Porcine circovirus vaccines – where are we?

Porcine Circovirus 2 (PCV2) was first isolated in 1997. Now, over a decade later, four vaccines against the viral disease have been developed. Overall, all of these offer an excellent opportunity to control PCV2 associated diseases and the distressing effects they have had on pig production – all in their own ways.

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It has taken a long time, some would say too long, for the new Porcine Circovirus type 2 (PCV2) vaccines to arrive in Europe, but at last they are now being registered there as well. Four vaccines have been available in North America for the last couple of years, so most of the field information has come from there, although series of trials have been carried out in the EU for regulatory purposes and positive field-experience information is starting to come through.

Vaccine concepts

There are two major approaches to controlling PCV2 infections in pigs, the first one being by vaccinating the sows and allowing maternally derived antibodies to protect the piglets and allow them to build up their own immunity naturally from natural virus exposure. The alternative is to vaccinate the piglets directly and early, before the virus has had a chance to multiply significantly, and thereby stimulate a more complete immune response. Whether one needs to use a one-shot or two-shot vaccine approach is also a point for discussion but possibly depends on the efficacy of the vaccine and the weight of the challenge.

Four vaccines

An overview of the four vaccines is presented in *Table 1*. Merial's vaccine **Circovac®**, for use in sows, was the first to be approved in Europe (September 2007) although it had been used under special license for a couple of years in France, Germany and Denmark. The vaccine is based on PCV2, but it is a relatively slow growing virus, so other routes of production have been developed for the piglet vaccines, to speed up the process. The important part of the virus for stimulating immunity

Table 1. Current PCV2 vaccines and some characteristics.

Company	Product	Sow/piglet	Type of vaccine	Adjuvant	Number of injections
Merial	Circovac®	Sow	Killed – PCV2 virus	Mineral oil	2 + boosters each gestation
Boehringer Ingelheim	Ingelvac CircoFlex®	Piglet (2 weeks +)	PCV2 capsid	Aqueous polymer	1
Fort Dodge	Suvaxyn® PCV2 One Dose	Piglet (4 weeks +)	Killed – chimeric PCV1 & 2	SL-CD aqueous	1 1
Intervet/SP	Circumvent® PCV	Piglet (3 weeks +)	PCV2 capsid Tocophorol	Diluvac	2

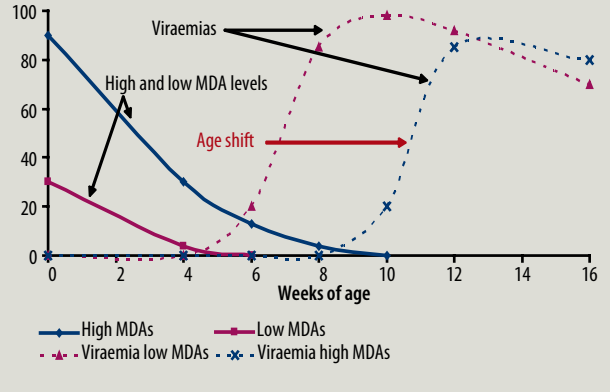
Table 2. Current PCV2 vaccine registrations around the world (up to July 20, 2008).

Region/ country	Circovac (Merial)	CircoFlex (Boehringer Ingelheim)	Suvaxyn PCV2 (Fort Dodge)	Circumvent (Intervet/ Schering-Plough**)
North America	Canada -	Canada USA	Canada* USA	Canada USA
Latin America	Brazil Colombia Costa Rica Panama	Mexico Colombia - -	Mexico Brazil - -	Mexico - - -
Europe	EU Switzerland - - -	EU Switzerland - - -	Czech Republic* Denmark* Slovakia* Ukraine United Kingdom*	- - - - -
Asia	Thailand Japan -	South Korea Japan Philippines	Thailand Singapore* Philippines	- - -
Oceania	-	New Zealand	New Zealand	-

* For these states, a special import permit applies for this product.

** In 2009, the company will launch Porcilis PCV2 in the EU and Japan. This one- or two-shot piglet vaccine will be a different product from their North American vaccine Circumvent PCV.

Figure 1. The effects of low and high MDAs on age when PCV2 viraemia occurs.



appears to be the outer capsid protein, which is produced from the DNA genetic material contained in the open-reading frame 2 (ORF2). This is quite complex, but it is this genetic component, which has been inserted into other faster growing viruses to produce the capsid proteins more quickly and in a larger quantity. Boehringer Ingelheim's **Ingelvac CircoFlex®** and Intervet/ Schering-Plough's **Circumvent PCV®** use a plant baculovirus with the ORF2 component inserted into it and Fort Dodge's **Suvaxyn® PCV2 One Dose** uses PCV1, which is not pathogenic in pigs, with ORF2 inserted to produce a chimeric virus. Originally, it was thought it might be used as a live vaccine but it was neutralised by maternally derived antibodies (MDAs) and was subsequently developed as an inactivated or killed vaccine. The vaccines are being registered around the world and the process will take time, depending on the local regulatory authority.

Development of PCV2 infections

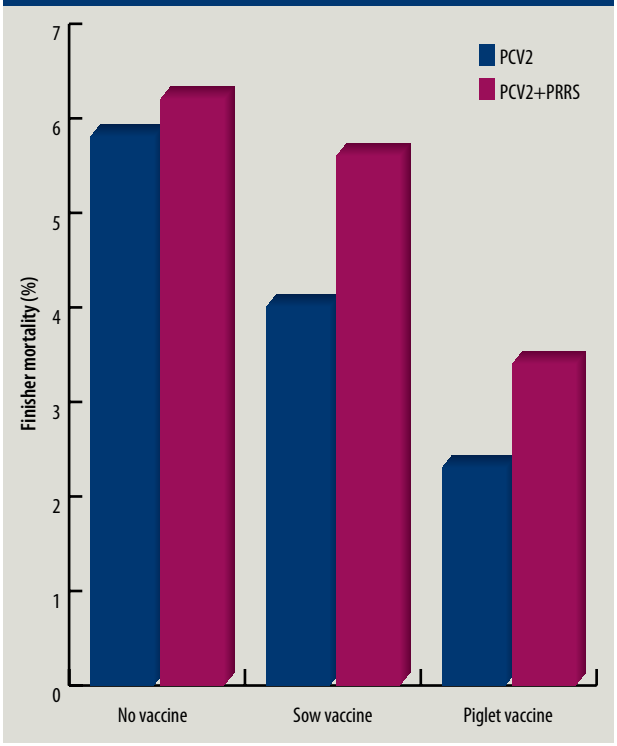
In the acute phase of the disease, when it first occurred, there was initially a very high mortality in piglets (30-40%) and wasting disease (Post-Weaning Multisystemic Syndrome) and then it gradually came down to a lower level (0-10% mortality) in the more chronic phase. The disease occurred later, as the sow herds built up their own immunity (see *Figure 1*). Depending on the individual farm and its production system (farrow to finish; 3-site, 2-site production) other management factors, housing (slatted or non-slatted floors), other infections (PRRS, enzootic pneumonia) and possibly vaccination programmes and stressors (moving, mixing, overcrowding), the resulting disease appeared to stabilise at a certain level. In the UK it was noted that the mortality in the weaner/grower pigs started to fall, from natural immunity, but the finisher pig mortality remained higher, at about 3% above normal.

This fits in with the development of maternal immunity and the basic control of the acute infection in the early weaner/grower stages in the majority of pigs, but subsequently the infection and resulting viraemia was delayed and occurred in the older pig (age shift), where the mortality was lower (possible age effect). Nevertheless, there was often a drop in growth performance in the finisher by as much as 7 kg/pig produced, as they fought against the viraemia and possibly up to 20% of the pigs were affected clinically.

Enhancing immunity in the sow population therefore reduces the effect of the virus in the breeding herd and would increase protection in the younger pig through MDAs and enables the majority of the pigs to develop some active immunity in the face of an early virus challenge. This controls the viraemia to a level that does not kill the pigs or cause severe wasting in most cases. The question mark remains over the protection being sufficient in pigs that take in low levels of MDAs and older pigs, which receive a later challenge and viraemia, especially in the finishing stages over ten weeks of age (see *Figure 2*). In the EU, the authorities gave approval for Circovac to give a duration of immunity up to five weeks after the transfer of passive antibodies to the piglets through colostrum uptake. In practice, the duration would appear to be longer but has not been defined. Older pigs seem to be less susceptible to PCV2 infection and farm results have indicated a satisfactory performance.

Piglet vaccines, by contrast, are given to stimulate immunity directly in the piglet. BI's CircoFlex, has EU approval for use in piglets from two weeks of age. It normally takes about two weeks for an immune response to develop so they are protected from four weeks of age. The duration of immunity for this piglet vaccine appears to last right through the finishing period.

Figure 2. Finisher mortality (%) in pigs from non-vaccinated sows, vaccinated sows and vaccinated piglets with PCV2 and PCV2 + PRRS herds, involving over 33,000 pigs in Canada (Cardinal and Jones, 2008).



Further vaccine developments

The capsid protein appears to be very antigenic and stimulate good immunity. The DNA, which codes for it (ORF2) can be transferred to other viruses to speed up production and alternatives are already being looked at. The development of so-called 'sub-unit' vaccines or multivalent vaccines containing antigens against more than one disease – e.g. PCV2, enzootic (mycoplasmal) pneumonia, *Actinobacillus pleuropneumoniae*, also would be possible. In some countries, where many other diseases are endemic (e.g. CSF, pseudorabies), it would be convenient, as many different vaccines are required and it is hard to fit them all in.

Future development will be primarily aimed at using the present vaccines in the most suitable and convenient vaccine programmes. Combined use of vaccines is being talked about e.g. giving two vaccines together but combination vaccines appear to be some way off, although they are available in several other species such as dogs, cattle and poultry. **PP**