig growth and decrease in antibiotic treatments. 5th International Symposium on Emerging and Re-emerging Pig Diseases: Krakow, Poland, June 24-27th, pp. 127

McCullough KC, Vincent IE and Summerfield A (2007) The immunology of PCV2 infections. Proceedings of the 38th AASV meeting, March 3-6th, Orlando, Florida, USA, p 497-506

Muirhead MR and Alexander TJL, (2002) Managing Pig Health and the Treatment of Disease. A Reference for the Herd. 5M Enterprises Ltd, Sheffield, UK

Nerem J (2007) PCV2 Experience with sow and pig vaccination, AD Leman Conference, 34: 115-116

Reynaud G, Boeuf-Tedeschi L, Bublot M and Charreyre C (2001) Maternally derived protection against PCV2 experimental challenge in 3 week old piglets. Proceedings of the ssDNA Viruses of Plants, Birds, Pigs and Primates, St Malo, France September 24-27th, p137

Rose N, Larour G, Le Diguerber G, Eveno G, Jolly JP, Blanchard P, Oger A, Le Dimma M, Jestin A and Madec F (2003) Risk factors for porcine post-weaning multisystemic wasting syndrome (PMWS) in 149 French farrow-to-finish herds. *Prev Vet Med* 61(3): 209-225

Vincent IE, Carrasco CP, Guzylack-Piriou L, Herrmann B, McNeilly F, Allan GM, Summerfield A and McCullough KC (2005) Subset-dependent modulation of dendritic cell activity by circovirus type 2, *Immunology*, 115:388-398

Vincent IE, Carrasco CP, Herrmann B, Meehan BM, Allan GM, Summerfield A, McCullough KC. (2003) Dendritic cells harbor infectious porcine circovirus type 2 in the absence of apparent cell modulation or replication of the virus. *J Virol* 77(24):13288-300