RESEARCH REPORT
SWINE HEALTH

Title: Development of standard methods to compare surveillance between regional porcine reproductive and respiratory virus control projects **– NPB #12-179**

Investigator: Derald Holtkamp[1]

Co-Investigators: Robert Morrison[2] , Leigh Rosengren[3]

Institution: Iowa State University[1],University of Minnesota[2], Rosengren Epidemiology Consulting Ltd.[3]

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INDUSTRY SUMMARY

The North American Swine industry is engaged in a conversation on a national porcine reproductive and respiratory syndrome virus (PRRSV) strategy. The parties involved in the conversation clearly recognize that effectively monitoring the PRRSV status of herds over time is a prerequisite for successfully controlling the virus. Because diagnostic testing can be expensive, the challenge is to design effective monitoring strategies for minimal cost. Regional PRRSV control and elimination projects are adopting and testing various monitoring strategies.

This project developed a data collection tool, methods of analysis, and standardized reports to help regional PRRSV control and elimination projects monitor the PRRSV status of the region and benchmark their monitoring efforts against each other. The project is designed to help participants and leaders of regional control and elimination project answer, “How much testing is enough?” A description of the region and information on each swine herd is needed. This can be submitted using the data collection tool, which is available as an excel spreadsheet, or by electronic file transfer. These data are collected initially and can be updated at any time. Diagnostic and clinical data describing the PRRSV circulation can be submitted at any time.

The developed methods classify each herd as PRRSV circulation positive, negative, or unconfirmed. The status is updated each week. A core principle of this project is that while a single positive test, where the possibility of a false positive has been ruled out, proves a herd is PRRSV circulation positive it is difficult to prove a herd is PRRSV circulation negative. To do so would require a perfect test be applied to every animal on a continuous basis. A major focus of this project is the process and caveats used for ongoing classification of herds as virus circulation (VC) negative.

Herds are initially classified as PRRS VC-negative after conducting diagnostic testing equivalent to the guidelines to classify a breeding herd as positive-stable (IIA, IIB, III or IV) or a growing herd as negative as described in the American Association of Swine Veterinarians (AASV) herd classification system (Holtkamp, et al., 2011). Once classified as VC-negative, herds must conduct ongoing testing to maintain this status. Ongoing testing is required because information is discounted over time to account for the chance the herd may have become infected since testing. The amount of ongoing testing may vary by the type of herd (breeding vs. growing) and type of production (commercial vs. genetic). It is determined by the desired level of confidence in the negative status and is communicated to participants as a baseline threshold. Establishing the standards for ongoing claims of VC-negative status is novel and helps address the problem of when to consider a herd's status and regional maps outdated.

Each month the prevalence of PRRS VC-negative herds in the region is estimated along with 95% confidence intervals. Higher participation rates narrow the confidence intervals so this gives perspective on the estimate's precision. In regions with no known positive herds, the probability the region is PRRS VC-negative is calculated. The probability the region is PRRS VC-negative increases with the proportion of known PRRS VC-negative herds in the region and with the intensity of ongoing testing of herds in the region.

While the methods developed and described in this report are relatively technical, the herd-level reports are designed to return meaningful information to participants so that regional activity can be considered in each herd's monitoring decisions. The regional reports developed for this project are designed to deliver monitoring information that will help regions track trends and progress toward goals. Because the process is standardized, the reports can be compared between PRRSV regional control and elimination projects to stimulate discussion and innovation. This is facilitated by an inter-regional report which is generated quarterly and can be opted into by interested regional control and elimination projects.

Participation in PRRSV regional control and elimination projects is voluntary and herds vary in the frequency and intensity of PRRSV monitoring. These methods are designed to use all diagnostic and clinical information about PRRSV circulation without restriction on choice of test, timing or amount of sampling. This allows participants to select the best monitoring regime for their herd and provides them with feedback to use in future monitoring decisions. The regional reports will help determine if a region is conducting enough monitoring to meet its goals, to identify herds where more testing is needed, and to evaluate if monitoring dollars are being spent effectively.

This project leveraged prior work and expertise of a working group established by the PRRS Coordinated Agricultural Project (PRRS-CAP) project (USDA NIFA Award 2008-55620-19132). The project also built on existing programs in Canada that have been supported by the Canadian Swine Health Board (Development of a PRRS-Free Certification Project & Sustainability and Enhancements of the PRRSV Free Certification Project).

This project provides value to PRRSV regional control and elimination projects. Freedom from disease modelling is a rapidly developing field that is becoming accepted in international trade. The reports provided by these methods will be required by regions achieving and claiming PRRSV freedom. Until that happens, the reports will provide useful information to regions striving to control PRRSV.

KEYWORDS

PRRSV; surveillance; monitoring; prevalence; disease-freedom

SCIENTIFIC ABSTRACT

The North American Swine industry recognizes the potential value of a porcine reproductive and respiratory syndrome virus (PRRSV) control and elimination strategy. As for any disease control, methods to track changes in prevalence and detect herd status changes will be required. Surveillance is expensive. Methods are needed to ensure it is cost effective. These methods can be piloted and applied in regional PRRSV control and elimination projects that are actively engaged in PRRSV monitoring.

This project developed a data collection tool, methods of analysis, and standardized reports to help regional PRRSV control and elimination projects monitor the PRRSV status of the region and benchmark their monitoring efforts against each other. The methods are unique because no monitoring protocols are dictated. Rather, each herd sets its own monitoring strategy. This helps ensure the strategy is appropriate and cost effective for each herd. The methods quantify the information provided by each herd's monitoring activities to describe the regional status without dictating herd monitoring protocols.

This project is based on the following three principles: i) A herd or region cannot be absolutely proven to be free of disease; ii) The degree of confidence that a herd or region is disease free can be described; and iii) A disease free status can be inferred on herds or regions exceeding an agreed-upon confidence. These methods describe a region's PRRS virus circulation (VC) status by compiling the confidence about the VC-status of the herds in the region. The confidence in each herd's status is adjusted each week by discounting the prior knowledge and by adding any new knowledge generated through diagnostic testing or clinical reporting. Confidence accumulates with supporting evidence such as negative diagnostic test results or a continued absence of clinical signs. Confidence erodes over time because the chance that a change has occurred which makes the information incorrect increases as time passes. This can be thought of as a leaky bucket; Information must be continually added to maintain the desired level of confidence.

This project designed reports to facilitate comparisons between herds within the region and between projects. As the Swine Industry expands its PRRSV control and elimination efforts PRRSV status must be measured clearly, consistently, and transparently so that discussions about regional spread are valid and interventions can be evaluated for efficacy. These reports can facilitate these conversations by ensuring regions are reporting current and comparable results. Reports are generated including the monthly trend in the prevalence of PRRS VC-negative herds in the region. For regions with no known positive herds, the probability the region is PRRS VC-negative is also reported. Regional PRRSV freedom can be claimed when the probability exceeds an industry accepted standard.

This project leveraged the prior work and expertise of a working group established by the PRRS Coordinated Agricultural Project (PRRS-CAP) project (USDA NIFA Award 2008-55620-19132). The project also built on existing programs in Canada that have been supported by the Canadian Swine Health Board (Development of a PRRS-Free Certification Project & Sustainability and Enhancements of the PRRSV Free Certification Project).

This project provides value to regional control and elimination projects. Freedom from disease modelling is a rapidly developing field that is becoming accepted in international trade. The types of outcomes provided by these methods will be required by regions that achieve and claim PRRSV freedom. Until that happens, the reports will provide useful information to regions striving to control PRRSV.

INTRODUCTION

Porcine reproductive and respiratory syndrome (PRRS) is endemic in North America. Losses are estimated at $664 million annually in the United States and $130 million annually in Canada (Holtkamp, et al. 2013, Mussell, et al., 2011). The swine industry has begun to speculate about the potential for PRRSV elimination. Clearly this will require epidemiological tools to monitor PRRSV status and detect significant shifts in prevalence, incidence or severity. On a smaller scale, regional PRRSV control and elimination projects are testing these strategies. The same epidemiological tools that will be required at a national level will provide immediate value to these projects and offer an opportunity to validate the approach.

While PRRSV can be eliminated from individual herds with a high probability of success, herds in high-risk areas face uncertainty whether they will remain negative long enough to offset the investment (Dee, et al., 2001; Dee and Deen, 2001; Yang, et al., 2008; Linhares, et al., 2013). This area risk has been a catalyst for regional disease control efforts. Regional PRRSV control and elimination projects are voluntary initiatives. Producers in a geographical area work together to communicate PRRSV status and control inter-herd transmission through pig movements and biosecurity. Regional PRRSV control and elimination projects have been operating in North America for 15 years (Hurnik, 2001; Corzo, et al., 2010) and at the present time at least 37 projects are operating (11 Canadian + 26 American) (personal communication E. Mondaca).

Regional PRRSV control and elimination projects monitor herd PRRSV status' to describe the incidence, prevalence, and distribution of PRRSV in the region. As regions transition to PRRSV freedom the monitoring focus shifts to detecting new infections and substantiating ongoing claims of PRRSV freedom. An informal survey of regional project leaders in 2011 found that regions (and herds within regions) have different monitoring strategies (Unpublished survey Holtkamp & Rosengren). Most regions have a protocol to establish the status of herds at the start of the project but may not require it be followed precisely. Few regions have protocols for ongoing testing. This has made it difficult for regions to fully capitalize on the information provided by these diagnostic results. In response, this project offers methods to quantify the information provided by each herd's monitoring activities to describe the regional status without dictating herd monitoring protocols.

This project developed a data collection tool, methods of analysis, and reports to describe the PRRSV circulation status in regional control and elimination projects. Producers and their veterinarians can continue to select the most appropriate tests, animals, and sample size to monitor PRRSV in the herd. Standardized reports are created using all diagnostic information available. These reports are designed to facilitate inter-herd and region communication and sharing.

This project leveraged prior work and expertise of a working group established by the PRRS Coordinated Agricultural Project (PRRS-CAP) project (USDA NIFA Award 2008-55620-19132). The members of this working group met once in person, and three times through conference calls. Feedback from this group is incorporated throughout the methods development and validation. The project also built on existing programs in Canada supported by the Canadian Swine Health Board (Development of a PRRS-Free Certification Project & Sustainability and Enhancements of the PRRSV Free Certification Project).

OBJECTIVES

To establish methods for regional PRRSV control and elimination projects to compare surveillance between regional projects and to make claims of PRRSV freedom.

METHODS

This project offers methods to describe a region's current PRRSV circulation status. The methods include the process to collect, manipulate, analyze and report on PRRSV monitoring data. The objective is to describe the probability that the region is free of circulating PRRSV if no herds are known to be PRRS virus circulation (VC)-positive *or* the prevalence, incidence and trends of PRRS infections if herds with circulating PRRSV are known to be present in the region. To do this, the PRRSV circulation status for each herd in the region is summarized weekly and these are combined to determine the region's status (Figure 1).

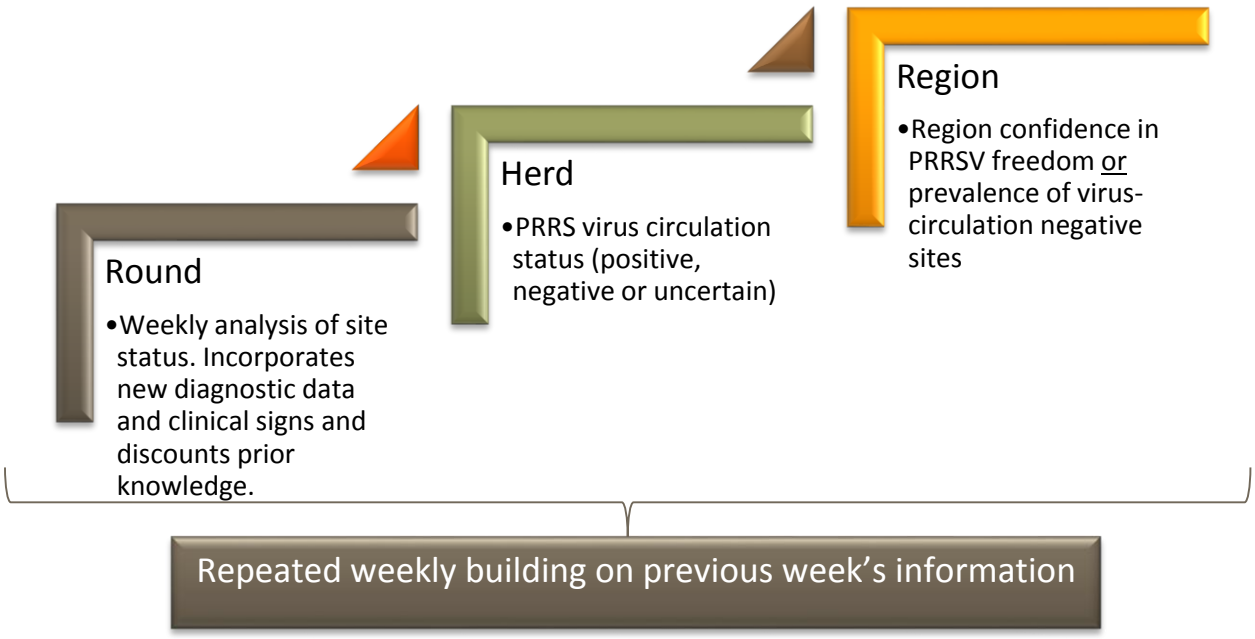


Figure 1. Process to determine herd and regional PRRSV circulation status.

POPULATION & OUTCOME OF INTEREST

All swine herds within the boundaries of a regional control and elimination project form the population of interest. The boundaries of the region are defined by the user and can change over time. Knowledge of the herds' PRRSV status can be acquired through any combination of disease investigations, routine monitoring, clinical reporting, or systematic surveys of the region.

Herds are classified based on the presence or absence of circulating PRRSV. The terminology for classifying swine herds by PRRSV status developed by a joint AASV and PRRS-CAP working group is used in this process (Holtkamp, et al., 2011). Throughout this report, this is referred to as the AASV herd classification system.

Growing herds classified as negative under the AASV herd classification system are classified as VC-negative in this project (Table 1). Likewise, sow herds that are classified as positive stable or higher (category IIA to IV) using the AASV herd classification system are classified as VC-negative (Table 2).

Table 1. Comparison of AASV Herd classification system and virus circulation status used in developed methods for growing herds.

AASV Herd Classification System	Virus Circulation Status
Positive	Virus circulation positive
Negative	Virus circulation negative

Table 2. Comparison of AASV Herd classification system and virus circulation status used in developed methods for breeding herds.

AASV Herd Classification System	Virus Circulation Status
Positive unstable	Virus circulation positive
Positive stable (IIA) Positive stable undergoing elimination (IIB) Provisional negative (III) Negative (IV)	Virus circulation negative

TEST SENSITIVITY

These methods accept diagnostic tests for which the test sensitivity can be estimated. The criteria for test selection and test sensitivity described in this section have been established for the current project as well as a related project supported by the Canadian Swine Health Board (Sustainability and Enhancements of PRRSV Free Certification Project).

The accepted diagnostic test / specimen combinations include ELISA or PCR tests on unpooled oral fluids or serum in pool sizes ≥10 (Table 3). The test sensitivity (Se_T) is assigned for each test / specimen combination based on published research. Test specificity is fixed at 1 because it is assumed that any unexpected positive results would be followed up ensure there are no false positive rounds.

To determine the test sensitivity, a literature search was performed to capture relevant peer reviewed papers, peer reviewed trade publications, and non-peer reviewed publications using Google Scholar, PubMed, and EBSCO HOST. Additionally, searches were conducted using the Google search engine and within the American Association of Swine Veterinarians E-Library. Terms used alone and in combination are provided (Table 4).

Search results were screened to restrict publications to those evaluating diagnostic test sensitivity. Analytical sensitivity papers were excluded. The remaining literature was categorized according to publication type including peer-reviewed, peer-reviewed conference proceedings, peer-reviewed trade publications, and non-peer reviewed. Spreadsheets were created to capture relevant information for each piece of literature which included, when available; type of diagnostic sample, sample collection method (individual, pooled, or grab), diagnostic test, pig type (boar, sow, hog, etc.), sensitivity, specificity, estimate confidence intervals, sample timing (days post inoculation, days post-vaccination, etc.), literature reference, and comments (study objective, methods, sampling procedure, specific diagnostic test (i.e. commercial name), comparison method (gold-standard, pseudo-gold standard).

A summary spreadsheet was compiled by type of diagnostic sample, diagnostic test, sample collection method, and sensitivity. The sensitivity estimates were noted as reported or calculated if the values were not reported in the paper but could be calculated from data in results section. Final sensitivity estimates were determined by a

consensus based process in which three epidemiologists blindly submitted their best, worst, and most likely sensitivity values. The estimates were then discussed until group consensus was achieved (Table 5). For oral fluids testing, a conference call was held with researchers actively investigating the sensitivity and specificity of PRRSV testing to validate and improve the estimates and approaches.

Table 3. Accepted test and specimen combinations, sensitivity estimates, and assigned point values per pig or rope.

Specimen	Diagnostic Test		Se[1]
Serum	ELISA	Pool of 1	0.95
		Pool of 2	0.91
		Pool of 3	0.87
		Pool of 4	0.83
		Pool of 5	0.79
		Pool of 6	0.75
		Pool of 7	0.71
		Pool of 8	0.67
		Pool of 9	0.63
		Pool of 10	0.59
	PCR	Pool of 1	0.95
		Pool of 2	0.93
		Pool of 3	0.90
		Pool of 4	0.87
		Pool of 5	0.84
		Pool of 6	0.81
		Pool of 7	0.78
		Pool of 8	0.75
		Pool of 9	0.72
		Pool of 10	0.69
Oral Fluid	PCR	Pool of 1	0.95
	ELISA/PCR	Rope with 20+ pigs	0.60[2]
Clinical signs	none	Pool of 1	.99[3]

[1] The worst case sensitivity estimate for individual serum ELISA and PCR tests is chosen from Table 1, as these estimates represented the most conservative value to ensure freedom from disease.

[2] Not a true test sensitivity, but is designed to give the correct number of points per pig where 22 ropes equals 95% detection at 5% pig prevalence and 10% pen prevalence [3] The test sensitivity for clinical signs is derived assuming the entire herd (≥500 animals) contributed to the test and the within herd prevalence is ≥0.1%.

Table 4. List of search terms used to determine test sensitivity (used alone and in various combinations)

Category	Search Terms (alone and in combination)
Pathogen Terms	
	Porcine Reproductive and Respiratory Syndrome / Porcine Reproductive and Respiratory Syndrome virus / PRRS / PRRSV
Diagnostic Test Terms	
	Antigen based immunochromatographic strip test / ICST
	Antigen Capture ELISA / ACE
	AriVac
	BioSign
	Enzyme-linked immunosorbent assay / ELISA
	IDEXX / IDEXX 2XR / IDEXX X3 ab / IDEXX HerdChek
	pen-side antibody test
	polymerase chain reaction / qualitative reverse transcriptase polymerase chain reaction / PCR / RT-PCR / qRT-PCR
	reverse transcriptase loop mediated isothermal amplification / RT-LAMP
	virus isolation / VI
Specimen Terms	
	blood
	buccal
	meat juice / meat transudate
	oral fluid / OF
	semen
	serum
	swab
Collection Method / Device Terms	
	capillary tube
	filter disc(s) / filter paper
	rope
	sample
	grab
Surveillance Terms	
	detection
	diagnostic
	gold-standard
	monitoring
	prevalence
	sensitivity
	specificity
	surveillance
	validation
Population of interest	
	boar
	field-based
	finish(er)
	gilt
	grow(er)

Category	Search Terms (alone and in combination)
	herd
	individual
	nursery
	pen
	pen-based
	pig(s)
	pool(ed)
	pre-wean(ed)
	post-wean(ed)
	sow
	swine
	viremic
	wean

Table 5. Consensus estimates of diagnostic sensitivity based on literature review.

Analyte	Diagnostic Test	Sample Method	Consensus Estimates of Sensitivity Best	Worst	Most Likely
Oral Fluid	PCR	Individual	0.99	0.50	0.95
	ELISA	Grab (rope)	0.99	0.50	0.84
	PCR		0.85	0.45	0.65
Serum	ELISA	Individual	0.99	0.90	0.95
	PCR		0.99	0.93	0.96
	ELISA	Pool of 3	0.98	0.69	0.83
		Pool of 5	0.99	0.69	0.84
	PCR	Pool of 5	0.92	0.74	0.85
		Pool of 10	0.91	0.68	0.82

*For freedom of disease surveillance systems, specificity can be assumed to be 100%

Sensitivities for tests on serum pooled from ≤10 pigs are proposed. Evidence was available to select test sensitivities for pools of 3, 5, and 10. Prior experience dictated that it is important to accept as many pool sizes as possible. Thus the sensitivity for pools of 2, 4, and 6 – 9 are modeled to decrease linearly by 4% and 3% for each additional sample included in the pool for ELISA and PCR tests respectively.

Clinical reports are a valid component of a surveillance system and regular reporting of both the presence and absence of clinical signs is encouraged in many control and elimination projects. No literature was identified describing the sensitivity of clinical reporting but there is precedent to include clinical knowledge in surveillance systems (Cameron, 2009). A report of the presence or absence of clinical signs consistent with PRRSV is considered a herd-level test. The test sensitivity (Se_T) for a clinical report is set at 0.99 which is calculated using a herd sensitivity formula with the herd design prevalence (P^*_H) used as the apparent prevalence of VC-positive herds in the region (Equation 1) (Christensen and Gardner, 2000). This value is proposed because for all combinations of herd design prevalence (P^*_H) ≥0.05 and herd sizes ≥100 the result is ≥0.99. Clinical signs are limited to one observation per week per herd.

$$Se_T = 1 - (1 - P_H^*)^n \quad \text{(Eq. 1)}$$

Data Manipulation

Round Sensitivity and Herd Status-Score

Each week all new monitoring data is combined with the previous knowledge to re-estimate the herd sensitivity. Each negative submission is awarded a round sensitivity (Se_R) equal to the probability that the submission outcome would have been positive (i.e. disease would have been detected) if the herd is truly infected at or above the herd design prevalence.

Submissions interpreted as positive had a Se_R equal to zero. The Se_R is calculated using the within-herd design prevalence (P^*_H), the number of tests (n), and the test sensitivity (Se_T) (Equation 2). When serum is the specimen one pig equals one unit and for oral fluids one pen equals one unit. The Se_R adjusts for pooled testing using the number of units sampled (u) and the pool size (ps) (Equation 3).

$$Se_R = 1 - (1 - P^*_H * Se_T)^n \quad \text{(Eq. 2)}$$

$$Se_R = 1 - (1 - (1 - ((1 - P^*_H)ps) - (1 - Se_T) * ps * P^*_H * ((1 - P^*_H)(ps - 1)))))^u \quad \text{(Eq. 3)}$$

Herd Sensitivity

A points-based system is used to approximate herd confidence. This system simplifies the combining of test results from a number of test types and from the same herd over time. The system is used in the Canadian PRRS-Free Certification Program (www.prrsfree.com) and is based on published literature (Cannon, 2002). Points are awarded for each submission proportional to the sensitivity of the test and design prevalence (Table 6). All points accumulated within a week are added together. The points accumulate over time resulting in a status-score. The relationship between status-score and herd sensitivity (Se_H) is logarithmic (Equation 4). The scales of these metrics differ as Se_H can range between 0 and 1 while the status-score can range from 0 to infinity.

$$\text{Status-Score} = -\frac{\ln(1 - Se_H)}{P^*_H} \quad \text{or equivalently} \quad Se_H = 1 - \left(e^{(-P^*_H * score)}\right) \quad \text{(Eq. 4)}$$

Each week the status-score is recalculated by combining any new knowledge generated with the knowledge from the week prior. A temporal decay is applied to the previous week's status-score. The temporal decay is determined by the herd's design prevalence (P^*_H), the previous weeks' (lag) herd sensitivity ($L.Se_H$) and the weekly probability that the herd became positive (R_H). The investigators propose that the herd risk (R_H) be based on the historical rate of outbreaks (as provided by the herd) adjusted for the level of regional risk. This process must be validated in multiple regions before being implemented in field projects.

The historical weekly probability of a breeding herd becoming infected with PRRSV is calculated by dividing the reported number of outbreaks in the last 5 years by 260 (i.e. the number of weeks in the period at risk). For growing herds the reported proportion of groups placed negative but positive at close is divided by 8 for nursery barns, 16 for finisher barns, and 24 for nursery to finisher barns (i.e. the approximate number of weeks the group is at risk). When herds do not provide a historical rate of outbreaks a default weekly risk of 3% is used.

Table 6. Value per test at recommended herd-level design prevalence.

Test	Analyte		Points per test at recommended design prevalence [a]			
			0.05	0.1	0.2	0.3
ELISA	Serum	Pool of 1	1	1	1.1	1.1
		Pool of 2	1.9	1.9	2	2.1
		Pool of 3	2.7	2.7	2.9	3.1
		Pool of 4	3.4	3.5	3.7	3.9
		Pool of 5	4.1	4.2	4.4	4.7
		Pool of 6	4.6	4.8	5.1	5.8
		Pool of 7	5.2	5.3	5.8	6.2
		Pool of 8	5.6	5.9	6.4	7
		Pool of 9	6	6.3	7	7.7
		Pool of 10	6.4	6.8	7.6	8.5
PCR		Pool of 1	1	1	1.1	1.1
		Pool of 2	1.9	2	2.1	2.2
		Pool of 3	2.8	2.8	3	3.2
		Pool of 4	3.6	3.7	3.9	4.1
		Pool of 5	4.3	4.4	4.7	5
		Pool of 6	5	5.1	5.4	5.8
		Pool of 7	5.6	5.8	6.2	6.6
		Pool of 8	6.2	6.4	6.9	7.4
		Pool of 9	6.7	7	7.6	8.3
		Pool of 10	7.2	7.6	8.3	9.1
PCR	Oral fluids	Pool of 1	1	1	1.1	1.1
ELISA /PCR		Rope with 20+ pigs	2.8	3	3.7	5
Clinical Report	none	Single test per herd	1	1	1.1	1.2

a: Refer to table 8 for proposed design prevalence by herd and business type.

The process to estimate the regional risk level is modeled after methods used to describe the prevalence of PRRSV outbreaks in sow herds (Tousignant, 2013). The methods are provided along with a comparison when appropriate (based on personal communication, S. Tousignant). The smoothing value (lambda, λ) is set at 0.279 as used by Tousignant. The starting value is calculated from the first half of the data, which differs slightly from the methods of Tousignant et al. whom use the cases observed over the summer months as the starting value. The expected PRRSV outbreaks per week (E_T) are calculated using an exponentially weighted moving average (Equation 5). Two weeks are forecast. The epidemic threshold is set at the median annual outbreak rate over the previous 5 years (R_{median}). Tousignant et. al. calculate the epidemic threshold from the data. The expected cases are converted to a rate (R_{est}) and adjusted by the epidemic threshold to establish the weekly risk index (R_{week}) (Equation 6). Finally, a regional risk level (R_{6w}) is calculated as a 6 week average of R_{week} using the 3 weeks prior, the current week, and the 2 week forecast (Equation 7). This level is multiplied by the herd risk (Equation 8).

The herd risk (R_H) dictates the temporal decay (D) rate; the higher the risk the more rapid past knowledge loses value. This downward adjustment reflects the loss of confidence in aging knowledge (Equation 9). The relationship between Se_H and status-score is logarithmic so the higher the previous week's Se_H the more the status-score declines. For example, a decrease is Se_H from 0.95 to 0.9 would cause a much greater drop in the status-score than a decrease from 0.25 to 0.2.

$$E_T = \lambda\gamma_t + (1-\lambda)E_{t-1,} \text{ for } t = 1, 2, \ldots \text{n} \quad \text{(Eq. 5)}$$

$$R_{week} = 1 + (R_{est} - R_{median}) \quad \text{(Eq. 6)}$$

$$R_{6w} = \frac{(\text{L3.R}_{week} + \text{L2.R}_{week} + \text{L1.R}_{week} + \text{R}_{week} + \text{F1.R}_{week} + \text{F2.R}_{week})}{6} \quad \text{(Eq. 7)}$$

$$R_H = R_{historical} * R_{6w} \quad \text{(Eq. 8)}$$

$$\text{Decay} = \frac{\ln\left(1+e^{\left(-P_H^*(M-L.Se_H)\right)}\right)}{P_H^*} \text{ where } M = -1 * [ln(R_H)/P_H^*] \quad \text{(Eq. 9)}$$

HERD STATUS

Herds can have one of three statuses; VC-positive, VC-negative, or VC-unconfirmed. Status is determined by the presence or absence of detected virus and the status-score. At enrollment, all herds are classified as VC-unconfirmed.

Herds that claim or detect circulating PRRSV (either report intentional exposure or submit positive diagnostic test results) are classified as VC-positive and the status-score is set to zero. No distinction is made between positive by vaccination or natural exposure because exposure by vaccination cannot be distinguished from a field strain without sequencing the virus. However, given vaccination is important in many regional control strategies, reports separate positive herds that report modified live virus vaccination from those that do not. The status of VC-positive herds can change only when a negative diagnostic submission is received. This results in the herd transitioning from a VC-positive status to a VC-unconfirmed status.

The methods use a threshold-score and a baseline-score. The threshold-score is the higher of the two and must be exceeded to first claim a VC-negative status (i.e. transition from VC-unconfirmed to VC-negative). Once classified as VC-negative the status-score must remain above the baseline-score to maintain this status.

Herds transition from PRRS VC-unconfirmed to VC-negative by conducting testing equivalent to the American Association of Swine Veterinarians (AASV) guidelines (Holtkamp, et al., 2011). For breeding herds these are the requirements described to claim positive stable (IIA or IIB). For growing herds they are the requirements to be classified as negative (Table 7). Herds must achieve an Se_H greater than or equal to the Se_H that would be achieved by following the guidelines exactly over a time period equal or greater to the time window stated in the AASV guidelines. While the AASV guidelines specify the population, sample size, tests and time intervals the methodology described in this report leave these to the herd veterinarians' discretion. During the transition period, which is equal to the time described by AASV guidelines plus 1 week, no temporal decay is applied.

The herd's VC-negative status will remain unchanged providing the Se_H remains above the baseline-score for that herd type and reason for production (Table 8). When a herd's Se_H fell below the minimum threshold, the herd

returns to a VC-unconfirmed status. In this situation, the herd is required to repeat the process described above to transition from VC-unconfirmed to VC-negative.

Table 7. Relationship between the AASV Guidelines for breeding herds to claim a positive stable status and growing herds to claim a negative status and the methods to claim VC-negative status

		Breeding herds	Nursery herds	Growing herds
AASV	Protocol	30 serum in pools of 5 with PCR from weaning-age pigs	30 serum samples from growing pigs with ELISA	30 serum samples from growing pigs with ELISA
	Stated design prevalence & confidence	10% / 95%	10% / 95%	10% / 95%
	Sampling rounds & time apart	4 (30 days)	2 (3 weeks)	2 (8 weeks)
Proposed Methods	Transition period (# weeks without decay)	14	4	9
	Threshold-score to claim VC-negative	103	60	60

Table 8. Proposed design prevalence, confidence levels and threshold-score to claim and baseline-score to maintain a virus circulation negative status.

Population	Activity	Score type	P^*_H	Confidence	Score Value
Growing herd	Claim	Threshold	0.5	0.95	60
	Maintain	Baseline	0.3	0.7	4
Gilt developer growing herd	Claim	Threshold	0.05	0.95	110
	Maintain	Baseline	0.2	0.8	8
Commercial sow herd	Claim	Threshold	0.1	0.95	103
	Maintain	Baseline	0.2	0.8	8
Nucleus or multiplier sow herd	Claim	Threshold	0.1	0.95	103
	Maintain	Baseline	0.1	0.9	23
Boar stud	Claim	Threshold	0.05	0.95	103[a]
	Maintain	Baseline	0.05	0.95	60
Region	Claim	n/a	0.01	0.95	n/a

*: these proposed values should be finalized after validation by a committee of stakeholders.
a : The AASV guidelines do not discuss testing to classify boar studs as negative. For the purposes of this project the threshold-score to claim a PRRS VC-negative status in a boar stud is set equivalent to a sow herd.

The baseline-score values are determined by the design prevalence and confidence to declare a herd VC-negative (Table 8). Values are proposed based on discussion among the authors. Setting the thresholds too high will lead

producers to spend more money than is necessary on diagnostic testing. Setting them too low will lead to a lack of confidence in the declared PRRSV status. These values should be subjected to a review by a committee of industry stakeholders .Until then, regions may select their own herd-level confidence and design prevalence. If this is done the corresponding baseline-score can be found using Table 9.

Table 9. Baseline-score associated with combinations of herd design prevalence and disease freedom confidence

		Prevalence								
		0.4	0.35	0.30	0.25	0.20	0.15	0.10	0.05	0.01
Confidence	0.7	3.0	3.4	4.0	4.8	6.0	8.0	12.0	24.1	120.4
	0.75	3.5	4.0	4.6	5.5	6.9	9.2	13.9	27.7	138.6
	0.8	4.0	4.6	5.4	6.4	8.0	10.7	16.1	32.2	160.9
	0.85	4.7	5.4	6.3	7.6	9.5	12.6	19.0	37.9	189.7
	0.9	5.8	6.6	7.7	9.2	11.5	15.4	23.0	46.1	230.3
	0.95	7.5	8.6	10.0	12.0	15.0	20.0	30.0	59.9	299.6
	0.99	11.5	13.2	15.4	18.4	23.0	30.7	46.1	92.1	460.5

Regional Outcomes

Regions are classified as VC-positive, VC-negative, or VC-unconfirmed. Any region with ≥1 VC-positive herds is classified as VC-positive. In VC-positive regions the prevalence of VC-negative herds may be calculated. A binomial distribution is used with exact 95% confidence intervals. Regions where all herds are VC-negative or VC-unconfirmed are classified as VC-negative if the regional confidence exceeds the threshold confidence at the design prevalence (P^*_R) ((Cannon, 2002). If the regional confidence is below the threshold the region is classified as VC-unconfirmed. The criteria to claim regional PRRS VC-negative status is proposed at 95% confidence for P^*_R ≥1%. The design prevalence is adjusted in small projects: For those with fewer than 100 herds the regional design prevalence is set at the reciprocal of the herds in the region. The regional confidence is not reported but rather is converted to the more intuitive metric of the probability the region is truly VC-negative given testing did not identify any VC-positive herds (Equations 10 & 11) (Cameron, 2009).

Regional Confidence = $1-(1-AvgSe_H)^D$ (Eq. 10)
where D = 1 (threshold number of diseased herds) and $AvgSe_H$ = average of Se_H in region

Probability Region PRRS VC-negative = $\frac{(1-P_R^*)}{1-(P_R^*-C_R)}$ (Eq. 11)

The VC-negative herd days is calculated in all regions. It is determined by multiplying the number of negative herds by the number of days the herds have been negative in the month. The herd-days-at-risk is the denominator: This is the population at risk and is the product of the number of herds in the region by the number of days in the month. (i.e. 30 herd-days could be 1 herd for 30 days, or 30 herds for 1 day, or any combination in between that multiplies to 30).

Assumptions in Methods

The project makes assumptions and set standards. The following discussion provides the reasoning behind these choices. The assumptions are easily altered and should be validated by a panel of industry stakeholders. Once

these have been reviewed and accepted it is ideal to use them consistently or the objective of creating comparative reports is lost.

It is impossible to prove disease freedom: A single positive result proves a population is infected but to claim PRRSV freedom with 100% confidence every animal would need to be tested on a continuous basis with a perfect test. Therefore, disease freedom claims are made with caveats about the confidence that a minimum level of disease would be detected if present. Many of the assumptions described relate to sensitivity / confidence at the level of the test, round, herd and region.

The confidence to claim regional PRRSV freedom is set at 95% confidence for ≥1% regional design prevalence. This is based on the recommendations of the OIE Ad Hoc Group on PRRS which recommended countries use an initial design prevalence of 5% and a confidence of 95% when the status is unknown and the objective is to determine the disease prevalence. Countries with prior evidence of a negative status or re-establishing a negative status after an incursion are recommended to use a design prevalence of 1% (OIE, 2008). We propose a design prevalence of 1% as the minimum criteria because peer-review publications have based models on standards accepted for other highly infectious diseases including national design prevalence levels of 0.1% and 0.2% (Corbellini, et al., 2006; Frossling, et al., 2009).

The AASV guidelines are recommended as the standard to claim a herd as VC-negative. These standards were developed by a group of industry experts and have been through a peer review process. Equivalent testing, rather than precisely following the guidelines, is in keeping with the objective of standardizing what needs to be shown but leaving flexibility in how it is accomplished.

Ongoing testing requirements are affected by the baseline-score and the temporal decay rate. The baseline-scores are proposed as a compromise between sufficient incoming information to the project and overly onerous requirements for participating herds. These baseline-scores differ by the purpose of production as is done in the Canadian PRRS Free Herd Certification Project. Higher standards are placed on boar studs and genetic breeding stock herds because the consequence to the region is greater if these herds are incorrectly classified as VC-negative.

The historical outbreak rate for a 5 year period is used to set each herd's baseline risk. A five year period is suggested because this is the time period that is currently reported in the Production Animal Disease Risk Assessment Program (PADRAP). When missing, a default rate of 3% per week is proposed to be used. This assumption can, and should, be adjusted to the best guess in regions that use the methods.

The regional risk is calculated using an exponentially weighted moving average formula that predicts the rate of outbreaks in the upcoming two weeks. This prediction is averaged with the current week and previous three weeks to generate a regional risk level. There are insufficient data to fully evaluate how well this concept will work. It is recommended that the outcome of this part of the model be monitored closely in any regions choosing to pilot this tool.

Together the historical and regional risk affects the temporal decay rate. This concept is based on the belief that the best predictor of a herd's risk is its past history. Regions may choose to monitor these risk estimates to determine if they are making progress towards the goal of PRRSV control.

Testing and demonstrating the Program

Data for an example region have been simulated to test the program and to demonstrate how the program works. Two additional regions were simulated for internal validation and to develop an example inter-regional report. Examples of the data entry forms and reports are provided in the results to illustrate what would be required to use the program.

Results

This project is based on the following three principles; i) A herd or region cannot be absolutely proven to be VC-negative; ii) The degree of confidence that a herd or region is VC-negative can be described; and iii) A VC-negative status can be inferred when herds or regions exceeding an agreed-upon confidence.

A region's status is described by compiling the confidence about the VC-status of the herds in the region. The confidence in each herd's status is adjusted each week by discounting the prior knowledge and by adding any new knowledge generated through diagnostic testing or clinical reporting. Confidence accumulates with supporting evidence such as negative diagnostic test results or a continued absence of clinical signs. Confidence erodes over time because the chance that a change has occurred which makes the information incorrect increases as time passes. This can be thought of as a leaky bucket; Information must be continually added to maintain the desired level of confidence (Figure 2).

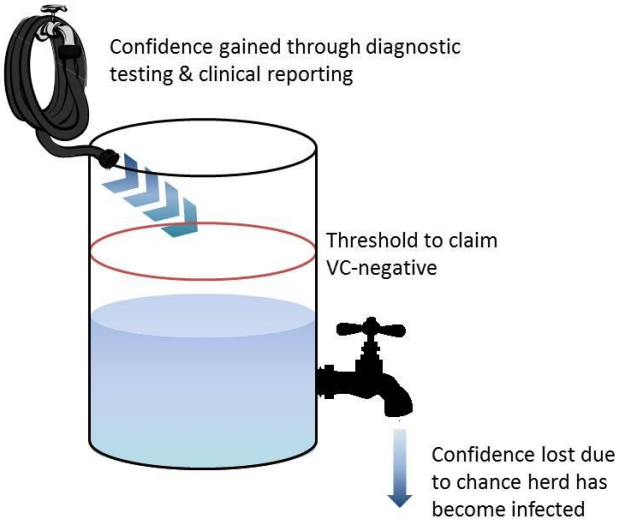


Figure 2. Illustration of the concept of continual loss and replenishing of confidence and requirement for a sufficient amount of confidence to claim disease freedom using water as a proxy for diagnostic information.

The objective is to describe the probability that the region is free of circulating PRRSV if no herds are known to be VC-positive. When herds with circulating PRRSV are known to be present in the region the objective is to report the prevalence, incidence and trends of PRRS infections. To do this, the PRRS virus circulation status for each herd in the region is summarized weekly and these are combined to determine the region's status. This process is summarized in Figures 3 & 4.

The methods simplify communication about status by converting the probability a herd is VC-negative to a points system. This can be thought of using sports terminology. The weekly calculation cycle is referred to as a round. The knowledge gained is referred to as points. Lastly, the net points are referred to as the status-score.

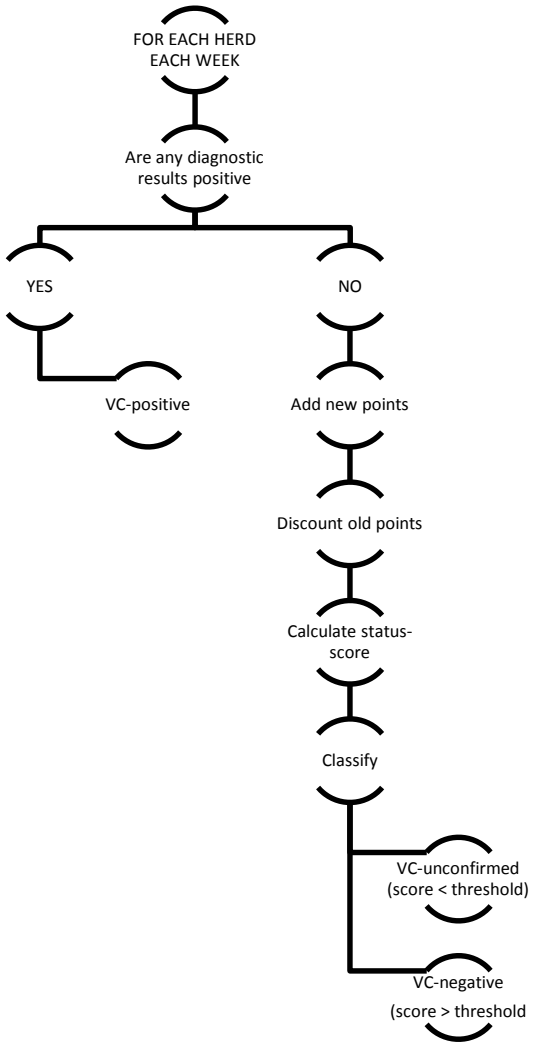


Figure 3. Flow chart of the weekly process to analyses a round of data and re-establish herd virus circulation status.

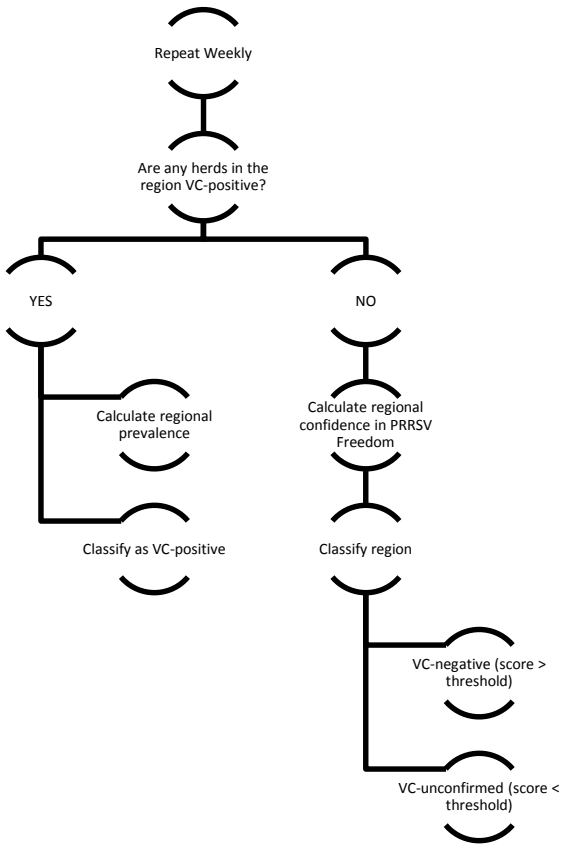


Figure 4. Flow chart of the weekly process to analyze herd status information and re-establish regional PRRS virus circulation status

Data Entry Forms

The data entry forms shown are available as an excel spreadsheet. The spreadsheet has validation rules to improve data quality and minimize time spent cleaning and verifying data. Regions that maintain data electronically can also transfer datasets into the tool without re-entry. A PRRSV regional control and elimination project wishing to use the program would first complete the regional description form (Figure 5). This collects the project start date, the number and type of herds in the region, the area (km^2) of the region, the regional design prevalence (P^*_R), and regional confidence (C_R). These last two values, which are proposed to be set at a design prevalence of 1% and a regional confidence of 95%, set the stringency at which regional claims of PRRSV freedom will be made.

A completed form is shown for the simulated Pacific Ocean Project (Figure 5). An option to use the default values for herd level design prevalence and confidence is included on this form. The lower the design prevalence and the higher the confidence the more intense the ongoing testing requirements are for a herd to maintain a VC-negative status. Users are recommended to use the default values to ensure inter-regional comparisons are valid. Once the default values have been reviewed by an Industry stakeholder committee and approved the option to select alternative values could be removed.

The herd-level form is completed for each known swine herd in the region (Figure 6). The geographical location (latitude and longitude) is the minimum data required to include non-participating herds. Participating herds can complete this at enrollment and can update it at any time. Each herd is described by one of the following phases of

production: farrow-to-finish, farrow-to-wean, farrow-to-feeder, nursery, wean-to-finish, finisher, boar stud, or isolation / acclimation. The purpose of production can be declared as commercial, multiplier, nucleus, or boar stud. The historical rate of outbreaks in the previous 5 years is requested for each herd. No formal definition is provided for an outbreak because projects often lack a case definition or differ slightly in their definitions. The current immunization practices can be declared as live-virus inoculation, modified live-virus vaccination, other or none.

For demonstration, the herd enrollment form is completed for a wean-to-finish operation in the Pacific Ocean Project (Figure 6). In practice, government issued premises ID should be used to ensure that each premises in the dataset is uniquely identified.

The PRRSV diagnostic and clinical data can be entered up to 5 years retrospectively as well as prospectively. Diagnostic testing does not need to follow a regular schedule; rather each time data about PRRSV circulation becomes available a form is completed (Figure 7). Data are requested on the current situation for PRRSV circulation, the presence or absence of clinical signs consistent with PRRSV since the last report, the diagnostic test results, and the reasons for any changes in PRRSV circulation. Diagnostic test results are collected at the case-submission level. For the purposes of this report, it is the responsibility of the investigators to classify a submission as positive or negative. For region's using the tool in the future this will be the responsibility of the herd veterinarian or project manager.

The example form has been completed for the same wean-to-finish commercial operation after serum from a new batch of pigs is tested with ELISA (Figure 7). Although not shown, this form could be completed to report the presence or absence of clinical signs without accompanying diagnostic information or change in PRRSV circulation. This is designed to provide value to projects that collect clinical reports.

The PRRSV status form collects four pieces of information that are not used in the any calculations but help with data interpretation and validation. These are the questions "What is the current situation for circulation of PRRSV", "Has the circulating PRRSV situation changed", and the last two question on how the change is determined and the cause of the change. These questions can be left blank in regions entering retrospective data if they are not available.

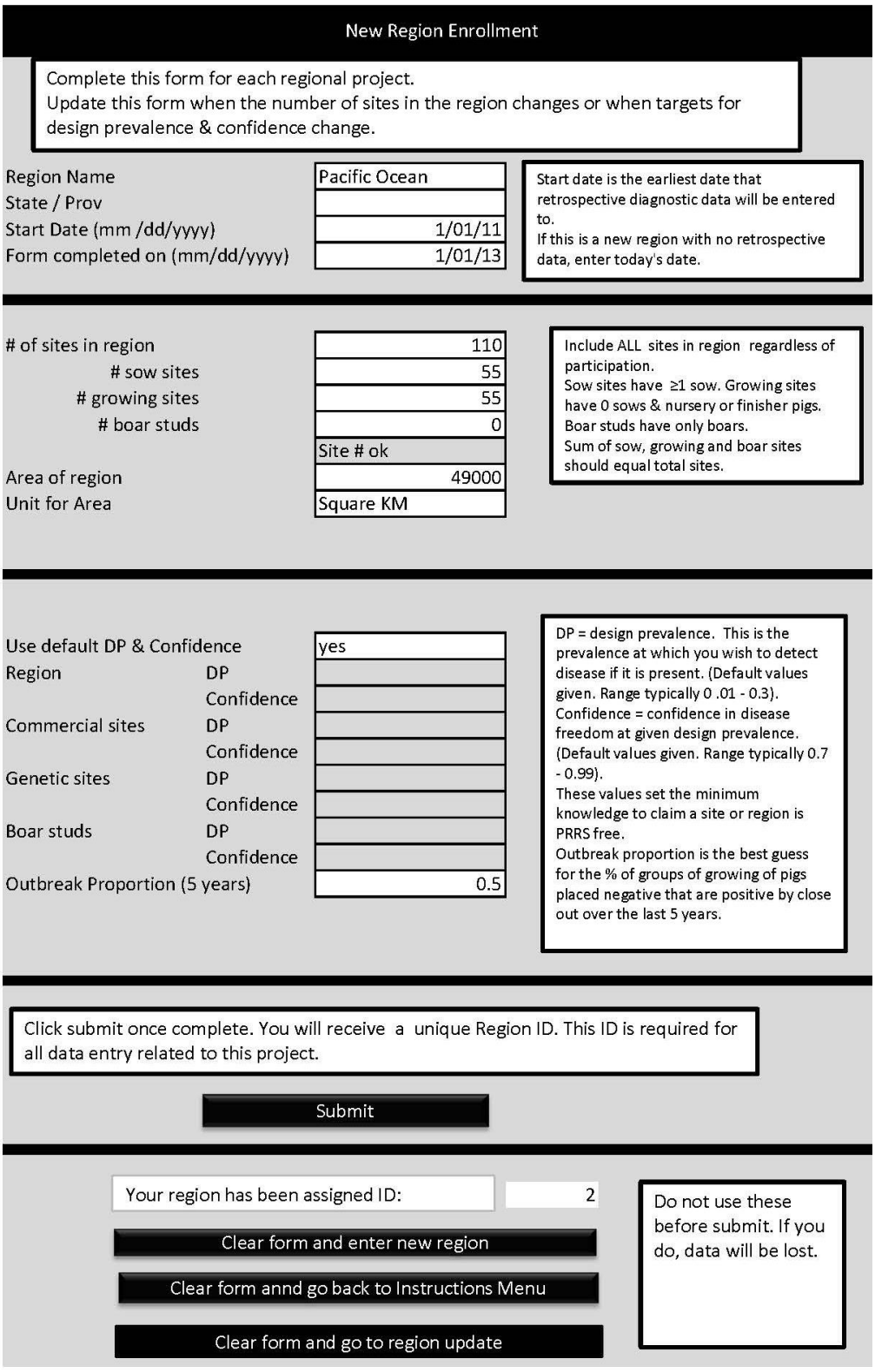


Figure 5. Regional enrollment form completed for an example region.

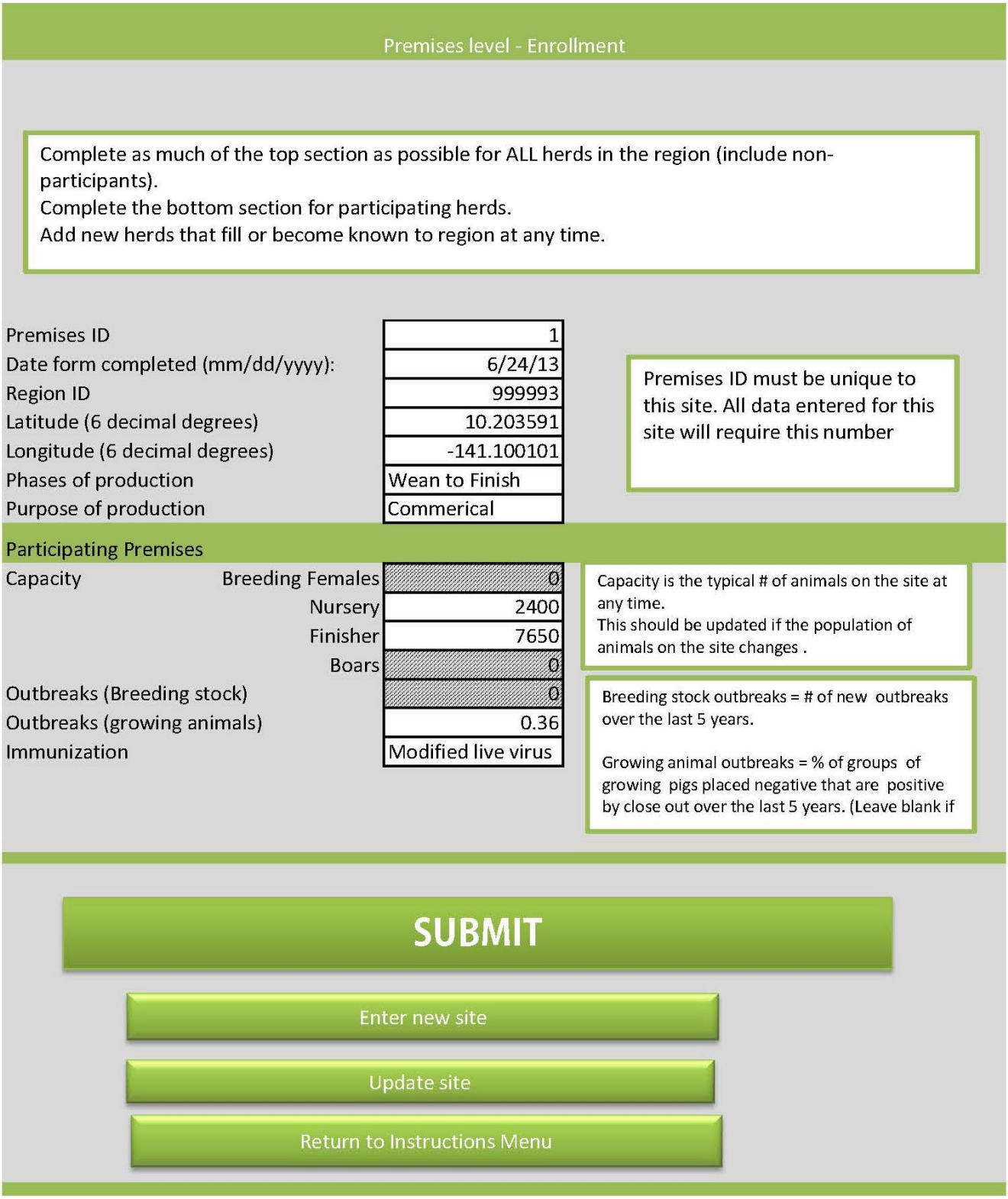


Figure 6. Herd enrollment form completed for an example herd.

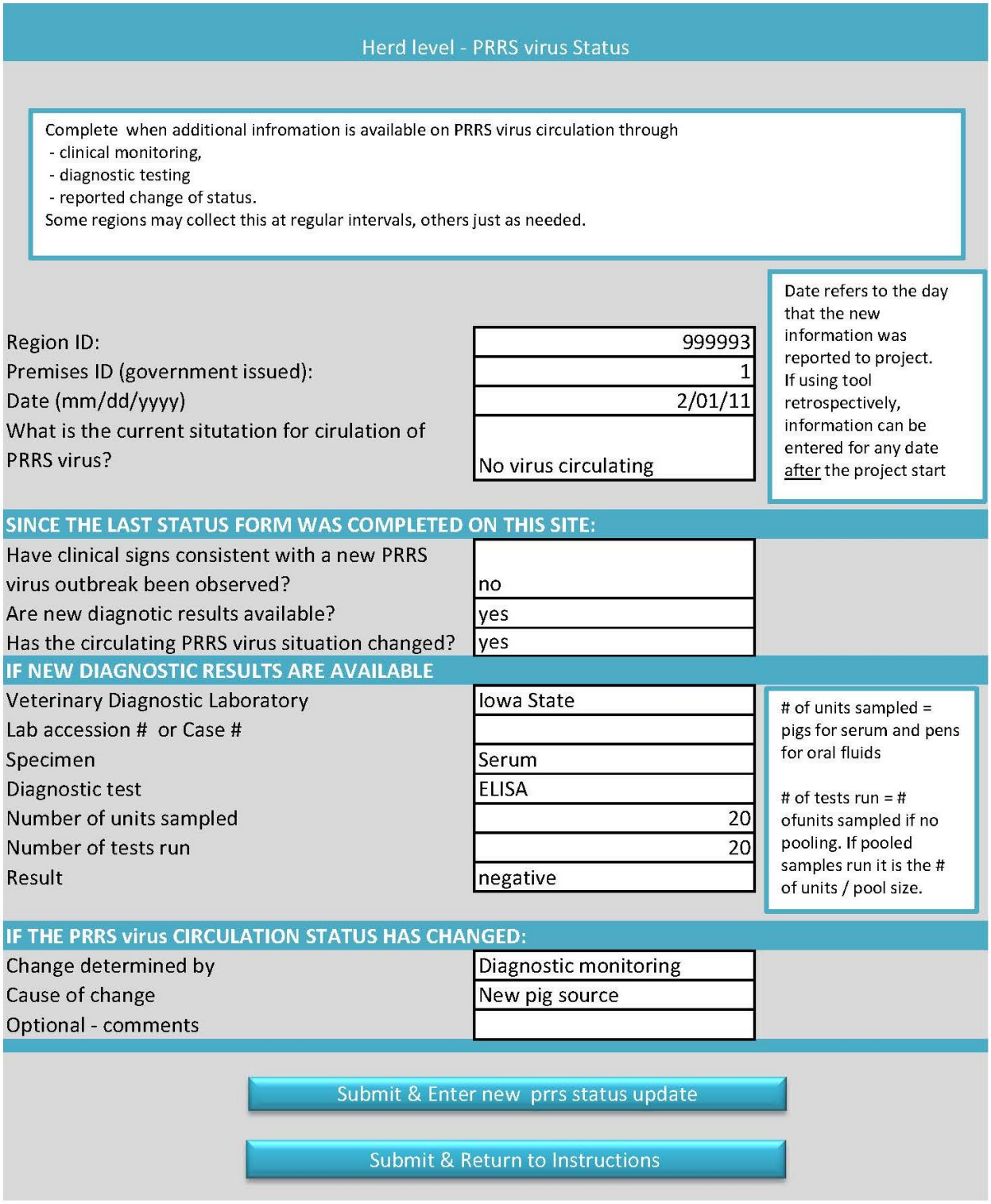


Figure 7. PRRSV update form completed for an example diagnostic submission from an example herd.

REPORTING

HERD REPORT

Reports can be generated as frequently as desired. A report for the example commercial wean-to-finish operation in the Pacific Ocean Project is provided as an example (Figure 8). The upper-left section of the herd-level report describes static information about the herd. This is provided so participants can notify the project if data are incorrect or outdated. This section also shows the threshold-score to claim and the baseline-score to maintain a PRRS VC-negative status. The bottom section of the report includes information on the current month, the quarter-to-date and the year-to-date along with the previous month, previous quarter and previous year.

As described in the methods, the confidence that a herd is PRRS VC-negative is transformed into a status-score. The center section of the herd-report includes a graph of the status-score accumulated through the submission of diagnostic test results and clinical reporting (Figure 8). The graph also includes the threshold-score to claim and the baseline-score to maintain a VC-negative status. Along the bottom axis a colored-coded bar indicates the status. The bar is grey when the herd is not participating, black when the status is VC-unconfirmed, green when it is VC-negative, blue when VC-positive and reporting modified live virus vaccination, and red when VC-positive without vaccination.

The graph of the status-score is provided to help producers make diagnostic monitoring decisions. The graph shows that the status-score does not decline during the transition-period when the herd is working towards claiming the VC-negative status. In the example report this occurs twice; once in the spring of 2013 and once in the spring of 2015. Once the transition period is past, the status-score is discounted each week to adjust for the aging or decay in the confidence of past results. When herds are VC-positive the status-score immediately drops to zero as is illustrated to have occurred in the fall of 2014. To re-claim a VC-negative status the herd must again exceed the threshold-score.

The top-center section of the herd report describes the most current PRRSV circulation status, the testing recommendation, and the current situation in nearby herds (Figure 8). The testing recommendation is reported as "yes" if any of the following are true when the report is generated: the herd has reported clinical signs consistent with PRRSV; there is knowledge of an outbreak in a herd within 5 km; or the herd has a VC-unconfirmed PRRS circulation status. This recommendation is included to emphasize testing decisions should include risk factors that affect the likelihood that the status of the farm will change over time.

The top-right section of the herd-level report describes the PRRSV circulation status of neighboring herds (Figure 8). This describes neighbors within 10 km for herds in low density areas and herds within 3 km for those in high density areas. A herd is considered to be in a high density area if there are 2 or more neighboring sites within three kilometers or 4 or more neighboring sites within 10 kilometers. These thresholds can easily be adjusted by each region. Directly below this the middle-right table provides information about the nearest 5 swine herds. This includes the herd type, distance to the neighboring herd and current virus circulation status. The status-score is provided for those neighboring herds that are VC-negative or VC-unconfirmed.

The bottom section of the herd-report describes the PRRSV circulation status of the herd over time (Figure 8). The last complete week of data are reported as "Current." The status at the end of the period can be one of the following: VC-negative, VC-unconfirmed, VC-positive (mlv immunized), VC-positive (no vaccination), or non-participant. The number of status changes, diagnostic submissions, clinical reports and a total of expenditures on diagnostic tests are reported for each time period. Of note, a status change is a change between VC-negative, VC-unconfirmed, or VC-positive. Herds changing from non-participant to participant and between positive with or

without vaccination are not considered status changes. Also note that a clinical report can be the presence or absence of clinical signs so the report describes the communication frequency not the frequency of clinical signs. The standardized expenditure is set at $40 per PCR test and $10 per ELISA test; no allowance is included for expenditures on virus sequencing.

Regional Report

The regional report is designed to be generated monthly. For this demonstration it is created at the end of June 2015 (simulated data) and includes information on the quarter to date, year to date, previous month, previous quarter, and previous year (Figure 9, page A). The report describes the herds, herd types, business purpose and density of the herds in the region.

The bottom of the first page of the regional report (Figure 9, Page A) includes tables to describe the number of herds in each PRRSV circulation status. This information is similar to what many regions already generate. These tables are included in the regional report to help users make the transition from the currently used description of the region to the proposed outcomes in the uppermost table. Users may find differences from their current status; exploring these differences can be a useful exercise to understand differences in how herds are classified.

Once regional leaders are comfortable with herd classification, the more novel components of the report can be used. In regions with known VC-positive herds the prevalence of VC-negative herds is reported along with 95% confidence intervals. The point estimate is the “best-guess” while the confidence intervals show the degree of uncertainty around the estimate. Currently most regions report the count or percent of negative sites. The prevalence of VC-negative sites provides similar information but allows the user to evaluate the certainty around the estimate. Uncertainty arises from several sources including the following: i) the results represent a sample rather than a census of herds; ii) the results are based on herd data collected at a point-of-time, iii) the specimens are collected from a sample of animals within those herds with different herds using different sampling strategies and intensities; and finally iv) diagnostic tests are imperfect and can give false results. These methods account for these uncertainties when providing the prevalence estimate.

For regions with no known VC-positive herds, the probability the region is free of herds with circulating virus is reported. This probability increases with the number of VC-negative herds, the confidence in the status of these herds and the number of herds in the region.

In all regions the percent of VC-negative herd days is reported. The VC-negative herd days is similar to the prevalence but describes the status over the entire month rather than a single day. Some regional project leaders have noted that although participating herds continue to experience PRRS outbreaks, they are returning to a negative status more quickly. The herd days may help to quantify and describe this activity.

The number of herds changing to VC-positive may be equivalent to the number of PRRS outbreaks in the period. The term outbreak, however, is not used because many regions consider outbreaks to be the occurrence of clinical disease regardless of whether the herd is previously positive or negative. The reported outcome is chosen because the number of new positive herds reflects the change in status in the region.

As described under the herd-report, herds without circulating virus accumulate points for diagnostic testing. The status-score to claim and maintain a VC-negative status differs by herd type and reason for production. To facilitate benchmarking between herds, the status-score is converted to an index with 1 equal to the baseline-score. This is summarized for the region as the median and interquartile range of the indexed status-scores for participating VC-negative or VC-unconfirmed herds (Figure 9 Page A). It is also illustrated in graphs with the index

status-score on the y-axis and time on the x-axis in Figure 9 Pages B & C. Spikes below the x-axis denote that the herd changed status.

Information on the indexed status-score is included to help regional leaders make monitoring decisions. Regional control and elimination projects that cover diagnostic testing using public or project funds need ways to measure and improve monitoring efficiency. The score-distribution in the region is paired with the graphs on pages B & C of Figure 9 because the distribution is used to decide what, if any, changes should be made in the monitoring strategy and the individual charts are used to determine where to best apply those changes. This information could be used to develop a least-cost monitoring plan. Therefore it is presented along with average expenditures per herd based on a standardized test cost of $10 per ELISA and $40 per PCR.

The final page (Figure 9, Page D) of the regional-report includes two graphs. The top graph shows the number of herds changing to PRRS VC-positive status each week. The bottom graph describes the reported historical rate per week of PRRS outbreaks for the previous five years. This graph could be changed to show the trend over time as data become available. These graphs are included for two reasons. First, these outcomes dictate the rate confidence decays over time. As the rate of outbreaks in the region increase, the rate of decay also increases so these graphs can be used to understand why more or less testing is being required. The trend in the rate of outbreaks can also be monitored; although not a perfect experiment the rate of outbreaks should theoretically decrease following the implementation of effective interventions.

Inter-Regional Report

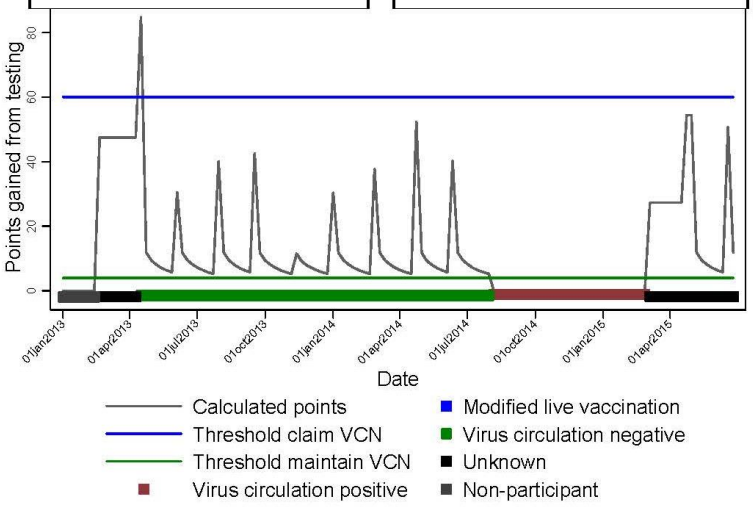
An inter-regional report is designed to be generated quarterly. The example provided includes the three simulated regions (Figure 10). In practice, regional control and elimination projects would need to provide permission for some or all of their information to appear on this report. The inter-regional report contains key outcomes from the regional report in the most recent quarter. The purpose of this report is to facilitate comparisons and stimulate discussion among regions without having to share any herd-level (and thus potentially confidential) information.

PACIFIC OCEAN—SITE 3

Herd Description	
Herd Type	Wean to Finish
Business Type	Commercial
Immunization	none
Score claim negative	60
Score to maintain negative	4
Historical weekly risk	2.5%

Current Status & Risk 06/25/15	
Current Status	Unknown
Days since status change	112
Testing Recommendation	Yes
Herds within 10 km reporting clinical signs	0
Herds within 10 km reporting change to Virus Circulation Positive	0

Herds within 10 km	
Number of Sites	2
# vaccinating	0
# wild strain positive	1
# negative	0
# unknown	1
# non-participating	0



Nearest **Neighbors**		
Herd Type	Distance (km)	Status (score)
Farrow to finish	7.5	Pos-wild
Farrow to feeder	6.0	unknown
n/a		
n/a		
n/a		

	Current			Previous complete		
	Month to date	Quarter to date	Year to date	Month	Quarter	Year
End Date in report period	25-Jun-15	25-Jun-15	25-Jun-15	28-May-15	26-Mar-15	24-Dec-14
Status at end of period	Unknown	-	-	Unknown	Unknown	Pos-wild
Average score over period	19	23	16	9	8	7
# Status changes over period	0	0	1	0	1	1
# Diagnostic submissions	1	2	4	0	2	7
# Clinical reports	0	0	0	0	0	0
Expenditure (standardized)	90	140	280	0	140	950

Generated for demonstration only using simulated data

Figure 8. Herd Report for an example herd in an example region.

PACIFIC OCEAN PROJECT— Report for June 25, 2015

Description	
Density (herd / $km^{2)}$	$6.2*10^{-3}$
Total herds	110
Breeding	51
Growing	59
Other	0
Commercial	90
Genetics	20

PRRS virus Status	Current Month	Prior Month	Prior Quarter	Prior Year
End Date	25Jun2015	28May2015	26 Mar 2015	24Dec 2015
Prevalence VCN (95% CI)	4.5 (1.4—10.3)	6.8 (2.8—13.5)	8.7 (4.1—15.9)	6.8 (2.8—13.5)
Probability PRRS-Virus Free	0	0	0	0
% VCN Herd Days	5.2	6.6	7.3	5.2
# herds changing to VCP	14	3	0	9
Median Index Score (*IQR*)	1.7 (0.8—3.1)	1.5 (0.6—2.3)	6.7 (2.0—4.7)	2.0 (1.3—3.6)

Breeding & High Health Herds

	Current	Prior Month	Prior. Quarter	Prior Year
Number (%) participating	51 (100%)	46 (90%)	46 (90%)	49 (90%)
Number Unconfirmed Status	37	29	29	28
Number virus-circulation negative	3	3	4	3
Number Positive (Wild Virus)	25	19	18	18
Number Positive (Vaccination)	9	7	7	7
Average expenditure / herd over period	565	155	747	3307

Growing Herds

	Current	Prior Month	Prior. Quarter	Prior Year
Number (%) participating	59 (100%)	57 (97%)	57 (97%)	57 (97%)
Number Unconfirmed Status	43	39	40	42
Number virus-circulation negative	2	4	5	4
Number Positive (Wild Virus)	24	18	18	21
Number Positive (Vaccination)	17	17	17	17
Average expenditure / herd over period	364	128	448	2014

Figure 9 – Page A. Regional Report for an example region.

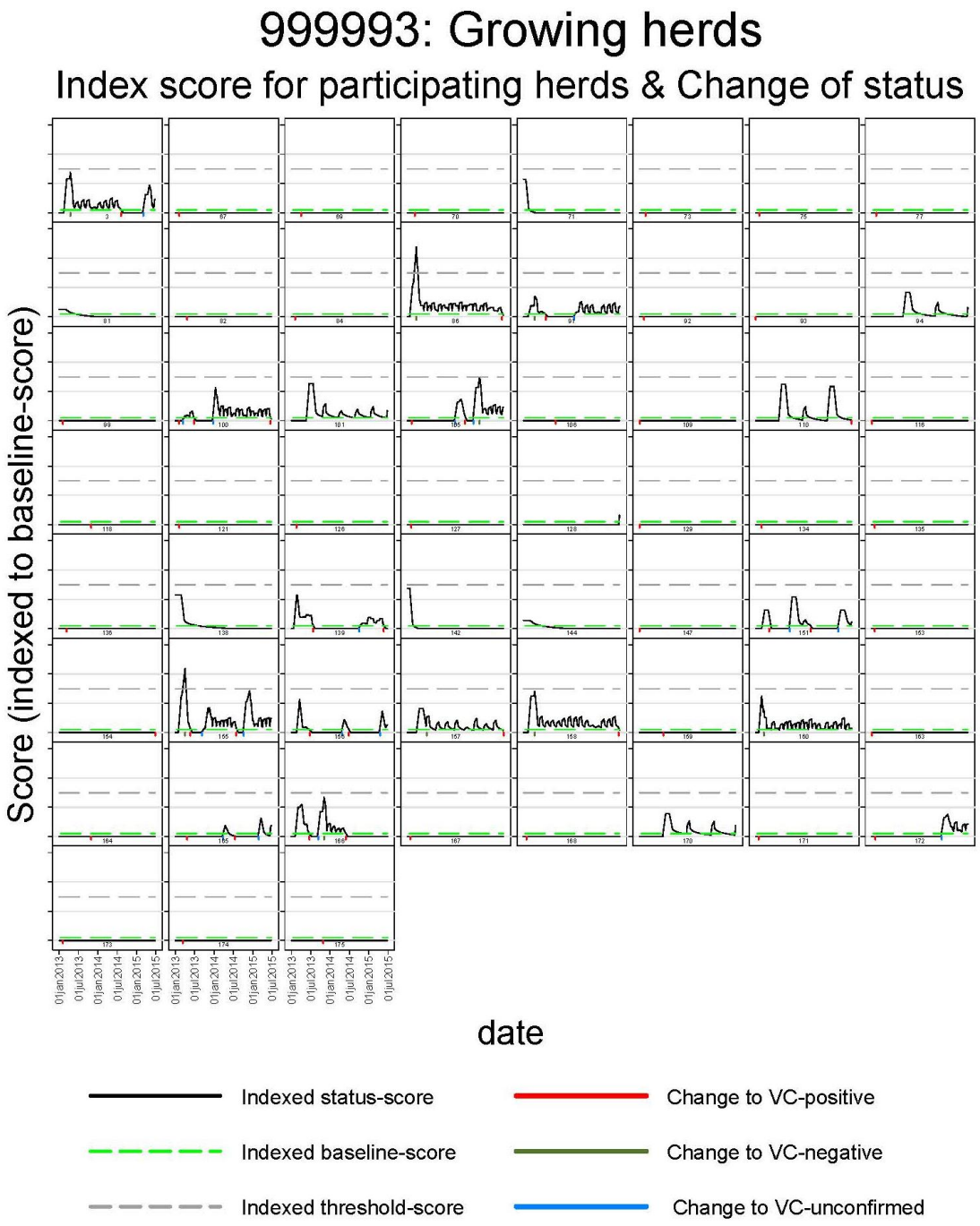


Figure 9 – Page B. Regional Report for an example region.

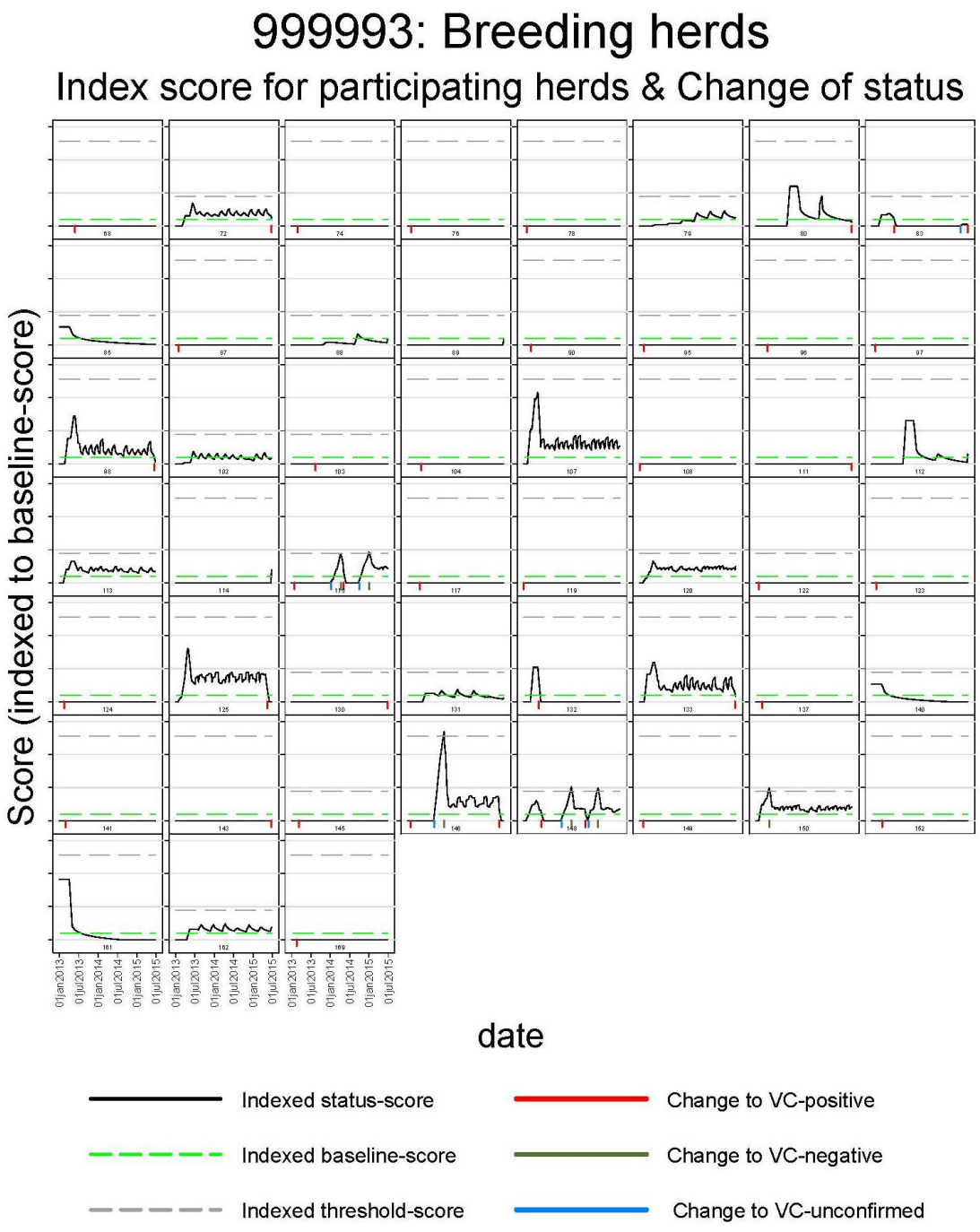


Figure 9 – Page C Regional Report for an example region.

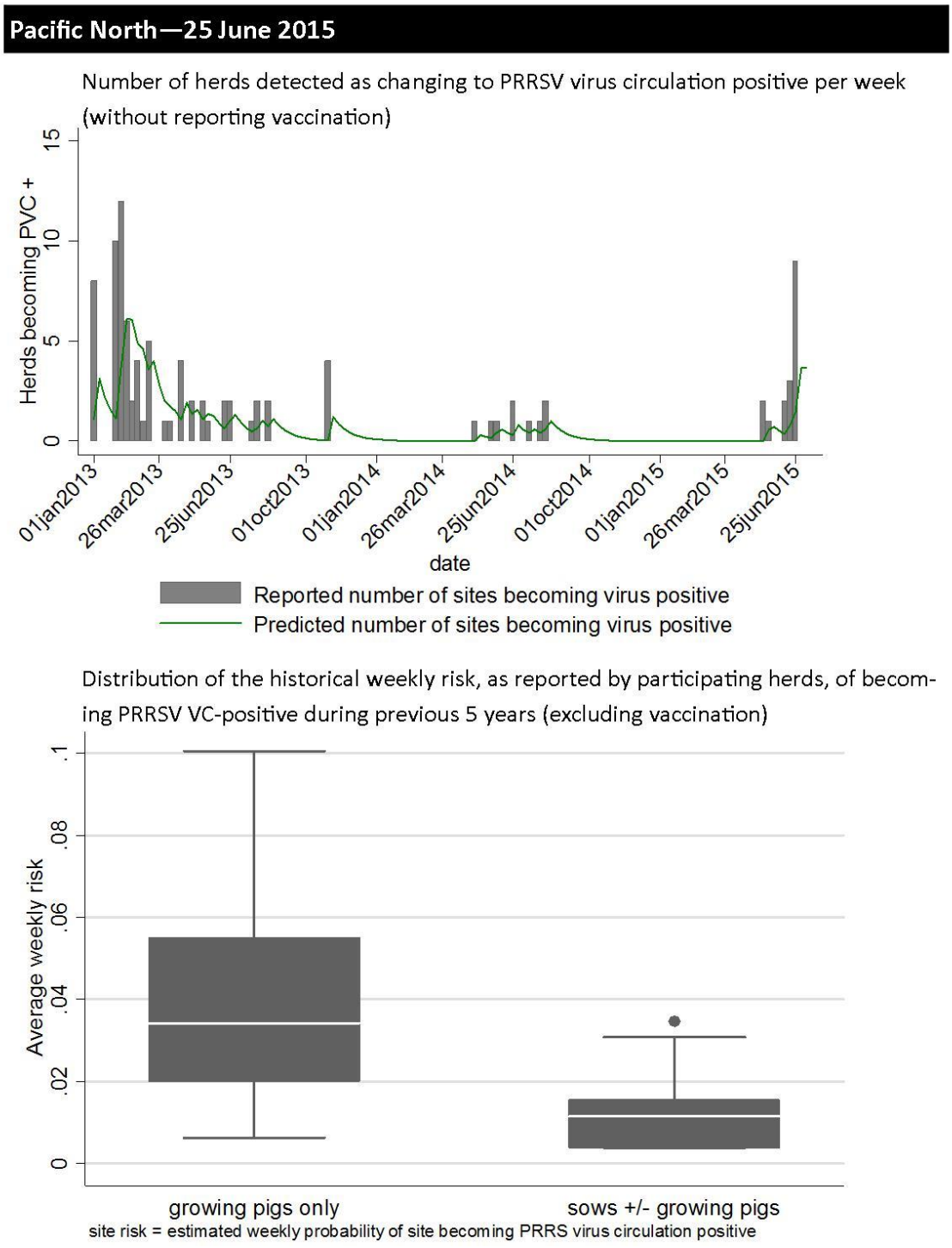


Figure 9 – Page D. Regional Report for an example region.

INTER-REGIONAL REPORT - QUARTERLY - JUNE 2013

	North Atlantic	Indian Ocean	Pacific Ocean
Density (herds / km^2)	$1.0*10^{-2}$	$2.5*10^{-1}$	$6.2*10^{-3}$
Area (km^2)	1963	176	17671
Total Herds	20	45	110
Breeding Herds	10	21	51
Growing herds	10	24	59
Other	0	0	0
Participating herds (%)	20 (100%)	45 (100%	110 (100%)
Known status (%)	10 (50%)	37 (82%)	80 (73%)
PRRSV Status			
Prevalence VC-negative (95% CI)	45 (23—68)	2.2 (0—12)	4.5 (1.5—10)
Probability PRRSV Circulation Free	0	0	0
Percent VC-negative herd days in previous quarter	45%	2.2%	6.6%
Changes to VC-positive (vaccine)	0	1	11
Changes to VC-positive (infection)	0	0	6
Median Index Score (*IQR*) in herds with score>0	3.7 (2.8—5.0)	4.3 (2.6—4.9)	3.2 (1.8—4.3)
BREEDING HERDS			
Number VC-negative	2	0	9
Number VC-positive (Wild Virus)	0	10	25
Number VC-positive (Vaccination)	0	8	9
Avg. $ / breeding herd	719	1412	995
GROWING			
Number VC-negative	7	1	2
Number VC-positive (Wild Virus)	1	16	24
Number VC-positive (Vaccination)	0	2	17
Avg. $ / growing herd	239	527	710

Figure 10. Inter-Regional Report for an example region.

DISCUSSION

Regional control and elimination projects differ from research studies or surveys because participation is voluntary and sampling is determined by the herd owner rather than the project. Analysis is complicated by non-random sampling, a hierarchical data structure, and repeated measures. This project attempts to apply statistically valid methods to data typically collected by PRRSV regional control and elimination project to facilitate comparisons over time and regions. The objective is to make regional PRRSV status descriptions standardized and transparent while maintaining flexibility in how regions obtain the information.

The methods use the framework of the PRRS-Free Herd Certification project. This Canadian program has established a process for ongoing declarations that herds are PRRSV exposure negative. This project builds on that tool by (1) extending PRRSV-status classification from herds to regions (2) incorporating the AASV standards to classify herds by PRRSV status (3) developing a process to declare herds as PRRS VC-negative (rather than PRRSV exposure negative), (4) utilizing the herds' and regions' history of outbreaks to adjust the temporal decay, and (5) incorporating testing options that have been recently recommended to the PRRS Free Certification Program.

In this project, herds are classified according to their virus circulation status. This differs from the PRRS Free Certification project which uses virus-exposure status. The outcomes differ because the purpose of classification differs. This project classified herds to describe regional status and understand area risk. The PRRS Free Certification classifies herds to facilitate trade in Canada. Herds that are PRRSV exposure positive but circulation negative (i.e. IIA, IIB, or III) have a greater potential for misclassification than herds classified as positive unstable (I) or negative (IV). This misclassification risk is considered unacceptable in the PRRS Fee Certification Project. However, for this project it is considered acceptable because herds with and without circulating virus pose very different area risks while those with virus exposure but no circulation (i.e. IIA, IIB or III) do not pose a substantially different area risk from negative (IV) herds.

These methods generate reports for regional project participants and leadership teams. The regional report provides the information to compare the PRRSV status of the region over time and between regions (Figure 9). This information was the impetus for this project and there are several metrics included, that to the authors' knowledge, have not previously been generated by regional control projects. Below are our opinions on how the information could be used.

The regional report includes the prevalence of VC-negative herds. Regions may shift to using prevalence estimates instead of herd-status counts to describe their region because it more precisely defines the VC-negative status. The confidence intervals may be used to help make monitoring intensity decisions. A region could plausibly set targets that trigger more sampling if uncertainty about the prevalence becomes too great or if the upper limit exceeds a level which would dictate the region should be taking different actions.

The regional report includes a line describing the probability the region is PRRS VC-negative. Few, if any, regions will receive a result other than non-applicable. However, we believe it is important to retain this line in the report. Freedom from disease modeling is a rapidly evolving field which many international bodies now recognize as a valid. This will be useful for informing participants about the difference in VC-unconfirmed and VC-negative at the herd level and may initiate conversations about the monitoring that will be needed if and when elimination is successful.

The regional report includes the percent of PRRSV-negative-days because we believe this can be used to motivate or encourage participants. When herds become infected with PRRSV it is demotivating. This is particularly true in small regions where a few herds may represent a substantial proportion of participants. The PRRS-negative-days

counteracts this because the effect is cumulative daily so it is less subject to sudden changes. In regions striving to mass-vaccinate this could easily be replaced with PRRS-vaccinated pig days.

Lastly the median index status-score is included in the regional report because it can be used in conjunction with the prevalence confidence intervals. This metric is most useful in regions that are mature and relatively stable for PRRSV. In these situations, few herds will be doing intense testing to demonstrate PRRS VC-negative while most will be working to maintain their status. Regions could encourage monitoring strategies that have a median slightly above one with a narrow inter-quartile range. This would indicate that sufficient but not excessive information is known about most herds.

This project was initiated because the question had been posed "How much testing is enough in a PRRSV regional control and elimination project?" The methods are intentionally designed for use in existing projects. So, two regional projects were approached to pilot these methods. Up to five years of retrospective data, or retrospective data to the start of the project, were requested. One project elected to participate by providing electronic records. The other chose to participate by providing raw retrospective data. Neither project used the developed data collection tool.

In the region that provided electronic records retrospective data to the beginning of the regional project were used. The data were manually manipulated, cleaned and validated. While this was feasible for a pilot it would not be practical ongoing or for multiple regions. Feedback was sought from the regional leaders and their consultants on the herd and regional reports. They noted the reports contain different information than they currently generate and provided an alternative way to examine their monitoring strategy. They also noted that the criteria to claim and maintain a VC-negative status is more stringent than the region is using. Finally, the herd status of vaccinated herds was different in this project than they are using. This meant that the region was described quite differently. This was potentially confusing for users but re-enforced our belief that there is a need for standardized reporting methods to facilitate communication among regional projects.

In the region that provided raw data, the authors compared the data available to the required variables and decided that there were too many missing variables to proceed. This confirmed our prior belief that regional projects differ both in what and how they collect and manage data. For regions that are currently managing data manually (i.e. without customized databases) these methods could provide an inexpensive way to generate more information from their current diagnostic monitoring results. However, to do so the project may need to change or increase the data currently being collected.

Overall, by piloting these methods in existing projects the following lessons were learnt. First, more than one data entry method will be required in order to accommodate existing electronic and manual systems. Secondly, communication and consensus is needed on what variables should be collected in a minimum dataset to enable inter-regional comparisons. Finally, regions differ in how herds are classified. Standardization is needed to facilitate inter-regional communication, evaluate the effects of interventions, and track progress in control and elimination on a national scale.

This project provides value to regional control and elimination projects. Freedom from disease modelling is a rapidly developing field that is becoming accepted in international trade. The types of outcomes provided by these methods will be required by regions achieving and claiming PRRSV freedom. Until that happens, the methods will provide useful information to regions striving to control PRRSV.

REFERENCES

Cameron, A., 2009. Risk-Based Disease Surveillance. A Manual for Veterinarians. FAO, Rome, Italy.

Cannon, R.M., 2002. Demonstrating disease freedom - combining confidence levels. Prev. Vet. Med. 52, 227-249.

Christensen, J., Gardner, I.A., 2000. Herd-level interpretation of test results for epidemiologic studies of animal diseases. Prev. Vet. Med. 45, 83-106.

Corbellini, L.G., Schwermer, H., Presi, P., Thur, B., Stark, K.D., Reist, M., 2006. Analysis of national serological surveys for the documentation of freedom from Porcine Reproductive and Respiratory Syndrome in Switzerland. Vet. Microbiol. 118, 267-273.

Corzo, C.A., Mondaca, E., Wayne, S., Torremorell, M., Dee, S., Davies, P., Morrison, R.B., 2010. Control and elimination of Porcine Reproductive and Respiratory Syndrome virus. Virus Res. 154, 185-192.

Dee, S., Deen, J., 2001. Establishment of a PRRS virus ELISA-negative boar population using previously exposed boars. Vet. Rec. 149, 678-680.

Dee, S.A., Bierk, M.D., Deen, J., Molitor, T.W., 2001. An evaluation of test and removal for the elimination of Porcine Reproductive and Respiratory Syndrome virus from 5 swine farms. Can. J. Vet. Res. 65, 22-27.

Frossling, J., Agren, E.C., Eliasson-Selling, L., Lewerin, S.S., 2009. Probability of freedom from disease after the first detection and eradication of PRRS in Sweden: Scenario-tree modelling of the surveillance system. Prev. Vet. Med. 91, 137-145.

Holtkamp, D., Polson, D., Torremorell, M., et al., 2011. Terminology for classifying swine herds by Porcine Reproductive and Respiratory Syndrome virus status. JSHAP 19, 44-56.

Hurnik, D., 2001. A producer supported regional program for PRRS and TGE control and eradication. AASV Swine Library 19, 23-24.

Linhares, D., Torremorell, M., Morrison, R., 2013. Time to produce PRRSV-negative pigs from infected breeding sites. AASV 59-60.

Mussell, A., Oginsky, A., Grier, K., Morin, M., Lachance, M., Whittington, L., Friendship, R., 2011. A risk, benefit, strength, weakness, opportunity and threat analysis for the control and possible eradication of Porcine Reproductive and Respiratory Syndrome (PRRS) virus within the Canadian swine herd. 1-122.

OIE, 2008. Appendices IV and V of the report of the OIE *ad hoc group* on Porcine Reproductive and Respiratory Syndrome. PRRS: The disease, its diagnosis, prevention and control. Paris, 9 - 11 June 2008.

Tousignant, S., 2013. Sow herd incidence and prevalence study. Proc AASV Conf 419-420.

Yang, J.S., Moon, H.J., Lee, C.S., Park, S.J., Song, D.S., Kang, B.K., Choi, J.U., Park, B.K., 2008. Elimination of Porcine Reproductive and Respiratory Syndrome virus from a seedstock breeding farm and a supplying boar stud by a modified test and removal method. Vet. Rec. 162, 333-337.

APPENDIX 1 - DEFINITIONS & ABBREVIATIONS

Term or abbreviation	Definition
Region	A geographical area with boundaries defined by the users of the methods. All swine herds within these boundaries form the population of interest.
Premises	Buildings or areas containing pigs at contiguous locations with common employees, management, or both. Equivalent to site in this paper.
Herd	The population of animals at a defined premises.
Round	The diagnostic samples, and the diagnostic test results associated with those samples, collected within one day.
Breeding Herd	A herd with one or more sows or boars (with or without growing pigs)
Growing herd	A herd with no sows or breeding boars
AASV PRRS herd classification	As defined in Holtkamp DJ, Polson DD, Torremorell M, et al. Terminology for classifying swine herds by Porcine Reproductive and Respiratory Syndrome virus status. *J Swine Health Prod.* 2011; 19(1):44-56
PRRS virus Circulation status	Positive - Presence of circulating PRRSV (including vaccine) Negative – Absence of circulating PRRSV at given confidence and design prevalence Unconfirmed – Insufficient knowledge of circulation of PRRSV to claim negative but no evidence of virus circulation.
PRRSV	Porcine Reproductive and Respiratory Syndrome Virus
ELISA	enzyme-linked immunosorbent assay
PCR	polymerase chain reaction
Specificity	P (T-|D-) Probability that a test will be negative given the sampled unit is negative.
Sensitivity	P (T+|D+) Probability that a test will be positive given the sampled unit is positive.
Confidence	P (T+|D+) Probability the system will detect at least one (true?) positive test given the population is positive at or above the design prevalence Equivalent concept to the sensitivity of a test at the population level.
Apparent prevalence	The proportion of animals testing positive either due to being truly positive or false positive.
Design prevalence	A hypothetical prevalence that sets the standard for surveillance
Disease Freedom	P (D-|T-) Probability the region is negative given that no positive herds are detected.
VC-positive	Virus Circulation Positive - Presence of circulating PRRSV (including vaccine)
VC-negative	Virus circulation negative - Absence of circulating PRRSV at given confidence and design prevalence
VC-unconfirmed	Virus circulation unconfirmed – no evidence of circulating PRRSV but insufficient evidence to claim VC-negative
P^*_R	Regional Design Prevalence: the theoretical prevalence of infected herds that sets the standard for regions to claim PRRSV circulation negative
C_R	Regional Confidence: the confidence with which regions claim PRRSV circulation negative

Se_T	Test sensitivity
Se_R	Round sensitivity – net sensitivity from all tests in a round
Se_H	Herd sensitivity – net sensitivity from ongoing rounds
P^*_H	Herd design prevalence
n	number of tests
u	number of units (serum; 1 pig = 1 unit, oral fluids; 1 pen = 1 unit)
ps	pool size: number of units included in each pool
Score	A translation of herd sensitivity Status-score: a herd level description of the degree of confidence the herd is truly negative Threshold-score: the score that must be exceeded in order to classify a herd as VCN Baseline-score: the minimum score that must be maintained to continue classifying a herd as VCN
E_T	Estimated number of PRRSV outbreaks in week T
$R_{historical}$	Historical rate of PRRSV outbreaks in each herd (as reported by the herd)
R_{est}	Estimated rate of PRRSV outbreaks in week T
R_{median}	Median weekly outbreak rate in region over prior 5 years
R_{week}	Level of weekly PRRSV outbreak rate relative to median of historical rate
R_{6w}	Average of weekly risk for 3 weeks prior, current week, and 2 weeks forecast
R_H	Estimated herd weekly risk of PRRSV outbreak
D	Temporal decay rate