Field experience with PCV2 vaccination

by F. Joisel, C. Charreyre, Merial SAS, Lyon, France, H. Too, Merial Asia Pte Ltd, Selangor, Malaysia, and S. Longo, BPC, Labruguière, France.

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 necrotising pneumonia, porcine respiratory disease complex (PRDC), abortion and reproductive problems.

Porcine dermatitis and nephropathy syndrome (PDNS) and a new ear necrosis syndrome have also been associated with PCV2, but today there is not yet definite evidence that PCV2 is the major cause of these syndromes.

Since the end of 2004, Merial's Circovac, a PCV2 vaccine dedicated to sows and gilts to control PCVD in the whole herd, has been largely used in several parts of the world.

This article reviews the large scale studies of PCV2 vaccination in Europe.

PCV2 vaccination

PCV2 is a very small, stable and resistant virus. It is ubiquitous in the pig rearing environment. In PMWS affected farms, piglets are exposed to PCV2 very early in their life. An early uncontrolled PCV2 load can be found within the dendritic clls (DC), a particular type of immunological cells 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.

Further on, 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. Such 'immuno-compromised' status would result in the pig being susceptible against infectious diseases including PMWS/PCVD and other bacterial and viral infections for the rest of its life.

Maternally derived immunity has been demonstrated to be protective. Numerous case control studies have repeatedly identified poor colostrum intake as a risk factor for the clinical expression of PMWS.

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 immunocompetent cells. In species having an epithelio-chorial placenta, like swine, it has been largely demonstrated that colostrum from vaccinated mothers contains antigen specific maternal immunoglobulins which have an important role in the passive protection of newborn animals.

However, it has been found that colostrum also contains T and B lymphocytes. Recent functional experiments in SPF sows clearly showed that colostrum from sows vaccinated with Circovac contained INFγ 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 defence against infections in neonxates 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 faecal excretion both by sows and by the young piglets. 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 successfully been used.

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.

Although both maternal immunity and compromised early immunity due to uncontrolled PCV2 exposure will hinder somewhat the efficacy of the piglet vaccination, satisfactory results can be obtained as the vaccine will draw on remaining immune cells.

A global picture is given in Fig. 1, based on the available knowledge, it is an attempt at the best known description of pathogenesis when pigs face PCV2 exposure.

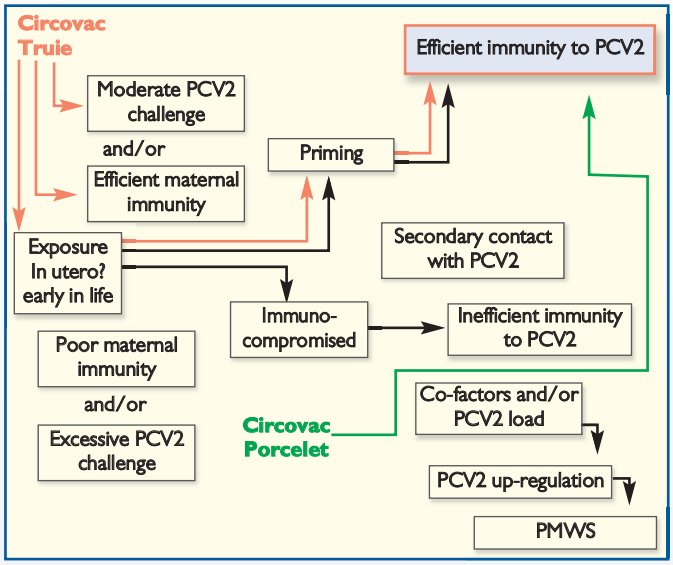

Fig. 1. Pathogenesis and vaccination effects.

Field results in France

Two large studies were conducted in France using the records of the national data programme 'Gestion Technico-Economique' (GTE) focusing on production data and 'Gestion Technique des Troupeaux de

Continued on page 19

Table 1. Economic estimate of the benefit of the vaccination of sows with Circovac per present sow per year in the 'GTE' study.

	Improvement (%)	Average added value (€) (source: IFIP/ITP, France)
Decrease in mortality rate in the nursery	1.0	14
Decrease in mortality rate in the finishing barn	1.0	19
Increased feed efficiency	0.1 unit	36
Results	**Statistically significant improvement**	**Added value or benefit for the considered index**
Additional benefit for nursery	1.4%	1.4 x 14 = 19.6
Additional benefit for finishing	2.2%	2.2 x 19 = 41.8
Increased feed efficiency 8-105kg	0.11 unit	0.11 x 36 = 39.6
Average benefit/sow/year	Total	101

	No.			Total number of sows	Average number of sows	Monitoring	
	F-to-F	Farrowing farms	Finishing units			GTE	G3T
Vaccinated	21	9	6	8719	3030	14	28
Non-vaccinated	10	3	7	291	379	17	9

Table 2. Types of farm in a recent GTE and G3T Circovac efficacy study.

Continued from page 17

Truies' (GTTT or G3T) focusing on reproduction parameters.

The first study included 24 of the very first herds that have been using sow PCV2 vaccination. Included in this study were the farms for which GTE results were available for at least a one year period from pigs born to non-vaccinated sows and at least for a six month period in which results were entirely attributable to pigs born from vaccinated sows.

The farms were diversely affected with other pathogens as PRRSV, M. hyo, APP and SIV, but all had a clinical and post mortem diagnosis of PCVD recently confirmed by laboratory examination in 40% of the cases.

The study regrouped 7,750 sows (mean = 310 per farm). Vaccination with Circovac took place from December 2004-February 2005. Significant improvements were found in:

- Post-weaning mortality rate: from 3.6-2.2% (-1.4 points).
- Fattening mortality rate: from 7.2-5.1% (-2.2 points).
- Weaning to slaughter mortality rate: from 10.6-7.1% (-3.5 points).
- Standardised feed efficiency: 2.75-2.64 (-0.11kg feed per kg of pig meat).

A financial analysis of the benefits brought by the improvement of parameters that showed significant differences between 'before' and 'after' PCV2 vaccination was done. 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 bring an average benefit of €101 per present sow per year.

Second study

The second study gathered the GTE and G3T results of 36 vaccinated farms and compared those obtained in a similar 20 farm non-vaccinated control population.

Vaccination started from January 2004-February 2006.

The type of farms are summarised in Table 2.

After validation of the GTE and G3T data farm by farm, an analysis of the evolution in both population was performed and the main results are shown in Tables 3, 4, 5 and 6.

Not all data were available for each farm. No improvement or any significant difference was found in the control population.

In vaccinated farms, 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 was down by 1.1% (NS) from around 7-6% (Tables 3, 4).

Despite the rather low number of farms in which data were usable, this study clearly shows the dramatic improvement in growth with 38g per day increase of the weaning to slaughter ADWG and a reduction of the presence of the pigs in the barns.

Comparison of the G3T results showed significant positive effects on reproduction. Results for vaccinated and non-vaccinated farms are presented in Tables 5 and 6, respectively.

The financial analysis of the benefits brought by the improvement of parameters that showed significant differences or a strong tendency between 'before' and 'after' Circovac vaccination was performed.

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.

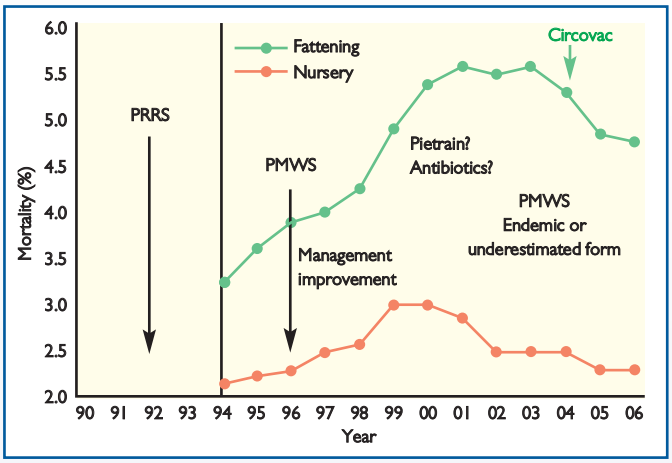

Fig. 2. Records of mortality in average in Brittany in post-weaning and fattening (IFIP/ITP, Paris and EDE, Chambre d'Agriculture de Bretagne, May 2007).

Circovac vaccinated farms	No.	Before ± sd*	After ± sd*	Difference
Mortality rate (%)	13	7.1[a] ± 2.51	6.0[a] ± 2.71	-1.1
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
ADWG 8-115 (g/d)	13	685 ± 39.18[a]	723 ± 31.43[b]	+38
Age at 115kg (days)	6	180 ± 4,59[a]	174 ± 5.5[c]	-6
Duration of présence (days)	13	165 ± 10.44[a]	160 ± 9.44[b]	-5

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

Table 3. Second French GTE study, results in the vaccinated farms. Not all data were available for each farm.

Table 4. Second French GTE study, results in the non-vaccinated farms. Not all data were available for each farm.

Non-vaccinated farms	No.	Before ± sd*	After ± sd*	Difference
Mortality rate (%)	15	6.0[a] ± 2.80	5.8[a] ± 3.23	-0.02
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 ± 7.11[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]	-0.08
ADWG 8-115 (g/d)	15	686 ± 50.07[a]	679 ± 61.29[a]	-7.0
Age at 115kg (days)	10	188 ± 12.97[a]	192 ± 19.17[a]	+4
Duration of presence (days)	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)*

Benefit of Circovac

The benefit brought by sow vaccination with Circovac was calculated to be on average €74.24 and 73.60 per present sow per year for the GTE (production) and the G3T (reproduction) parts, respectively.

In addition to these study results, the GTE national/regional programmes deliver on a yearly base consolidated information regarding all the different criteria.

Fig. 1 shows average mortality rates in post-weaning and fattening during the last 12 years, in relation to the major events concerning the last emerging diseases, such as PRRS and PMWS.

Around 3-3.5% additional mortality may be attributed to PCVD and despite many different attempts to control mortality, the rates did not evolve much.

Weaning to slaughter mortality was almost steady around 8% for 2001-2004. Vaccination started at the end of 2004 and today, 28-30% of the sows are routinely vaccinated with Circovac.

Since the autumn of 2004 and even if other factors may have

Continued on page 20

	No.	Mean	Sd*	Difference	p value
Live born piglets per litter					
Before	28	11.83	0.86	+0.44	p=0.046
After		12.27	0.75		
Weaning to fecundation interval (days)					
Before	27	10.62	4.8	-1.35	Tendency p=0.191
After		9.27	2.24		
Farrowing rate (%)					
Before	14	85.96	5.09	-1.9	NS p=0.260
After		84.06	3.5		

**Standard deviation; NS: non statistically significant*

Table 5. G3T results in vaccinated farms.

Continued from page 19
helped to improve the situation, sow PCV2 vaccination is likely to have had a prominent effect.

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 individual situation, these commercial farms used to be affected with current pathogens, such as, PRRS, M. hyopneumoniae, APP, S. suis and H. parasuis.

Depending on the herd, vaccination with Circovac thus started from the last quarter of 2004.

A standard questionnaire was designed and filled in by the veterinarians and the farmers for each of the farms where Circovac was used.

Results were communicated to the German authorities and the synthetic analysis was also presented. In the more advanced stage of this large survey, for example, end of 2006, completed questionnaires had been received from veterinarians responding for 233 farms located in all parts of Germany.

Mortality rates, average daily weight gains (ADWG) and frequencies of medication and antibiotic use before or during vaccination, for example, one year before and – months to one year after, were compared in the suckling, post-weaning and finishing age groups, using the appropriate statistical techniques. Comparison before versus during vaccination for mortality rates, average daily weight gains and treatments are shown in Tables 5, 6 and 7 respectively.

Mortality (Table 5) significantly decreased in the three groups of age: 2.9, 4.8 and 2.6 points of mortality in the suckling, post weaning and finishing phases, respectively.

The most striking and consistent finding was that mortality rates reached 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, 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 are protected against the deleterious impact of PCV2 during their whole life span.

Table 6 summarises the results of the average daily weight gain (ADWG) before and after vaccination in the farms 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 ($p<0.05$) ADWG improvement of 7.6, 25.9 and 33.2g/day were reported in suckling, post-weaning and fattening groups after vaccination respectively.

Although all medications appeared to be less used after vaccination in all groups of ages -3.2, -8.4 and -5.6% in suckling piglets, post-wean-

Table 6. G3T results in non-vaccinated farms.

	No.	Mean	Sd	Difference	Statistical difference
Live born piglets per litter					
Before	8	12.34	0.69	+0.09	NS
After		12.43	0.75		p=0.806
Weaning to fecundation interval (days)					
Before	9	8.27	2.24	+0.89	NS
After		9.16	4.43		p= 0.598
Farrowing rate (%)					
Before	7	82.63	10.00	+0.31	NS
After		82.94	10.08		p=0.955

**Standard deviation; NS: non statistically significant*

	No.	Mean (%)	Sd*	Decrease: 'Delta %'
Suckling piglets				
Before vaccination	198	13.9	5.6	2.9±4.9
During vaccination	198	11.0	3.8	(p<0.05)
Weaning to fecundation interval (days)				
Before vaccination	198	8.0	6.9	4.8±5.8
During vaccination	198	3.1	2.3	(p<0.05)
Farrowing rate (%)				
Before vaccination	109	5.7	4.1	2.6±3.9
During vaccination	109	3.0	1.7	(p<0.05)

**Standard deviation;*

Table 7. Mortality rates before and during vaccination in the German study (233 farms).

	No. of farms	Mean	STD*	Difference in ADWG
Suckling piglets				
Before	91/233	172.0	121.4	+7.6g/day[a]
During	91/233	179.6	126.0	
Weaning to fecundation interval (days)				
Before	116/233	345.3	143.1	+25.9g/day[a]
During	116/233	371.2	151.3	
Farrowing rate (%)				
Before	77/233	715.9	92.0	+33.2g/day[a]
During	77/233	749.0	91.8	

**STD: Standard deviation, ADWG = average daily weight gain. [a] = (P=0.000)*

Table 8. Average daily weight gain per group before and during vaccination in farms in the German study (233 farms).

ing and fattening respectively (Table 9), 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).

Under conditions of this very large study gathering results from 233 farms, around 66,700 sows and some 2,000,000 pigs, vaccination of the sow herds with Circovac resulted in a marked improvement of the sanitary and economical status of the farms with a decrease in both mortality and the use of medications especially antibiotics and a significant increase of ADWG at all stages of the pig's production cycle.

Decrease of mortality rates and improvements in performances and health status in post-weaning and finishing were expected since these age groups are those well known as being hit by PCVD.

Such a clear improvement in the early stage of life is much more 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.

Results in other EU countries

Other countries having used Circovac have been reporting similar results.

In Denmark, mortality was already down to a low level when Circovac was introduced in the field. Beside better growth and homogeneity of pigs, the first effect noticed by the veterinarians and farmers was a quick and clear improvement in the reproduction parametrers.

Today, between 15-20% of the Danish sows are vaccinated with Circovac. In the UK, the vaccine was introduced at the beginning of 2007 with individual special import permits.

The first farm having got the permit to import and use the vaccine was a 2,800 sow farm in four separate units. In an attempt to test how PCV2 sow vaccination was working, sows were vaccinated in a 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 8-13 weeks of age, including PMWS and PDNS. Vaccination of the sows with Circovac was started batch after batch from early January 2007.

The farmer and the veterinarian reported from the first vaccinated sows, the following effects:

- Healthier and more lively baby pigs from birth.
- Three first batches slaughtered with weaning to slaughter mortality down to 3%.
- Weaning weight: increased at 8.4 vs 8.2kg prior to vaccination.
- Only one or two runts per pig batch.
- No PDNS any more.
- Late abortions stopped.
- Piglets born alive per litter 14.7 vs 11.8 prior vaccination (a record).

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

Field results in Canada

Canada, as well as the United states, has recently suffered from acute PMWS outbreaks.

Due to the emergency of the situation, Circovac was introduced in Canada in April 2006 using a special import permit.

At the end of 2006, the first preliminary efficacy results were collected using a phone survey and an evaluation of the mortality after about six months use of Circovac were obtained for 77 farms representing 51,050 vaccinated sows and approximately 500,000 pigs.

Range of mortality rates

Weaning to slaughter mortality rates were often expressed as a range with a maximum (max) and a minimum (min) values for mortality before and during vaccination.

This led to calculate min and max means and confidence intervals for the periods before and during vaccination. Although these very preliminary results were obtained during a period in which pigs born from vaccinated and non-vaccinated sows were still both present in the farms a significant decrease of mortality and a recovery to 'close to normal' rates for commercial farms was seen.

The regression between mortality before vaccination and the Delta% decrease of mortality was applied.

The R^2 found was 0.76 and the regression line equation was: $Y = 1.05 X + 5.12$.

The basic weaning to slaughter mortality was, on average, 5.12% and the approximated predictive mortality reduction found was then 95% above the basic mortality.

These results are in accordance with what was found in the studies run both in France and Germany.

Conclusion

PMWS/PCVD are still major causes of impaired economical performances 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' situation (even sometimes better than before the PCVD outbreak), due to an almost total reduction of 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 life.

The data regarding reproduction are in contradiction with other recently presented observations in the United States, using the PigChamp system, 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 sanitary status of the farms/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 is inducing 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 are available from the authors on request.

Table 9. Distribution of percentage of medication recorded in the different groups of pigs from farms that gave information before and after vaccination in the German study (233 farms).

		Participating farms		Use of medication			Use of antibiotics		
		No.	%	No.	%	Decrease	No.	%	Decrease
Suckling piglets	Before	186/233	79.8	161/186	86.6	3.2%	124/186	66.7	-1.1%
	During			155/186	83.3	p=0.384	126/186	67.7	p=0.825
Post-weaned pigs	Before	202/233	86.7	189/202	93.6	8.4%	175/202	86.6	7.9%
	During			172/202	85.1	p=0.006	159/202	78.7	p=0.035
Fattening pigs	Before	125/233	53.7	65/125	52.0	5.6%	59/125	47.2	10.4%
	During			58/125	46.4	p=0.376	46/125	36.8	p=0.096