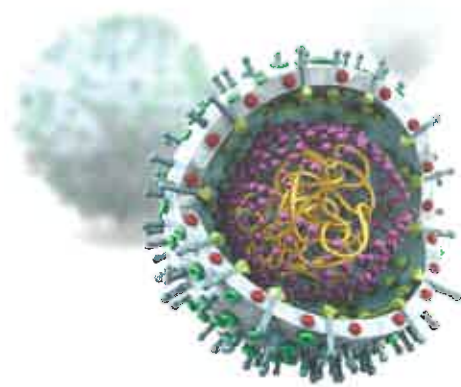


# The milestones in 30 years of PRRS control strategies



**A** landmark anniversary in pig health occurs this year as it is 30 years since the first pigs in the United States suffered a previously unknown disease that we now call the porcine reproductive and respiratory syndrome or PRRS.

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After the arrival of PRRS as a clinical entity in US pigs in 1987, a similar syndrome emerged in Europe by 1990 and Asian countries started to see outbreaks about a year later. By 1995 the disease was generally considered to be endemic throughout pig-producing territories on three continents.

The past three decades have brought a series of milestones or key moments in the development of our knowledge about what causes the disease and how to control it. The battle against PRRS continues and it remains probably the most economically damaging pig disease at world level.

This anniversary prompts us to reflect on those milestones and what we have learned regarding PRRS control strategies both in individual herds and in zones or regions.

## Profiling the virus

The first milestone had already arrived in 1991, when separate studies by Dutch and US researchers identified the cause as a virus. Comparisons revealed that the European and North American isolates were genetically distinct. Later, it became common to refer to the European genotype as Type 1 and the North American genotype as Type 2.

While causing similar clinical symptoms, the genomes of these two genotypes diverged by 40%. Investigators learned too, that a greater genetic diversity existed within the Type 1 classification than in Type 2. As a single-stranded RNA virus of the Arterivirus family, PRRSV can change its form constantly through mutation and recombination. What started 30 years ago as a relatively simple classification of two

basic types now recognises a genetic diversity of forms that grows bigger every day. Moreover, both genotypes are found internationally and not just in the continents where they were first identified. Type 2 also circulates predominantly in Asia and has been detected in European countries. A single sub-type of Type 1 has occurred in five countries outside Europe.

## Tracking the genetics

Genotyping of porcine viruses has become invaluable in tracking changes in the PRRS evolution over time. The tests have shown that although some herds have a stable resident infection, in many other instances there is an ever-changing viral population in which newcomer forms of PRRSV establish themselves and become dominant or rapidly disappear.

Studies comparing early and late isolates have suggested a rate of divergence averaging as much as 0.5% per year.

Because of the variability, the veterinarian may submit samples of virus from a farm for genetic identification (sequencing), which determines the gene sequences encoding a variable region of the specific viruses.

Results from sequencing can help to answer major questions such as whether a PRRS-positive herd is under attack from a new variant and how an infection has moved through the production system. But sequencing cannot be used to determine which vaccine is more appropriate in each herd.

## Developing protection

The outstanding milestone in PRRS control must be that vaccination quickly became available once the virus was characterised and the first modified live virus vaccine to be produced and approved – Ingelvac PRRS MLV – has continued to protect over 20 years later, despite the ever-changing nature of the PRRSV challenge.

This pioneering vaccine uses a modification of a live Type 2 seed virus to mimic the way in which a wild-virus infection triggers the pig's immune responses, but without causing disease.

Over the years it has reliably provided effective protection against Type 2 wild infections wherever it is applied.

The vaccine was introduced in the USA in 1994 and is today marketed in 19 countries of Asia, Europe and North America. Since 2000 the main extension of the PRRS vaccines range has been the debut of products directed against the European Type 1 virus.

## Protecting the whole herd

A shift in vaccination targets occurred around the mid-2000s. Before then the main application of vaccines was against reproductive losses in the breeding herd. But the realisation grew that it was not enough to control PRRS only in sows.

A whole-herd approach was needed, extending protection also to weaned and growing pigs.

Clinical signs in growing pigs may be less evident than in sows. With experience, however, came recognition that growing-finishing contains many more pigs and these harbour more virus that they can spread, so it represents a large reservoir of potential infection. Giving a modified live virus vaccine to pigs at weaning was demonstrated to directly improve growth performance and also indirectly influence against possible transmission by reducing the shedding of virus.

## Persisting threat

Another reason for recommending whole-herd vaccination is to avoid the formation of sub-populations of pigs that differ in their immune status. Where such sub-populations exist, they offer PRRSV a route to long-term survival in the herd by passing from infected carriers to susceptible pigs.

From 30 years of PRRS we have learned that the virus can persist for long periods, mainly in pigs' lymph nodes and tonsils, and that this poses a constant threat of transmission to unprotected animals or herds. The major problem confronting attempts at control is that carrier pigs are not easily detected.

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Transmission by carrier pigs is one of the main explanations for the fact that infected herds rarely rid themselves of PRRSV without some form of intervention, particularly in large farms. The virus tends to circulate indefinitely in a breeding herd once it has become infected. Clinical outbreaks of PRRS then reappear periodically as the infection reaches a susceptible sub-population of gilts or sows.

### Load, close and expose

A major milestone has been the success of production systems in beating the circulation/re-infection cycle and therefore controlling PRRS by applying a procedure commonly called load, close and expose. Loading means that the herd brings in as many gilts as it can accommodate in order to meet breeding targets. Once loaded, it is closed temporarily to the entry of all new pigs.

As practised especially by American veterinarians, herd closure is followed by the deliberate exposure of the resident animals to PRRSV in order to increase the level of immunity across the pig population on the site. This exposure can be done in various ways, but the most widely used is by the mass vaccination of the animals using a modified live virus vaccine.

Possibly the most referenced of all veterinary research publications on PRRS in recent years has been an account from the USA of an extensive trial on 61 farms to investigate load-close-expose procedures for stabilising the PRRSV status of the breeding herd. Vaccination was compared with exposing the breeding herd using serum containing live virus.

Two metrics were used to assess the outcome of these exposure techniques. The first was the time until the herd had stabilised after an outbreak, defined as weaning PRRSV-negative pigs in at least three consecutive months. As an alternative, the study also looked at the time that elapsed before a herd returned to its baseline level of productivity after experiencing an outbreak.

Achieving stability took 26 weeks on average with serum exposure and 33 weeks with vaccination, both methods showing large farm-to-farm variations. Only half of all farms were stabilised by 210 days and several others needed considerably longer, which is worth noting when planning the introduction of PRRSV-negative gilts into a previously infected herd.

But with the measurement of time to return to baseline, the study found that vaccinated herds recovered more quickly than those exposed by live-virus inoculation. The difference was marked – just 12 weeks on average after receiving the modified live virus vaccine compared with 20 weeks after serum exposure. The gap in time was calculated to represent a gain

through vaccination worth 1,443 pigs extra produced for every 1,000 sows.

### Improving diagnosis

Diagnostic methods for PRRS control have undoubtedly improved over the years. At the start the ELISA assay for antibodies was usually the only option to test pigs. While widely available and rapid, ELISA is limited: it demonstrates exposure and not the actual presence of virus, the immune response varies from pig to pig and antibody counts do not always relate to the virulence of the isolate. Another milestone was the realisation that detecting antibodies through an ELISA assay after wild-virus infection does not correlate with protection. One of the special features of PRRSV is its ability to induce an unusual immune response in the pig and so evade the normal defence mechanisms. Infection leads to antibody production, but the antibodies generated 7-14 days post-infection play no protective role. Neutralising antibodies are not induced until at least 21 days after infection and with some viral strains even these are not produced in significant quantities.

It indicates a demand for another form of test that can determine neutralising antibodies and cellular immunity. The commercialisation of new tests currently under development may be the next milestone. Direct viral detection is likely to be a better choice for a full diagnosis in persistently infected herds and that means the test method known as PCR. More expensive yet highly sensitive, it can detect PRRSV in a range of tissues. In addition to a conventional use on blood samples it has therefore been applied increasingly to oral fluids. In the USA, the use of oral fluid analysis has risen more than 10-fold since 2010 due to the easier sampling it involves.

A combination of these diagnostic tests may be used to determine a herd's status to PRRSV regarding exposure or the active circulation of virus in breeding animals.

Typically this might start with testing sample groups of weaned pigs by PCR and adding a monthly ELISA check on sows. As a further refinement, some herds include a few ELISA checks in late finishing to verify a flow or check if groups of pigs had been exposed to the virus. A combination of these diagnostic tests may be used to determine a herd's status to PRRSV regarding exposure or the active circulation of virus in breeding animals.

### Analysing control options

The development of knowledge on PRRS has presented a range of choices for actions to control the disease. A systematic approach to options analysis developed over the past 10 years by Boehringer Ingelheim's technical team marks a further

milestone by putting structure into the decision-making process.

Called the PRRS Five Step Process, it begins with the necessity that goals must be agreed. Someone in an area of low pig density may even want to eliminate the virus, in other circumstances the aim could be to minimise the risk of transmission or to reduce the economic impact of infection felt by the farm.

With the target identified, Step two considers the information from diagnostics about the current status of the production chain. Step three talks about understanding current constraints such as farm layout or location. Step four assesses the possible solutions to prevent infection, maximise immunity and reduce exposure. Finally, Step five implements the chosen path and monitors the outcomes.

Fundamental principles underpin the whole process. Firstly, that every farm is different and all control measures must be customised. Secondly, that control is not just a matter of vaccine application, there has to be a properly targeted vaccination programme backed by good biosecurity and diligent management.

### Mapping epidemiological data

First in the USA and now in Europe, veterinarians fighting PRRS are finding internet assistance in locating disease data for their own area and nationally or globally. It comes from a web-based system developed at the University of California-Davis, USA, as the Disease Bioportal.

This portal offers layers of information on PRRS outbreaks locally and in regions, both for geographic location and for details such as the viral strains involved. Its value in describing epidemics and how they are spreading is particularly clear for those who want to try controlling the disease across multiple herds in a defined area.

### Working together

Big improvements have been achieved in managing PRRS over the past 30 years, but the journey continues as global challenges remain massive. Co-ordinated herd control ensuring the full protection of all pigs in the population, including growing pigs, still is not widespread. On the other hand, the appeal of area control is increasing as pig producers and their advisers realise that PRRS is not something you can fight on your own. Unless your farm is in a zone of low pig density, one of the main lessons from 30 years of PRRS is that you will have a hard time keeping out the infection without working with your neighbours and sharing information with them.

It is a milestone moment whenever herd operators co-operate to fight the disease, because that is most definitely the way forward for long-term PRRS control. ■