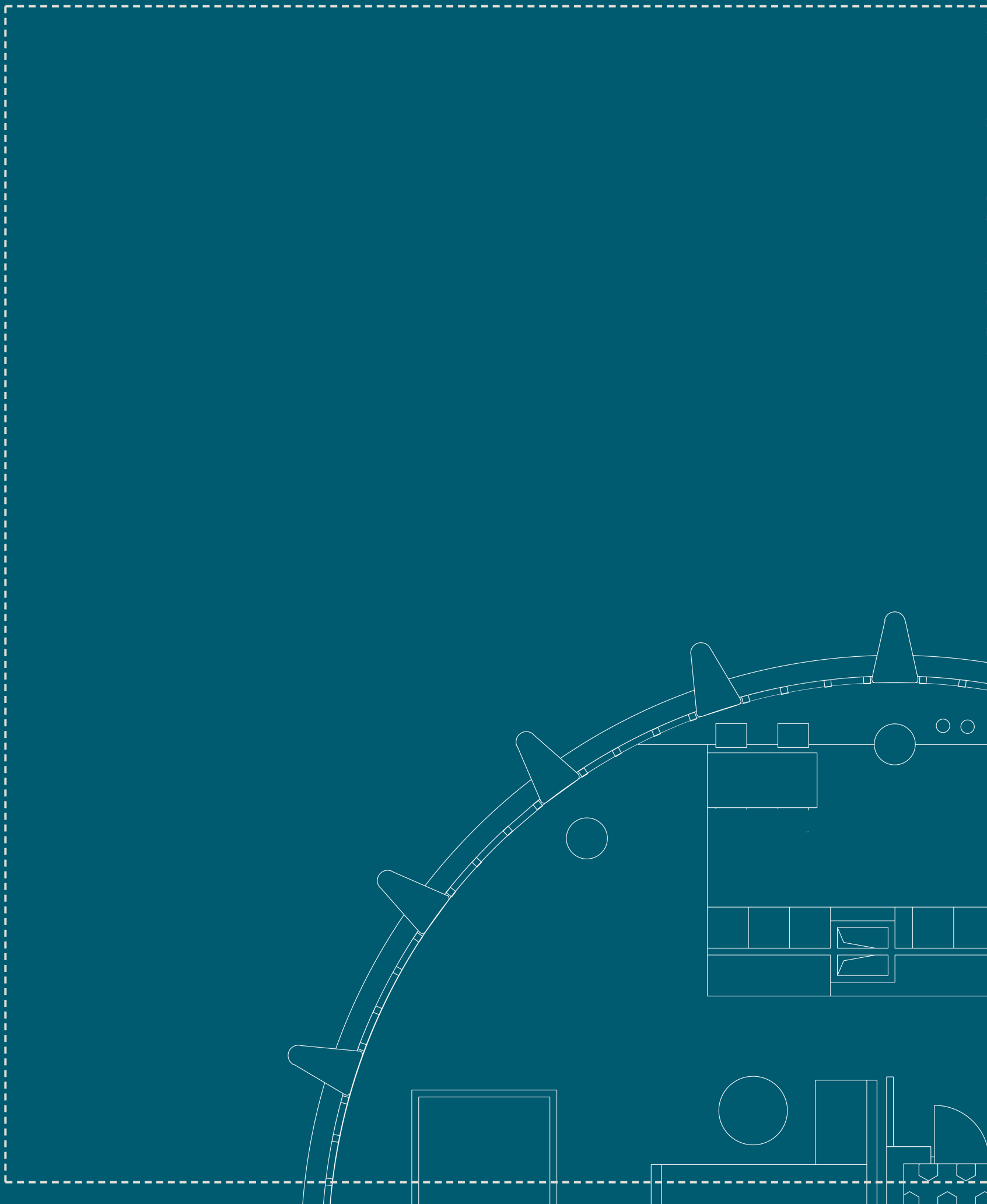
PIG HEALTH TODAY

CONFERENCE REPORT

FRAMING THE FUTURE FOR PRRS

NAPA, CALIFORNIA • 2017



LUCIANA GALINA, DVM, PHD

FRAMING THE FUTURE FOR PRRS

WELCOME

In 2017, Zoetis hosted a two-day symposium called "Framing the future of PRRS." The idea was to bring together the industry's top PRRS experts, draw on their expertise and frame out a plan for controlling and perhaps one day eliminating this costly swine disease.

Between the insightful presentations and thought-provoking discussions, I left the conference with a renewed sense of optimism about a future without the devastating losses associated with PRRS.

Two days later, we received word that one of our distinguished speakers — Dr. Bob Morrison of the University of Minnesota — had perished in a car accident in Prague. The news left us numb.

Only days earlier, Dr. Morrison had spoken passionately about the Swine Health Monitoring Project, which he helped launch in 2011. What's now known officially as the Morrison Swine Health Monitoring Program is helping the US pork industry monitor the prevalence of PRRS and, more importantly, draw a blueprint for improved control.

"We focus on methods of data capture and then, finally, visualization and reporting of those data. That's what gets us up in the morning," he said in what turned out to be his final industry presentation.

This summary of our conference's technical presentations is dedicated to the spirit of Dr. Morrison. His example and inspiration will be with us all for many years to come. We are also grateful to our other presenters for contributing to the success of this conference.

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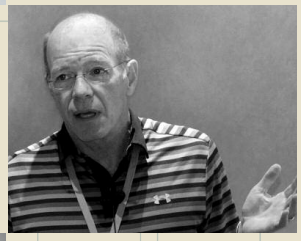
FRAMING THE FUTURE FOR PRRS

SCOTT DEE, DVM, PHD



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JAY CALVERT, PHD

DERALD HOLTKAMP, DVM

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PRESENTATION HIGHLIGHTS

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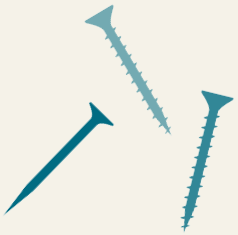
PIG HEALTH TODAY

SCOTT DEE, DVM, PHD

17 years of detective work, shared experiences helping pork industry get ahead of PRRS

KEY POINTS

- Blood swabbing of boars and oral-fluid sampling are two of the most effective means of determining whether risk is occurring through direct animal movement or semen.
- PRRS virus infections take much longer to become established in barns with air-filtration systems.
- PRRS can be successfully controlled and eliminated on a large scale, but it requires a serious commitment.



The evolution of knowledge about porcine reproductive and respiratory syndrome (PRRS) is now enabling pork producers and their veterinarians to make headway combatting this difficult and costly disease.

"You might lose a battle now and then, but overall, I'd say we're winning the war," said Scott Dee, DVM, PhD, director of research, Pipestone Applied Research, Pipestone, Minnesota.

Dee recalled the time in 1990 he encountered his first case of "mystery swine disease," or what was later dubbed PRRS.

A distraught producer had summoned him to a sow farm where all the sows had aborted and many had died. The setting was eerie, Dee recalled, because there were no animal sounds. All he could hear was the producer, who was on his knees crying at the devastation.

The virus hadn't yet been identified and diagnostics revealed no etiology. "It happened over and over, and I couldn't do anything about it," Dee said.

The good news was that although he was distressed and depressed by the carnage, it prompted him to search for answers.

Not long afterward, the virus was identified, and the disease's name had been changed to "swine infertility and respiratory syndrome." Dee continued to meet with colleagues and researchers and attend lectures about the disease.

VIRUS TRANSMISSION

The veterinarian focused on the persistent infection that characterizes PRRS — "the fundamental mechanism of this virus" that makes PRRS so difficult to manage — and decided to investigate the disease from all angles. In the process, he learned about *in utero* infection of piglets, PRRS virus shedding and viral shedding in semen. Most important, he learned about PRRS virus transmission from persistently infected pigs. By then polymerase chain reaction, or PCR, testing and the swine bioassay had come into play.

Less was known about indirect PRRS virus transmission, however, so Dee, by then on faculty at the University of Minnesota, and

his colleagues embarked on a series of sometimes quirky experiments, including one he called "the snowball from hell," designed to determine if the PRRS virus could be moved from place to place.

Using a seemingly random combination of carriers — Dee's SUV, work boots and the bathroom in Dee's house — they demonstrated how the PRRS virus on a snowball dropped off the wheel well at a truck wash could be picked up by boots and transmitted to another farm, packing plant or anywhere the producer traveled, particularly in cold weather. In warm weather, Dee said, they learned it was possible but not as easy to transmit the virus.

In other experiments conducted by Dee's students, he learned that certain strains of the PRRS virus — in this case MN184 — could also be transmitted via air and that flies could transmit it too.

GREAT INNOVATIONS

Fast-forwarding some 17 years, Dee said, "Oral-fluid sampling was a significant discovery in the battle against PRRS and for monitoring transmission. There's really nothing more simple yet so sophisticated." He added, "I put this at the top of the list of the innovations that have come forward. Just think how great our lives are now versus bleeding all those pigs."

Blood swabs are still important, however, along with oral-fluid sampling and quarantine to help protect the herd from PRRSV transmission when new stock is brought to the farm. He added, "Blood swabbing boars and oral-fluid sampling are two of the most effective means of determining whether risk is occurring through direct animal movement or semen."

Dee also pointed to early research showing the benefits of cleaning, disinfecting and drying trailers to prevent PRRS virus transmission. Recognized worldwide for his expertise in PRRS, he was also involved with a 4-year project showing that PRRS virus infections took significantly longer to become established in barns with air-filtration systems (Figure 1).

The cost of filtering a new construction project, he said, is about $1.50 per pig, and the return on investment if there's an annual

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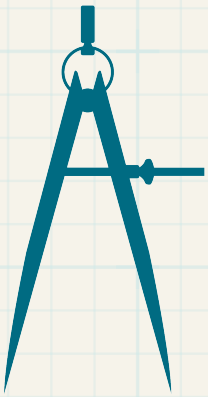
> "...ORAL-FLUID SAMPLING WAS A SIGNIFICANT DISCOVERY IN THE BATTLE AGAINST PRRS...THERE'S REALLY NOTHING MORE SIMPLE YET SO SOPHISTICATED."



SCOTT DEE, DVM, PHD

17 years of detective work, shared experiences helping pork industry get ahead of PRRS

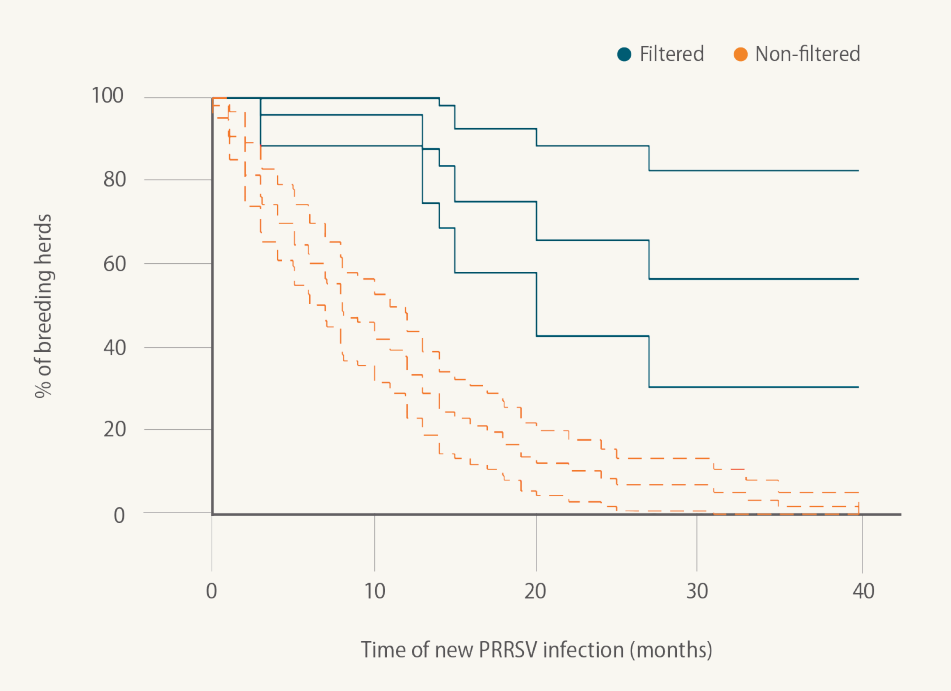
PRRS break is about 4:1. "So, it's a very, very good decision to make from the business standpoint if you are getting infected in a hog-dense region."

Dee noted the importance of having a room on the farm specifically for disinfection and drying — important components of biosecurity — along with quarantine and testing, sanitation of trailers and transport as well as air filtration.

Although PRRS remains the No. 1 disease target in the pork industry, he concluded, it can be successfully controlled and eliminated on a large scale. It requires an unwavering commitment from leadership, a significant investment, discipline, teamwork and a comprehensive approach toward biosecurity that considers all types of spread.

"You've got to have the whole package, with teams that will carry out protocols without fail," Dee said.

FIGURE 1. RESULTS WITH FILTERED VERSUS UNFILTERED BARNS



ALTHOUGH PRRS REMAINS THE NO. 1 DISEASE TARGET IN THE PORK INDUSTRY...IT CAN BE SUCCESSFULLY CONTROLLED AND ELIMINATED ON A LARGE SCALE.

FRAMING THE FUTURE FOR PRRS

BOB MORRISON, DVM, PHD

Swine Health Monitoring Project expanding but needs more industry participants

KEY POINTS

- The Swine Health Monitoring Project was established to monitor the incidence and prevalence of swine diseases and help with disease management.
- The project is expanding but needs data from 90% of the industry to reach its long-term goal of supporting the response to emerging pathogens.
- Disease control made possible by the project can help secure the nation's pork supply and bring more success to pork producers and swine veterinarians.

Editor's note:
Two days after the symposium, Dr. Morrison was killed in a car accident in Prague. He leaves as his legacy the Swine Health Monitoring Project, an endeavor that will continue under the direction of his colleagues as the Morrison Swine Health Monitoring Program.

The Swine Health Monitoring Project (SHMP)* continues to expand but ultimately needs data from 90% of the industry to reach its long-term goal of supporting the response to emerging pathogens, said the late Bob Morrison, DVM, PhD, professor, University of Minnesota, and coordinator of the project.

In the short term, the primary goal of SHMP, which began in 2015 with funding from the Swine Health Information Center (SHIC), is to monitor the incidence and prevalence of swine diseases and provide information to participants that help with disease management.

Currently, the project is gathering data on porcine reproductive and respiratory syndrome (PRRS), porcine epidemic diarrhea (PED) and Senecavirus A, he reported. "We focus on methods of data capture and then, finally, visualization and reporting of those data. That's what gets us up in the morning," he said.

SHMP is receiving data from 30 systems with approximately 1,100 sow farms representing 2.83 million sows. This includes 21 production companies, five veterinary practices and four regional projects. Data are provided voluntarily and, if desired, anonymously, he said.

WEEKLY REPORT

The project, which provides a weekly report to participants and about 300 non-participants, summarizes the latest findings on PRRS, PED and Senecavirus A. The report includes a "science page," available online, with a variety of topics ranging from the cost of PRRS to an article about unusual central nervous system cases.

SHMP is capturing swine-movement data and hopes to have a better understanding of how movement affects disease. It's also participating in collaborative studies with universities and a research institute. Studies under way include an investigation of a

continued

BOB MORRISON, DVM, PHD

Swine Health Monitoring Project expanding but needs more industry participants

> ...DISEASE CONTROL MADE POSSIBLE BY SHMP NOT ONLY SECURES THE NATION'S PORK SUPPLY, IT MEANS MORE SUCCESS FOR PORK PRODUCERS AND SWINE VETERINARIANS.

PRRS virus outbreak, detection of new and important PRRS viruses and an assessment of biosecurity.

Morrison indicated he was heartened no participants have withdrawn and said SHMP has enough data to understand what's going on with a limited number of diseases. However, he emphasized the project needs the large majority of the industry to participate if it's to reach its goal of responding to emerging pathogens.

Morrison said he's frequently asked why producers participate in SHMP. The answer is that producers benefit from sharing the benchmark data on PRRS and PED or, as one pork producer told him tongue in cheek, "That's a nice way to put it, but really, it's about sharing the misery. We really like to know that other producers are miserable, so it makes us feel good."

"Kidding aside, disease control made possible by SHMP not only secures the nation's pork supply, it means more success for pork producers and swine veterinarians," Morrison added.

FIVE VISIONS FOR THE FUTURE

Looking ahead, Morrison asked the audience of PRRS specialists for input on the project's future direction.

"Where would we like to be at the end of this project? Where would we like to be in 2020, which will be the fifth year of funding from SHIC? If you put on your dream caps, as I will, I'll be interested in your thoughts — how we build on and develop this aspect of regional and local health."

He then offered five visions of his own:

1

Develop hot and cold maps for PRRS, PED and emerging diseases. "By that, I mean where the disease is and where the disease isn't. That might help with pig placement. We have pieces of that now."

2

Produce transport heat maps. "I think we could produce transport heat maps, being aware of the pigs moving, that are positive and negative."

3

Develop more tools to supplement the veterinarian's outbreak investigation. "There's some fairly nice analytic capabilities that are out there, if you have the data," he said, citing the risks of transportation as one example. "Those tools all exist, but we don't have the data." Once we do, he added, "I think we'll be able to provide those tools to veterinarians."

4

Link SHMP data to the industry's Secure Pork Supply initiative. "This is something we're working on now — this aspect of business continuity or Secure Pork Supply," he said, referring to the National Pork Board's initiative to ensure pig flow from uninfected farms in areas with government-mandated quarantines following an outbreak of a foreign animal disease.

"Given that we have data for a fair number of producers in the industry, we can build on that," he said. "We have all of the sow-farm locations and identities," and it would not be that much of a reach to get

all the growing-pig locations. This will be even more feasible once the state testing laboratories complete efforts underway to standardize reporting.

But there's more to PRRS management than data analyses and sharing, Morrison said. "VDL (veterinary diagnostic laboratory) data is great for a new and emerging pathogen, but a pathogen like PRRS requires some interpretation on the part of the veterinarian," he continued. "Is the farm stable? Or is it stable vaccinated? So, we use PRRS as an example of building value for SHMP, and we require the veterinarian's interpretation of those data."

5

Gather and use more pig-transport data. "The one other piece you would need, as well as the analytical tools, would be the transport data," he said. "We can actually grab it today, but we're going to try and develop methods that grab it more conveniently in order to incorporate it into the health data, the location data, and create those tools or those capabilities that we hope will be useful."

** For more information about MSHMP, contact Carles Vilalta, DVM, PhD, at 651.352.7062 or cvilalta@umn.edu.*

Highlights

What's now known as the Morrison Swine Health Monitoring Program, or MSHMP, closed its pathogen year on June 30, 2017. Here are highlights on PRRS from the issued report:

EXPANDING ENROLLMENT

- Added four production companies
- Currently 33 systems with 1,092 sow farms and 2.96 million sows
- 161 non-participants receive weekly report

MONITORING AND INCIDENCE

PRRS incidence was 26% after 2 consecutive years at 28%.

"There are concerns that we have reached a threshold and that, for overcoming it and going into lower levels of incidence, we will have to improve collectively as an industry and make efforts to better understand how the disease spreads," the report said.

"One of the lessons learned during this (pathogen) year is that a given region and its features (weather and landscape) may shape disease incidence, e.g., having a different pattern in the Midwest and the Southeast of the USA."

PROSPECTIVE MONITORING OF PRRS VIRUSES

In a large-scale analysis of sequences coming from one system from the Midwest, MSHMP detected different characteristics that could help to differentiate endemic and epidemic strains.

The next step is to gather all the sequences from three different systems and analyze them monthly in an attempt to detect emerging strains and understand their spread in one area.

DEVELOP CAPACITY TO CAPTURE AND ANALYZE MOVEMENT DATA IN REAL TIME

A first version of a mobile app to collect truck movement and farm visits was developed and tested with promising results. A second version of the app with improvements is ready and will be tested in the following months.

EXPAND PARTICIPATION TO ALL PRODUCERS

Four production companies came on board during the last pathogen year. MSHMP now includes nearly 3 million sows or approximately 50% of the sows in the US.

"Following Bob's loss, a new plan for communication with the industry has been outlined and will be implemented in the second part of the year (2017) to sustain MSHMP's mission" and producers' collaboration with the ultimate goal to ensure "industry resilience and protection."

JAY CALVERT, PHD

Modified-live vaccines 'by far' most effective tool for combatting PRRSV

KEY POINTS

- PRRSV MLVs mimic natural infection and induce robust protection against PRRSV field viruses that are closely related to the vaccine strain.
- Most PRRSV vaccines can provide partial but significant cross protection against divergent PRRSV strains. Although the level of protection may drop as the degree of genetic relatedness between the two strains decreases, there is almost always a benefit to using a PRRSV MLV.
- Because MLVs are self-adjuvanting, only one injection is needed to provide lifetime protection against PRRSV to feeder pigs.

Modified-live vaccines (MLVs) are "by far" the most effective tool the industry currently has to control porcine reproductive and respiratory syndrome virus (PRRSV), said Jay Calvert, PhD, research director, Global Biologicals Research, Zoetis.

One of the key advantages of MLVs is their ability to mimic natural infections. They induce robust protection against reinfection with the same (homologous) PRRSV or closely related strains. The result can be "sterilizing immunity," which is demonstrated by the absence of detectible viremia and/or a lack of an increase in antibody titer.[1,2,3]

MLVs are also self-adjuvanting. They stimulate a cell-mediated immune response in addition to antibodies, and only one intramuscular injection is needed to provide lifetime protection in feeder pigs. This is in contrast to killed (inactivated) vaccines, which require an adjuvant to induce immunity and usually require two doses.

There are limitations, however, the scientist emphasized. All current MLVs for PRRSV are potentially prone to residual virulence in naïve herds, particularly in naïve third-trimester pregnant sows. Vaccination also results in seroconversion, which can complicate PRRSV surveillance.

It's also possible for MLVs to persist and spread to non-vaccinates, though not reliably enough to yield solid herd immunity. In addition, recombination may occur between vaccine and field strains, he said.

'GOOD NEWS, BAD NEWS'

Calvert reported "good news" and "bad news" regarding cross protection with MLVs for PRRSV. Most if not all PRRSV vaccines can provide partial, though statistically significant, cross protection against very divergent PRRSV strains.[4,5] However, the degree of protection drops off rapidly as the degree of genetic relatedness between the vaccine strain and challenge strain decreases from 100% identity (homologous challenge).

He considers genetic relatedness one of several predictors of whether a vaccine is going to protect well against a known challenge virus. However, "just how much relatedness is needed is a matter of debate and depends on where you live."

In the specific case of the US, the four licensed PRRSV MLVs are nearly equidistant genetically from the most common field strains. Any small differences in ORF5 sequence homology between a field isolate and particular vaccine viruses are irrelevant because they are swamped out by non-genetic factors, and because ORF5 only represents less than 4% of the viral genome, Calvert said.

VACCINE ATTENUATION

Most live PRRSV vaccines are attenuated, which means the virulence of a field strain is reduced, and they become "modified live," which makes them safe to use as vaccines. The attenuation process requires passing the field strain numerous times in a cell-culture system. Periodically, the virus is checked for both safety — the attenuation of disease — and efficacy.

At lower passages, the virus may be efficacious, but it's still not safe enough and needs more passages. If there are too many passages, it may be safe but no longer efficacious. When the virus is shown to be safe and efficacious, it becomes a vaccine candidate, he continued.

Calvert provided some basic knowledge necessary for understanding the attenuation of PRRSV vaccines. In pigs, the primary cells that PRRS viruses infect are macrophages. These are also the only cells that express a protein known as CD163, which is the primary receptor for all PRRS viruses. The CD163 PRRS receptor was discovered by Zoetis scientists in 2004.

Nearly all live, commercial PRRSV vaccines are field viruses attenuated by repeated passages on the MA-104 monkey kidney cell line, because this was the only cell line that would support the growth of a PRRS virus. However, it expresses a *monkey* version of CD163.

"By forcing the virus to learn how to grow on monkey cells, the PRRS virus forgets how to grow on pig macrophages. When you put it back into the pig (vaccination), it takes time and several generations of viral replication to learn how to adapt and grow on pig macrophages again. The attenuation is transient, and if you put the re-isolated vaccine virus into a naïve pig, it has different growth characteristics from the virus that's in the vaccine bottle," Calvert said.

continued

AN EXCEPTION IS FOSTERA® PRRS, A MODIFIED-LIVE PRRSV VACCINE DEVELOPED BY ZOETIS THAT'S PRODUCED WITH A UNIQUE ATTENUATION METHOD BASED ON BREAKTHROUGH RESEARCH... THE RESULT IS A VACCINE WITH IMPROVED SAFETY AND EFFICACY IN VERY YOUNG (PRE-WEANING) PIGS AND IS WHY THE FOSTERA PRRS VACCINE WAS THE FIRST OF ITS KIND TO BE LABELED FOR USE IN PIGLETS AS YOUNG AS 1 DAY OF AGE.

JAY CALVERT, PHD

Modified-live vaccines 'by far' most effective tool for combatting PRRSV

An exception is Fostera® PRRS, a modified-live PRRSV vaccine developed by Zoetis that's produced with a unique attenuation method based on breakthrough research. A field isolate known as P129 was attenuated by repeated passage on recombinant non-monkey cell lines. The CD163 that's expressed is the pig version. The virus replicates well in the pig straight out of the bottle, and the attenuation is not transient, he said.

The result is a vaccine with improved safety and efficacy in very young (pre-weaning) pigs and is why the Fostera PRRS vaccine was the first of its kind to be labeled for use in piglets as young as 1 day of age. This allows time for immunity to begin developing before weaning. The vaccine has a 6-month duration of immunity against respiratory disease and provides broad cross protection.

Although MLVs have limitations, Calvert said he believes they are the best option for PRRSV control and expects incremental improvements in these vaccines.

OTHER PRRSV VACCINE TYPES

Killed PRRSV vaccines are safe but, compared to MLVs, have poor efficacy in addition to their need for an adjuvant and multiple doses. Better adjuvants may improve them in the future, he said.

Recombinant live vaccines likewise have drawbacks. For instance, they have the potential for broadening cross protection, but so far, only modest improvements have been seen and may come at the expense of specific protection.

Calvert also reviewed several types of experimental PRRSV vaccines. Examples are subunit protein vaccines, which have issues similar to killed vaccines, and DNA vaccines, which are expensive to make and difficult to license.

Experimental vectored vaccines are similar to the DNA vaccines, but questions remain about which proteins from which strains to use, and poly-epitope vaccines need better adjuvants for cross protection, he said.

[1] Diaz I, et al. Characterization of homologous and heterologous adaptive immune responses in porcine reproductive and respiratory syndrome virus infection. Vet Res. 2012 Apr 19;43:30. doi: 10.1186/1297-9716-43-30.

[2] Batista L, Pijoan C, Dee S, Olin M, Molitor T, Joo HS, Xiao Z, Murtaugh M. Virological and immunological responses to porcine reproductive and respiratory syndrome virus in a large population of gilts. Can J Vet Res. 2004;68:267-273.

[3] Rahe MC, Murtaugh MP. Mechanisms of Adaptive Immunity to Porcine Reproductive and Respiratory Syndrome Virus. Dixon L, Graham S, eds. Viruses. 2017;9(6):148. doi:10.3390/v9060148.

[4] Charoenchanikran P, et al. Efficacy of Fostera PRRS modified live virus (MLV) vaccination strategy against a Thai highly pathogenic porcine reproductive and respiratory syndrome virus (HP-PRRSV) infection. Trop Anim Health Prod. 2016;48:1351-1359.

[5] Choi K, et al. Comparison of commercial type 1 and type 2 PRRSV vaccines against heterologous dual challenge. Vet Rec. 2016;178:291.

DERALD HOLTKAMP, DVM

Semi-annual report indicates progress combatting PRRSV

KEY POINTS

- The impact of PRRSV has been reduced by more than $83 million since 2010.
- Weaned-pig loss due to PRRSV has declined by more than 25% since 2010.
- Further progress will require a focus on elimination versus control of PRRSV, a continued focus on biosecurity and improved stabilization of sow farms.

Producers and veterinarians have reduced the impact of porcine reproductive and respiratory syndrome virus (PRRSV) by more than $83 million over the past 6 years, according to a semi-annual study conducted on behalf of the National Pork Board (NPB).

The annual incidence of PRRSV outbreaks has declined (Figure 1), and the loss of weaned pigs due to PRRSV declined by more than 25% as of October 2016 compared to 2010 baseline data, reported Derald Holtkamp, DVM, of Iowa State University.

To provide perspective, Holtkamp showed data comparing annual losses from PRRSV versus porcine epidemic diarrhea virus (PEDV). In 2010, PRRSV caused the loss of

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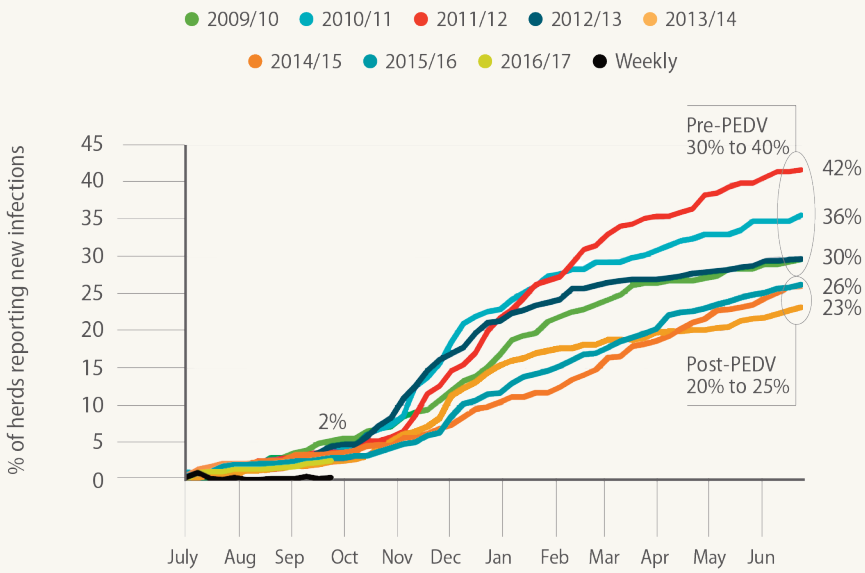
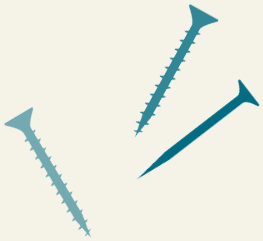
FIGURE 1. ANNUAL INCIDENCE OF PRRSV OUTBREAKS



DERALD HOLTKAMP, DVM

Semi-annual report indicates progress combatting PRRSV

> EVEN AT ITS WORSE, PEDV STILL DID LESS DAMAGE THAN PRRSV DOES YEAR AFTER YEAR



8.3 million pigs weaned and 9.9 million pigs marketed. In contrast, PEDV caused losses of 4.7 million to 6.4 million pigs weaned and 4.7 million to 6.4 million pigs marketed in the year of peak losses following its arrival in the US in 2013.

"Even at its worse, PEDV still did less damage than PRRSV does year after year," Holtkamp said.

NPB'S STRATEGIC PLAN

The PRRSV progress reports are provided as part of NPB's strategic 2020 goal to reduce the annual economic impact of PRRSV by 20% (as adjusted for inflation and measured against baseline data).

In his presentation, Holtkamp said there were four factors used to determine the overall impact of PRRSV on the value of lost productivity:

- **Herd distribution** — the percentage of breeding females and growing pigs in PRRSV-affected and -unaffected herds
- **Productivity** — the productivity of breeding herds and growing pigs in PRRSV-affected herds compared to unaffected herds
- **Prices and costs** — pig prices, input prices and costs
- **National herd inventory** — the size of the national herd

The report does not include factors such as treatment costs or the impact of PRRSV on the supply of pork and market-hog prices, Holtkamp said.

BIGGEST CHALLENGE: DATA

Incorporated into the report is analysis of farm-production records from 64 US breeding herds with known PRRSV status

...PROGRESS REGARDING PRRSV HAS NEVER FOLLOWED A STRAIGHT LINE...

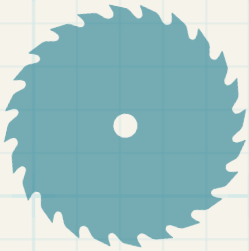
and outbreak histories, he said, noting that pig, feed-ingredient and diet prices for the October 2016 update were higher than they were for the 2010 study. Breeding-female inventory and pigs marketed also increased in 2016 compared to 2010.

The more recent updates are based on less production data than the 2010 baseline data, he said, adding that obtaining production data is the biggest challenge faced regarding compilation of the PRRSV reports.

All the progress made regarding PRRSV, he said, has been due to reduced productivity losses in PRRSV-affected herds relative to unaffected herds. This was especially so in PRRSV-positive breeding herds that hadn't experienced an outbreak for at least 12 months — a finding he theorized may be due to a shift from live-virus inoculation to the use of PRRSV vaccines as well as improvements in bio-management.

OPPORTUNITIES FOR IMPROVEMENT

Holtkamp emphasized that progress regarding PRRSV has never followed a straight line, but he identified some opportunities for more strides forward.



The studies indicate the industry has favored PRRSV control instead of elimination in breeding herds. That's resulted in fewer unaffected PRRSV herds, but further progress will require favoring elimination in the future, he said.

Progress will also require a further reduction in the incidence of PRRSV outbreaks and a continued focus on biosecurity. In addition, to achieve more PRRSV-negative pigs at placement, there needs to be an increased effort to stabilize sow farms, Holtkamp said.

JEFF ZIMMERMAN, DVM, PHD

Tips for successful oral-fluid sampling for PRRSV

KEY POINTS

- Oral fluids are an easy way to surveil or monitor PRRSV infections.
- When using oral fluids, "fixed" spatial sampling is as good or better than random sampling.
- For effective surveillance and monitoring, both PCR and antibody tests are needed.

Oral-fluid sampling is an easy way to detect porcine reproductive and respiratory syndrome virus (PRRSV) or track changes in PRRSV infections in populations — and it can optimize your survey efforts by keeping a few simple tips in mind, said Jeff Zimmerman, DVM, PhD, a professor at Iowa State University.

Oral fluids contain local and serum-derived antibodies and pathogens from the pig, but they also contain whatever other pathogens happen to be in the pen environment. This combination makes them a good diagnostic specimen, Zimmerman said.

Oral fluid is more efficient than bleeding pigs for detecting PRRSV and other pathogens. For example, if 20% of the pigs in a pen were PRRSV-positive, the probability of detecting the infection using one oral-fluid sample is over 90% — actually, 98% by polymerase chain reaction (PCR) and 94% by ELISA. To match that probability of detection, you would need to bleed at least 10 pigs (Table 1), he said.

SAMPLING PROCEDURE

Zimmerman advised obtaining oral-fluid samples first thing in the morning, when pigs are most active. It's important to use cotton rope, which gives better PCR performance than ropes made with synthetic fibers, and to cut the length of the rope so that the pigs need to raise their heads just a little to reach it.

After fluids are extracted from the rope and poured into a tube, they should be chilled immediately and kept cool until they get to the lab. If there will be more than a 72-hour delay, it may be better to freeze the samples, he added.

"Fixed" spatial sampling — that is, sampling pens throughout the barn (or air space) and at equal distances from each other — is easier than trying to randomly select pens and is actually as good as or better than random sampling or risk-based sampling. Sampling the same pens the next time and every time is best.

"This is a new idea for us, but it works well for both detection and monitoring," he said.

TABLE 1. PRRSV DETECTION (PRRSV RRT-PCR OR ELISA) USING ORAL-FLUID SAMPLE VERSUS SERUM SAMPLES; FAR FEWER ORAL-FLUID SAMPLES ARE NEEDED TO MATCH THE PROBABILITY OF DETECTION WITH SERUM SAMPLES.[1]

WITHIN-PEN PRRSV PREVALENCE*	PROBABILITY OF PRRSV DETECTION WITH ONE ORAL-FLUID SAMPLE		NO. OF SERUM SAMPLES NEEDED TO MATCH ORAL-FLUID DETECTION	
	RRT-PCR	ELISA	RRT-PCR	ELISA
5%	0.31	0.17	8	5
10%	0.79	0.59	11	7
15%	0.94	0.85	12	9
20%	0.98	0.94	13	10
25%	0.99	0.97	13	11
30%	1.00	0.99	12	10

** Assumption is that pigs are both viremic and antibody positive.*

If only one sample is going to be collected, he recommended sampling pens in the middle of the barn. "That's the spot where you'll have the highest likelihood of detection," Zimmerman said.

SAMPLE SAME PENS

For surveillance or monitoring, sampling the same pens each time will make it easier to interpret results. "If you mix different pens, they're going to be at different stages of infection, and you have a more difficult time understanding what the results are telling you over time," the veterinarian explained.

Repeated sampling over time is critical. "One sample is a picture that's static and historic, while sampling over time is a movie that's dynamic and predictive," Zimmerman explained.

One of the biggest challenges, he noted, is determining the best strategy for monitoring presumed-negative populations. In this case, Zimmerman recommended collecting six, eight or 10 samples initially and then one or two more samples every week or two. Collecting from all barns exponentially increases the probability of detection.

"I'd rather see fewer samples — even one sample — collected every week or 2 weeks from all or most barns versus more samples collected less often," he said.

continued

JEFF ZIMMERMAN, DVM, PHD

Tips for successful oral-fluid sampling for PRRSV

> **I'D RATHER SEE FEWER SAMPLES — EVEN ONE SAMPLE — COLLECTED EVERY WEEK OR 2 WEEKS FROM ALL OR MOST BARNS VERSUS MORE SAMPLES COLLECTED LESS OFTEN.**

DON'T ABANDON ANTIBODY TESTS

Testing of oral-fluid samples for PRRSV can be done by PCR. Test results can vary depending on the PCR protocols and kits used. "That's something to bear in mind when you look at your data. There are differences between labs and between kits," Zimmerman cautioned.

A problem with PCR testing for PRRSV is that not all labs are running the same protocol. Results can therefore vary with each lab. "There's still some work to be done to find the best protocol and get all the labs to run the same protocol," he said.

Samples also can be tested for PRRSV antibodies, Zimmerman said, adding that the antibody response is more definitive than PCR results for a number of different pathogens. "We've had a tendency to abandon antibody tests, but it may be premature. Antibodies are detectable even after nucleic acid disappears. For effective surveillance and monitoring, we need both nucleic acid [PCR] and antibody tests," he emphasized.

One problem with antibody testing occurs when maternal antibody (IgG) is present. IgG declines but can be detected for a long time. If there is doubt about a positive antibody result, a PRRSV IgM/IgA ELISA can be used to determine whether the antibody is from the sow (IgG) or from the pig (IgM and/or IgA), Zimmerman said.

[1] Olsen C, et al. Probability of detecting porcine reproductive and respiratory syndrome virus infection using pen-based swine oral fluid specimens as a function of within-pen prevalence. J Vet Diagn Invest. 2013;25(3): 328-335.

DANIEL LINHARES, DVM, PHD

'Nuts n' tails' fluid testing is promising, practical method of PRRSV monitoring

KEY POINTS

- Conventional serum monitoring for PRRSV is time consuming and will likely not detect the virus when the prevalence is low.
- PRRSV was more often detected in fluids obtained from routine castration and tail docking than it was in serum.
- Testing of fluids obtained from routine castration and tail docking holds promise as a practical and affordable way to improve PRRSV monitoring.

Testing fluids obtained from rout-ine castration and tail-docking procedures looks to be a promising, practical and affordable way to improve monitoring for porcine reproductive and respiratory syndrome virus (PRRSV), reported Daniel Linhares, DVM, PhD, from Iowa State University (ISU).

The fluids used for testing are aggregate samples — each sample has fluids from several pigs — comprised of serosanguineous drainage gathered during castration and tail docking, Linhares said.

The procedure, which Linhares said was developed by his PhD student Will Lopez, DVM, is simple:

- A bucket is lined with a disposable plastic bag, followed by a piece of cheesecloth.
- A large rubber band is placed around the outside top of the bucket to secure the bag and cheesecloth.
- Removed testicles and tails are placed in the bucket so their fluids drain through the cheesecloth into the plastic bag.
- The plastic bag is removed and a small hole is made in the bottom of the bag so the fluids can be funneled into testing vials.

"Put them on ice and you're ready to submit the samples to the lab," Linhares said.

The lab treats the samples similarly as it would treat serum and tests for PRRSV RNA by quantitative polymerase chain reaction (qPCR). The ISU lab is currently working on optimizing the diagnostic assays used to detect viral RNA and antibodies from processing-fluid samples, he noted.

MONTHLY SERUM-TESTING PROBLEMS

The veterinarian cited problems with the current method of statistical sampling that depends on conventional individual pig-serum testing. Serum taken monthly from 30 individual piglets provides a 95% probability of detecting PRRSV when the prevalence is 10% or higher. However, it is well established that the chance of detecting PRRSV based on individual blood samples is poor when the prevalence of the virus is low, Linhares said.

continued

DANIEL LINHARES, DVM, PHD

'Nuts n' tails' fluid testing is promising, practical method of PRRSV monitoring

> **TO IMPROVE THE PROBABILITY OF FINDING VIRUS WHEN THE PREVALENCE IS LOW, WE NEED TO SAMPLE *MORE PIGS, MORE FREQUENTLY.***

He said he's often asked if the likelihood of detecting PRRSV at near-zero prevalence could be improved by blood sampling 30 or 60 pigs weekly or bi-weekly instead of monthly. "The short answer is no," Linhares emphasized, because the same population isn't being sampled.

"Pigs are born every day. You wean every week. Sows move in and move out. So, those results don't add up. To improve the probability of finding virus when the prevalence is low, we need to sample *more pigs, more frequently*."

Conventional sampling of more pigs more frequently, however, isn't practical considering that trained personnel are required and that it's a two-person, time-consuming and costly job to get blood from individual pigs.

RESULTS WITH FLUIDS, SERUM COMPARED

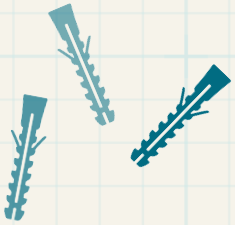
The herd sensitivity of processing-fluid testing is still being evaluated, but so far, it appears to be not only simpler but better than serum testing, he said.

To compare results, Linhares, Lopez and colleagues intentionally obtained weekly samples from several breeding farms where they expected to have a PRRSV prevalence of about 10%.

For each sampling, they collected blood serum from 30 pigs and divided it into six pooled samples, each with blood from five pigs. They also obtained one aggregate fluid sample from all pigs castrated and tail docked on each sampling day. In total, they had 10 sets of processing-fluid samples from the farms to compare to 10 sets of serum samples, Linhares said, noting that up to 600 piglets contributed to each of the processing-fluid samples.

TABLE 1. PRELIMINARY RESULTS COMPARING PROCESSING FLUIDS WITH SERUM TESTING FOR PRRSV

SAMPLING SET	RESULT OF PRRSV PCR OF PROCESSING FLUIDS	RESULT OF PRRSV PCR OF SERUM SAMPLES
1	Positive	1/5
2	Positive	1/5
3	Positive	2/5
4	Positive	2/5
5	Positive	1/5
6	Positive	1/5
7	Positive	Not detected
8	Positive	Not detected
9	Positive	1/5
10	Positive	2/5



Only one qPCR test was required to test each aggregated, processing-fluid sample compared to six qPCR tests needed to test serum samples from 30 pigs. "Overall, only 20% of the blood-serum samples tested positive compared to 100% of the processing-fluid samples (Table 1)," Linhares said.

In addition, anti-PRRSV antibodies using an IDEXX ELISA were detected in processing fluids, he said.

Linhares and colleagues hope that testing processing fluids can help detect PRRSV even when the prevalence is low. Toward this end, they plan to evaluate this monitoring method on farms with a low PRRSV prevalence.

WINDOW OF OPPORTUNITY

Testing of processing fluids, Linhares continued, could help producers resolve a common problem on farms undergoing PRRSV elimination: Piglets are born negative for the virus but test positive at weaning.

The animals might be infected due to management practices, pig or people movement and other factors between birth and weaning. That leaves a 10- to 12-week period of time when producers have a window of opportunity to prevent horizontal transmission of PRRSV to piglets.

What he called "nuts n' tails" monitoring could make it easier to pinpoint when pigs are becoming infected and when farms need to get aggressive about correcting problems so that pigs born PRRSV-negative remain so at weaning.

Linhares said he and colleagues are also conducting a retrospective study aimed at identifying the best control strategies to reduce the production impact of PRRSV. Their preliminary results indicate the impact is greater in systems that permit cross-fostering after 24 hours, in systems with poorly cleaned farrow-barn hallways and alleys and due to some gilt-acclimation practices.

The impact of the virus on production is less in herds with previous PRRSV exposure, with PRRSV-monitoring programs in place and when there is a PRRSV immunization strategy, he said.

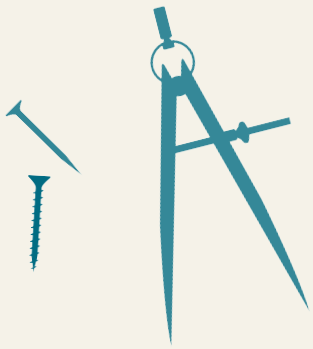
> **"OVERALL, ONLY 20% OF THE BLOOD-SERUM SAMPLES TESTED POSITIVE COMPARED TO 100% OF THE PROCESSING-FLUID SAMPLES."**

MONTSERRAT TORREMORELL, DVM, PHD

PRRSV in finishers may contribute to the disease on sow farms

KEY POINTS

- Efforts to control PRRSV have largely focused on sows herds, not on finishers.
- PRRSV in finishers may pose a risk to sow herds.
- Identifying risks for PRRSV infection and control of those risks in finishers may help lower the prevalence in sow herds and bring PRRSV control to the next level.



It's time to consider the role finishing pigs play in the spread of porcine reproductive and respiratory syndrome virus (PRRSV) to sow farms, said Montserrat Torremorell, DVM, PhD, University of Minnesota.

Most PRRSV-control efforts have focused on sow herds. As examples, Torremorell cited gilt acclimatization, PRRSV stabilization and herd closure — all aimed at protecting the sow herd and producing a PRRSV-negative pig.

Likewise, she said, biosecurity investments have focused on protecting sows. Examples include air filtration; disinfection of supplies; showering in; bench-entry systems; cleaning, disinfection and drying of weaned trailers; as well as downtime, dedicated personnel and dedicated transport.

Despite these efforts, various studies indicate the annual incidence of PRRSV hasn't dropped significantly and is still found in 20% to 30% of US sow herds (Figure 1).

The focus on protecting sow herds is a starting point, but to further improve PRRSV control, there needs to be a focus on PRRSV in finisher pigs, Torremorell asserted.

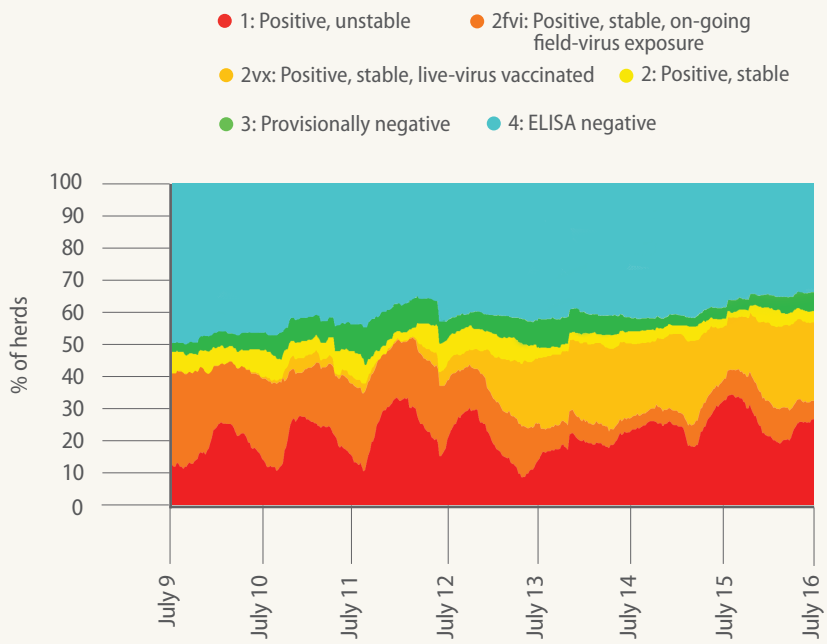
Currently, there's little effort to prevent infections in finishing sites, yet there is evidence that PRRSV is a growing problem in finishers and that these animals pose a risk for infection to sow farms, she said.

PRRSV IN GROWERS

In one study, 38% of finishing-pig groups (243/639) negative for PRRSV at weaning were positive at marketing; 39% (247/639) of groups were positive at both weaning and marketing.[1] In another study, 26% (31/120) of groups negative at weaning were positive at marketing.[2]

Annual losses due to PRRSV based on records from 2005 to 2010 were $664 million, and 55% of that amount was attributed to losses in growing herds. Data from 2016 indicates that losses due to PRRSV were $581 million (adjusted for changes in prices and the national herd size), and the percentage attributed to

FIGURE 1. PRRS AGGREGATE PREVALENCE IN SOW HERDS (N = 577) SINCE JULY 1, 2009
Source: Morrison Swine Health Monitoring Program, July 2017



losses in growers had risen to 62%,[3] Torremorell said.

The prevalence of PRRSV in finishers varies widely by region and may be as high as 62% to 84% based on information Torremorell obtained from colleagues at the Ohio State University.[4] "So, there's a lot of PRRSV in the finishing population," she said.

SPREAD TO SOW FARMS

In addition, emerging data from investigators at the University of Minnesota[5] indicate that when pigs are moved to finishing sites near sow farms, they may introduce pathogens to sows through area spread. In other words, when pigs positive for PRRSV move into a farm "neighborhood," there's an increased risk that neighboring sow farms will become infected with the virus, Torremorell said, noting that the median number of pigs moving weekly into an area can range from under 2,000 to tens of thousands.

Unfortunately, not much is known about risk factors for PRRSV infection in finishing pigs, she continued, but her personal experience indicates biosecurity is sorely lacking on many finishing farms.

"I don't go to any sow farms in the US where I don't have to shower. I can't say the same for most of the grow-finish sites I visit," she continued. "We don't even try to do some of the basic things on finishing farms…and don't really monitor them."

The failure to aggressively prevent PRRSV on finisher sites could be due in part to mindset. Producers may figure that if they'll be emptying the site in the weeks ahead, it doesn't matter if the animals get infected. "But if you start thinking in terms of implications for the neighborhood, then that assumption isn't very good," Torremorell continued.

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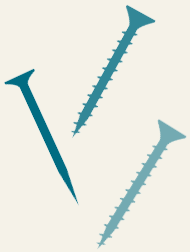
MONTSERRAT TORREMORELL, DVM, PHD

PRRSV in finishers may contribute to the disease on sow farms



> **I DON'T GO TO ANY SOW FARMS IN THE US WHERE I DON'T HAVE TO SHOWER. I CAN'T SAY THE SAME FOR MOST OF THE GROW-FINISH SITES I VISIT.**

EFFECT OF MARKETING PIGS

The veterinarian also addressed marketing strategies that may contribute to PRRSV infection. Anecdotal evidence indicates the virus in previously negative pigs is associated with marketing the first load of pigs. Infection with PRRSV could be linked to contamination of trucks, trailers and drivers, to loading procedures or perhaps to collection of cull animals at multiple sites.

Other marketing practices that appear to be linked to PRRSV infection in finishers include failure to wash the facilities between groups of pigs and poor employee retraining about biosecurity procedures, Torremorell said.

Because information about PRRSV in finishers is limited, the University of Minnesota has planned a study. It will focus on determining the PRRSV incidence among pigs in medium-density areas. The study will also evaluate risk factors associated with PRRSV infection in growers and the production and economic impact of the disease, she said.

"My assumption is that if we can control the risk of infection in finishers, we could potentially lower the risk of infection on sow farms," an approach that could bring PRRSV control to the next level, Torremorell said.

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[1] Holtkamp DJ, Kliebenstein JB, Neumann EJ, et al. Assessment of the economic impact of porcine reproductive and respiratory syndrome virus on United States pork producers. J Swine Health Pro. 2013;21(2):72-84.

[2] Robb C, Holtkamp D, Yeske P, Lower A, Lowe J, Polson D, Lasley P. Evaluation of biosecurity measures and management variables as risk factors for infection of growing pigs that are negative at placement with porcine reproductive and respiratory syndrome virus. Proc Am Assoc Swine Vet. p:75.

[3] Dr. Torremorell's personal communication with Derald Holtkamp, DVM.

[4] Dr. Torremorell's personal communication with Andréia Arruda, DVM, PhD.

[5] Morrison Swine Health Monitoring Program, Feb. 24, 2017.

JOSE ANGULO, DVM

Data can help improve PRRS control

KEY POINTS

- Decisions based on data from a production system affected by PRRS will be better than reactive decisions made when PRRS strikes.
- Implementing metrics, using predictive analytics and applying a proactive decision-making process can help pork producers improve management of PRRS.
- The value of applying data with a systematic approach has been demonstrated in the field.

Implementing metrics and utilizing predictive analytics can help pork producers improve their management of porcine reproductive and respiratory syndrome (PRRS), said Jose Angulo, DVM, a PRRS specialist for Zoetis.

"There are many lessons learned and fewer wasted efforts when decisions are made based on data generated from an affected production system," he said. "Producers can apply a systematic approach and make better decisions, in contrast to making reactive decisions when PRRS strikes."

Angulo defined a metric as a mathematical function that identifies a gap between the current state and a goal.

To apply metrics, he advised using statistical process control (SPC) charts — graphs used to study how process variation changes over time — to track performance data. SPC charts come in a variety of forms and are already used in the pork industry. They're a good way to plot and compare past and current pig performance and monitor the progress of PRRS-control programs. The charts can be especially helpful for identifying variation, which he called the enemy of swine production.

SELECT KEY PERFORMANCE INDICATORS

To start the process, a few important key performance indicators should be identified. These might include weekly data on abortion rates, live-borns or piglet mortality rates as well as total pigs weaned. Historical information for each indicator is charted and provides baseline data to compare with new information that's collected after PRRS-control plans are initiated, Angulo said, noting that the charts can also be used to generate metrics, such as the average time between PRRS outbreaks or time to baseline production, among others.

Zoetis has tested the value of this process in the field, he continued. One of the projects involved 9,000 sows on four breed-to-wean Iowa farms[1] where different strategies for PRRS control, including a killed PRRS vaccine, had been unsuccessfully used in the past.

The primary immunological tool of the new plan was use of a modified-live PRRS vaccine administered quarterly to the entire breeding herd and administration

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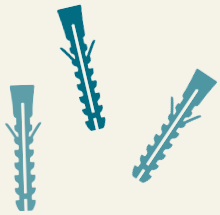
JOSE ANGULO, DVM

Data can help improve PRRS control



of two doses to replacement gilts, Angulo said. The goals were to develop a PRRS virus-control strategy to maintain breeding-herd stability, mitigate any potential wild-type PRRS virus (WT-PRRSv) re-circulation and/or new WT-PRRSv introduction and to establish standardized processes for measuring success in applied PRRS-control interventions.

Several key performance indicators were used to measure success and were compared to the previous 18 months of production data using SPC charts. Capability analysis — a set of calculations for statistical analysis — was also used.

The results demonstrated performance problems before the new PRRS-control plan was initiated and an improvement in performance and a reduction in variability after the plan was implemented (Figure 1). Breeding-herd stability was achieved on all four sow farms, evidenced by negative PRRS virus results on polymerase chain reaction testing of suckling pigs, he said.

Angulo showed SPC charts from the project (Figure 2), which he said demonstrated the value of applying a systematic approach to PRRS control in breeding herds.

FIGURE 1. RESULTS FROM A PROJECT INVOLVING 9,000 SOWS ON FOUR BREED-TO-WEAN IOWA FARMS BEFORE AND AFTER A NEW PRRS-CONTROL PLAN WAS INITIATED

KEY PERFORMANCE INDICATORS	BEFORE/STANDARD DEVIATION*	AFTER/STANDARD DEVIATION*	*p* VALUE
Abortion rate/1,000 sows	2.322 (9.431)	0.746 (0.698)	0.002
Farrowing rate	81.19 (10.88)	82.15 (7.00)	0.216
Average live born	11.78 (1.175)	11.96 (0.546)	0.016
Post-weaning mortality %	11.67 (8.795)	7.39 (2.014)	0.001

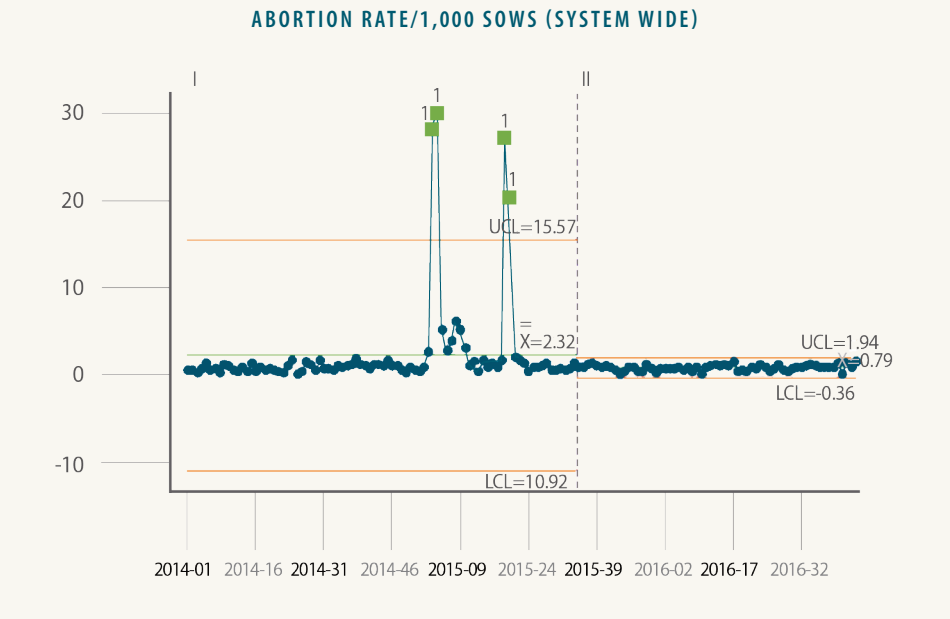
* Standard deviation from each period evaluated

Using a systematic approach to monitor and evaluate decisions also provides a building block for predictive analytics, Angulo said.

Predictive analytics is defined as a technology that learns from experience (data) to predict the future behavior of individuals in order to drive better decisions. The power of predictive analytics is already evident in other industries. In fact, most major retailers have a predictive-analytics department enabling them to improve their marketing.

In swine production systems, predictive analytics can be used to drive decisions about implementation of interventions that may minimize or even prevent disease outbreaks, he said.

FIGURE 2. AN XBAR VERSION OF AN SPC CHART SHOWING THE ABORTION RATE BEFORE AND AFTER INITIATION OF A NEW PRRS-CONTROL PLAN



Notes: UCL and LCL indicate a reduction in variation. The spikes show the severity of PRRS outbreaks before implementation of new PRRS-control strategies.

THERE ARE MANY LESSONS LEARNED AND FEWER WASTED EFFORTS WHEN DECISIONS ARE MADE BASED ON DATA GENERATED FROM AN AFFECTED PRODUCTION SYSTEM.

[1] Holtkamp DJ, et al. Terminology for classifying swine herds by PRRS virus status. J Swine Health Prod. 2011;19(1):44-56.