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Elimination of PRRSV from North America: Uniting the clans!

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University of Minnesota College of Veterinary Medicine

This lecture is dedicated to Drs. Tom Burkgren and Rod Johnson.
Thank you for all that you have taught me during the long, strange 20 year trip with PRRS.

Personal note: *This is a talk I have wanted to give for many years and today is the perfect time. Recent actions have confirmed my internal belief that when provided science-based facts upon which to base their decisions, veterinarians and producers are able to think rationally and act collaboratively in a manner that benefits the health and well being of man and animals. It is now my challenge to convince you today that the recent bursts of activity in the field of PRRSV elimination are realistic premonitions of a successful future and not the return of ghosts of failed efforts from the past….*

Chapter 1: What a long, strange trip it's been!

"Sometimes the light's all shining on me,
Other times I can barely see.
Lately it's occurred to me,
What a long, strange trip it's been…"
(J. Garcia, B. Weir, P. Lesh, R. Hunter)

The Grateful Dead, from the 1970 album
"American Beauty"

Those of you who are Grateful Dead fans will no doubt recognize the title to this first chapter of the lecture. While I am not personally a hardcore "Dead head", this excerpt from one of the most popular Dead tunes really hits home with me, particularly as it regards my experiences with PRRS, something which I have dedicated my entire professional life to solving. I graduated from veterinary school at the University of Minnesota in 1987 and had my first encounter with the disease in the early 1990s. Frustrated with my inability to solve the problem, I entered graduate school to pursue my PhD with Dr. Han Soo Joo in an effort to develop strategies to successfully control this monster that was engulfing my clients, one by one. I left practice after 12 years and joined the University of Minnesota because I was not able to focus all my efforts on solving the mystery of area spread of PRRSV. For the last 11 years as a faculty member, I have been focusing my research efforts of developing and validating biosecurity methods to reduce this risk. That's a total of 23 years (nearly 50% of my life) that has been spent trying to solve this problem.

Can you spell LOSER?

During this period, I am sorry to say that I have experienced the profession at its worst when it came to dealing with the challenge of PRRS, for example:

1. The initial attempts in the late 1980s and early 1990s to discover the etiology of the disease and all the battles that raged between the various Universities, everyone fighting each other instead of working together.
2. The 2004 AASV closed door session where cruel accusations were made, fingers were pointed and conflict of interest raised its ugly head.
3. The 2006 AASV annual meeting where dissention over the recently published AASV position statement that "Eradication of PRRS from the North American pig population was the long term goal" ran rampant throughout the membership.

What a mess!!….

I must tell you that these experiences caused me to have many sleepless nights pondering the impact of this disease on the industry and the role that our profession would play in either being part of the problem or part of the solution.

But now its 2010!

What a difference a few years make; talk about a change for the better! First of all, a resolution gets passed at the National Pork Forum calling for a united goal of eliminating PRRSV from the US swine herd. What makes this story even more intriguing is that producer delegates from several states worked together to amend its initial wording and the resolution passed. Unbelievable! Then, during the week of June 7-11, while at the World Pork Expo, I experienced this "series of very fortunate events":

June 7th: A meeting of PRRS CAP 2 and NPB funded researchers and stakeholders where a repeated message heard from CAP 2 leadership (Dr. Bob Rowland) throughout the day was that PRRSV elimination was an essential component of the CAP 2 effort.

June 9th: A meeting organized by Dr. Dale Polson and the BI Area Solutions Team in which over 100 veterinarians actually sat together in one room and calmly discussed the status of several area/regional control and elimination (ARC&E) projects currently underway in the United States and Canada (Figure 1).

June 10th: A meeting organized by AASV president Dr. Paul Ruen on the topic of PRRSV elimination for producers. Over 100 producers joined together to get updates on the latest developments regarding this controversial subject. In contrast to meetings over the past few years, the atmosphere was upbeat and many excellent questions were raised and issues of interest were discussed in depth.

June 11th: I was privileged to be a part of a discussion on ARC&E with an audience made up of media professionals from the major lay journals of our industry, such as Pork, National Hog Farmer and Farms.com, just to name a few. The outcome of this session was numerous articles on the potential for a life without PRRSV, all which contained a positive spirit with the hope of a better future.

"What a long, strange trip it's been!"

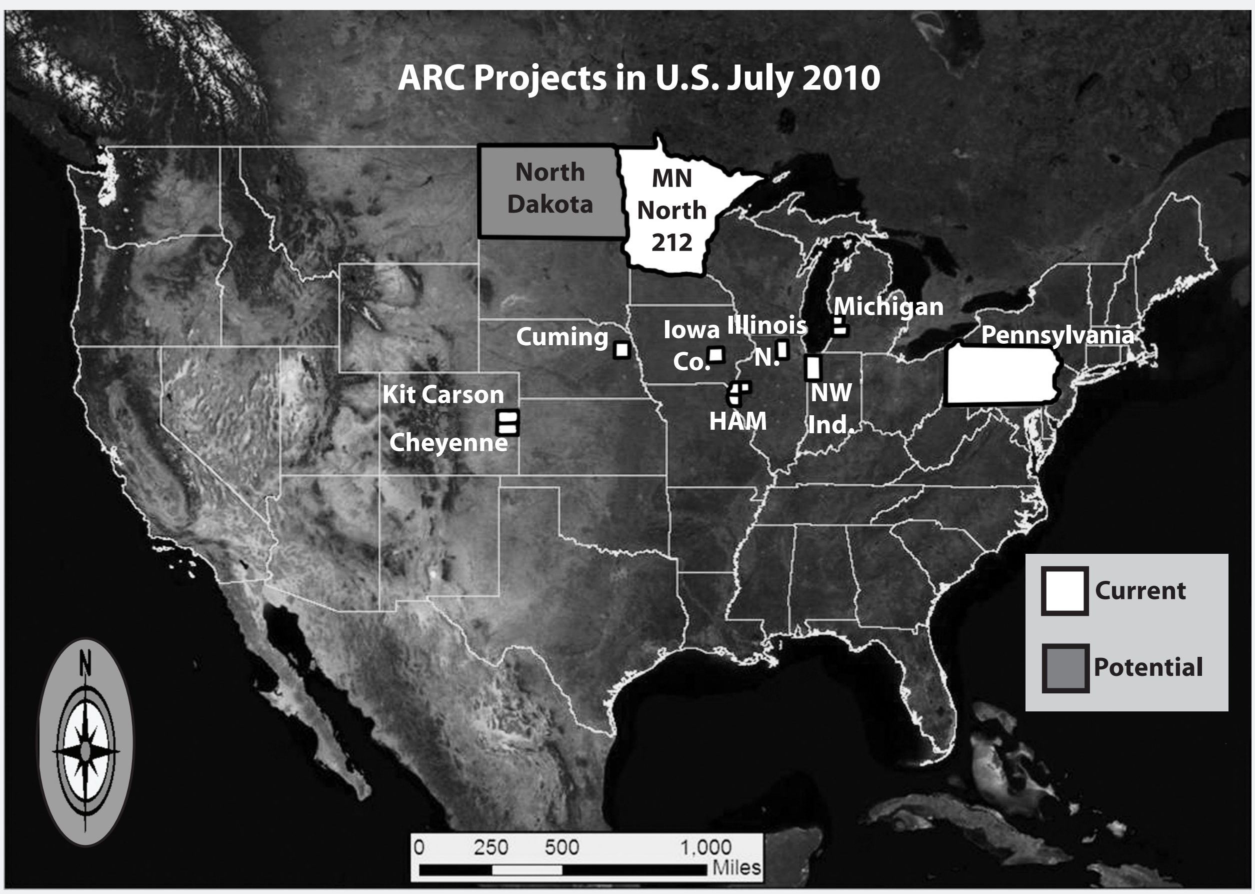
What happened?

I left Des Moines excited yet puzzled; enthused, yet confused. How could we suddenly go from such a negative attitude towards the future of PRRS in North America just a few years ago to the events of 2010? Well, after much contemplation, I have identified 5 "**Drivers of Change**" whose collective philosophy has propelled us to a new attitude towards the future of the disease never before achieved over the past 20+ years, including:

1. **UNDERSTANDING**
2. **NECESSITIES**
3. **INNOVATIONS**
4. **TEAMWORK**
5. **EDUCATION**

In my opinion, these "Drivers of change" have changed the way we think about the disease and our feelings regarding the ability to manage it in the future. While their significance is greater collectively, let's examine them individually:

Figure 1



Courtesy of Dr. Dale Polson and the BI Area Solutions Team

Chapter 2: The 5 drivers of change

Driver #1: UNDERSTANDING

We have come to an **UNDERSTANDING** regarding several key principles that are essential to our message regarding the elimination of PRRSV. These key principles must be translated clearly across all audiences, especially to producers, for example:

1. This is a voluntary effort. Nobody is proposing a regulatory program or any type of government intervention, other than potentially providing funding for research and surveillance. In addition, no one is proposing any restrictions on pig movement. This is not a PRV program by any means.

2. This will be market-driven, not federally mandated. In my opinion, as it did several years ago regarding the sale of PRRSV-infected breeding stock and semen, the market will drive the establishment of a PRRSV-naïve weaned pig market. Already throughout the industry, PRRSV-infected weaned pigs are being refused or being discounted on average at a rate of $4 dollars per animal (J. Waddell, personal communication 2010). No one will prevent you from selling them; however, there will be a significant economic disincentive. This will be especially apparent in shareholder-driven cooperatives that operate on weaned pig contracts as well as pigs crossing the US-Canadian border. The market pressure will result in clean-up of infected breeding herds along with the implementation of biosecurity practices to keep them (as well as down-stream pig flow) free of PRRSV.

3. This will be a strategic, science-based effort. This effort will be based on the use of carefully designed pilot projects, initially conducted in areas of low density which will then move into areas of high density, which will no doubt require different approaches than those in areas of low pig density. Furthermore, as new research data becomes available, protocols will be modified accordingly, resulting in an elimination plan that is a "living document", one that is extremely flexible and can be applied according to the unique needs of individual farms and regions.

4. This will be a team effort. No one can do this alone; we need to build teams. Teams of practices, teams of producers and teams of scientists. A spirit of collaboration and philosophy of mutual benefit for all must be established across the team. Clearly, this will be very difficult to do as it is against our nature; however, in the absence of this approach, the effort is doomed to fail.

Driver #2: NECESSITIES

We have come to a consensus that we now possess the **NECESSITIES**, i.e. the basic fundamental tools and knowledge to begin ARC&E projects. While it is true we do not have a perfect vaccine (I doubt that we ever will), we do have:

1. An effective means to eliminate PRRSV from individual farms in the technique known as "herd closure."

Previous publications proposed that the presence of breeding herd subpopulations in conjunction with the continuous introduction of replacement gilts promoted viral circulation within endemically infected populations.[1,2] In 1998, a proof-of-concept paper was published demonstrating successful elimination of PRRSV and showing the world that it could be done.[3] Building on this work, the pioneering efforts of Drs. Montserrat Torremorell, Butch Baker and Bill Christianson realized that the practice of preventing the introduction of replacement gilts into the breeding herd for a period of approximately 210 days was as an effective means to eliminate virus,[4] a strategy has proven to be highly repeatable in the field and is now the primary means of eliminating PRRSV from endemically infected breeding herds.

2. A means to diagnose and characterize viral infections in "real time" through the use of molecular diagnostics.

Advancements in molecular diagnostics, such as PCR and nucleic acid sequencing have made it possible to accurately diagnose new outbreaks faster than ever before, quantify viral load in samples and to track the movement of viruses in regional epidemics. In addition, the ability of diagnostic laboratories to provide electronic reporting of results in real time (12-24 hours post-submission) has been a tremendous advantage to practitioners and researchers. I would like to personally thank Drs Jim Collins and Kurt Rossow, along with Ms. Carrie Wees and her team of molecular diagnosticians at the Minnesota VDL for the outstanding service they have provided during my research efforts, especially over the past 4 years when I relied on real-time molecular diagnostics to make decisions.

3. The ability to make regional maps using Geographical Information Systems (GIS) technology.

In this case, "a picture is truly worth a thousand words" as the ability of practitioners to develop maps of their client farms through the application of GIS has been very helpful in understanding the status of herds within a defined region as well as track the spread of new PRRSV epidemics. Dr. Peter Davies' efforts in the development of a web-based GIS looks to be a great tool for coordinating efforts across clinics, systems and regions.

4. A tool to measure and manage internal and external PRRSV risk.

Thanks to the genius and generosity of Dr. Dale Polson and the efforts of Dr. Derald Holtkamp, the Production Animal Disease Risk Assessment Program (PADRAP) has been made available to AASV members. The mission of PADRAP is to support collaborative, epidemiologically-based initiatives to help producers and veterinarians manage PRRSV risk. It offers a series of risk assessment questionnaires, databases and reports for measuring and benchmarking disease risks. There are now web-based risk assessment programs for the breeding herd and grow-finish population. As of this writing, 229 veterinarians had been trained to use version 2 of the risk assessment program for the breeding herd, with 1981 assessments completed across 1161 sites. In regards to the grow-finish assessment which was completed in March 2009, 155 assessments and 120 sites had been completed when this manuscript went to press.

5. An improved understanding of PRRSV area spread.

Thanks to the tireless efforts of many people, we now have a very in-depth understanding of how PRRSV is transmitted between farms, critical knowledge that we must have in order to prevent re-infection. While the ability of PRRSV to be transmitted via direct (infected pigs and contaminated semen) routes[5,6] and mechanically via indirect routes (fomites, personnel, transport vehicles and insects)[7-15] is well-documented, perhaps the biggest breakthrough in this area has been the new knowledge regarding the aerobiology of the virus. The combined efforts of Dr. Jeff Zimmerman's group at ISU and our group at the SDEC have provided proof of the ability of this virus to spread via the airborne route. Some key facts from these efforts are as follows

A. Infectious PRRSV can be recovered from bioaerosols emitted from infected source populations of grow-finish pigs.[16]

B. The frequency of viral shedding in aerosols, the ID_{50} in aerosols and the transmission of PRRSV in aerosols is isolate-specific.[17-19]

C. The $T_{1/2}$ of PRRSV in aerosols is influenced by temperature and humidity.[20]

D. Risk factors associated with the presence of PRRSV in aerosols include winds of low velocity with sporadic gusts moving in the direction from a shedding source population to an at-risk population in conjunction with cooler temperatures, higher relative humidity and low levels of sunlight.[21] (Tables 1 and 2)

E. Long distance airborne transport of infectious PRRSV has been reported out to a 4.7 and 9.1 km.[22,23]

In summary, we now have proof that airborne spread of PRRSV is a reality; essential information for preventing area spread of the virus.

Driver #3: INNOVATION

Based on feedback from the field, there have been 2 key **INNOVATIONS** that have helped to elevate producer and practitioner confidence that we have the ability to successfully attempt ARC&E projects: oral fluid sampling and air filtration. At this time, I would like to provide an overview of the important messages that have come forward from this research that I believe will provide the greatest impact in the field.

1. Oral fluids

Derived from a technique commonly practiced in human medicine, the use of oral fluids appears to be a very effective means to evaluate the presence of pathogens in across large populations of pigs. In addition, the use of cotton ropes placed in pens to collect these samples has been an ingenious, cost-effective, labor-saving alternative to blood testing that has significant application to the success of ARC&E projects. Credit again goes to the efforts of Drs. Jeff Zimmerman and John Prickett for devising and validating this clever solution. Reviewing their published work, several key

Table 1: Differences in mean meteorological variables recorded on PRRSV-positive air days as compared to negative air days.

Variables	PRRS (+)mean	PRRS (–) mean	*P*
Temp (˚C)	1.1	6.3	.01
RH (%)	80	76	.002
Wind velocity (m/s)	1.7	2.1	.004
Gust velocity (m/s)	3.3	3.5	.23
Pressure (hPa)	981	979	.03
Precipitation (mm)	.002	.006	.08
Sunlight (watts/m^2)	139	165	.05
Sunlight (µmol/m^2/s)	403	480	.04

Table 2: Significant predictors of PRRSV-positive air days

PRRSV	Odds ratio	*P*
Building 1 shedding	3.63	.0002
Direction of wind	1.011 per degree	.0003
Minimum pressure	1.06 per hPa	.02
Mean RH	1.07 per %	.003
Mean wind velocity	.27 per degree	.002
Mean gust velocity	2.39	.002

take home messages that have immediate application the field include:

A. A standardized protocol for collection of oral fluids at the pen level and the individual animal level has been developed.[24]

B. PCR-based assays for testing oral fluid samples for PRRSV have been validated and its level of sensitivity is equal to that of serum.[25]

C. Antibody-based assays are currently being validated and preliminary data appear promising.[26]

D. PRRSV and PRRSV antibodies are stable in oral fluids and appropriate sample handling procedures will maintain integrity.[26]

I would like to congratulate and thank Jeff and John for the effort they put forth to bring this unique innovation to the industry.

2. Air filtration

Step 1: Identification of alternative filter candidates

Our group has spent the last 6 years evaluating the ability of air filtration to reduce the risk of the airborne spread of PRRSV and recent years, the spread of *Mycoplasma hyopneumoniae.* An idea originally pioneered by the French, it had little application to the US industry due to excessive cost and the requirement for positive pressure HEPA filtration systems. Therefore, we had a strong interest in developing not only an alternative system to better fit the facility designs and the budgets of our producers but we also wanted to develop a means to scientifically evaluate these alternative programs. The first step was to develop a dual chamber laboratory model to test and compare filter candidates.[27] This approach allowed us to challenge commercially available filters with artificial PRRSV aerosols of varying concentrations in order to identify candidates for use in negative pressure systems, such as mechanical filters (MERV 16 and MERV 14) and antimicrobial filters.[27]

Step 2: Application to AI centers

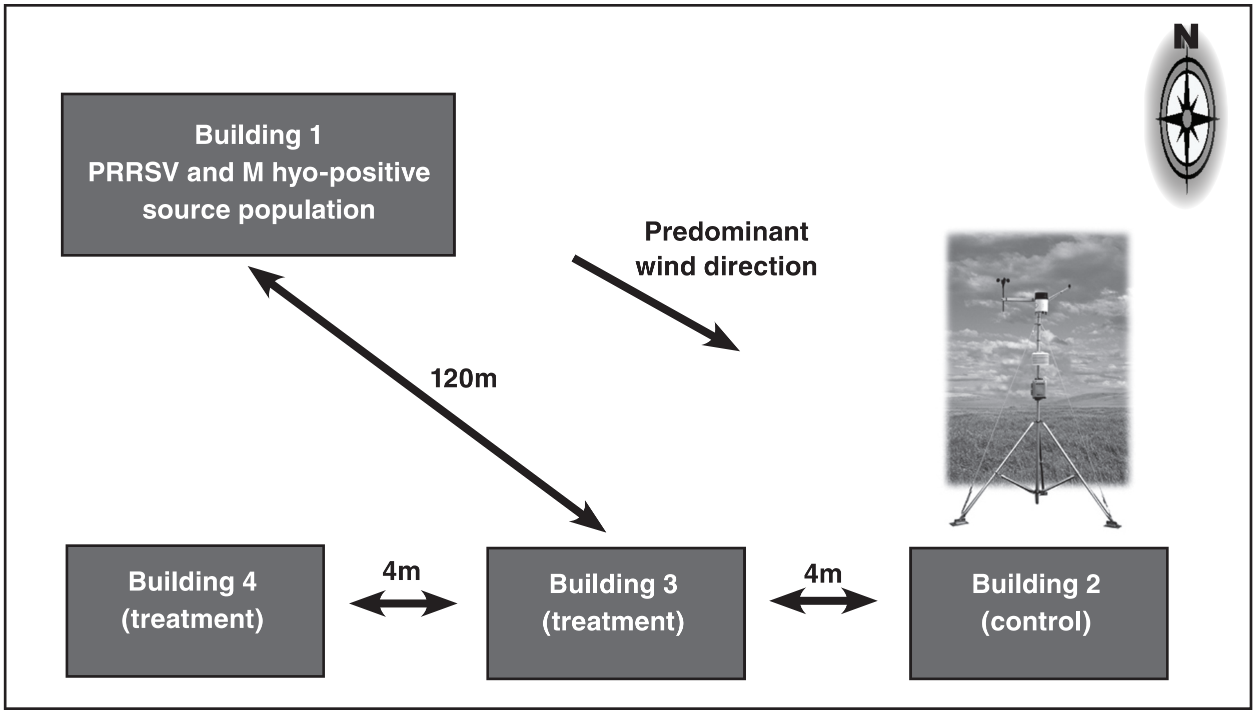
The first application of these new filter candidates was to AI centers and the results were amazing. Virtually "overnight", it became possible to consistently protect AI centers from the threat of annual external virus introduction, even when located in swine dense regions of southern Minnesota. As of this writing, there are over 25 boar studs under filtration which have been producing PRRSV-free semen for 5 years (D. Reicks, G. Spronk and C. Huinker, personal communication 2010).

Step 3: The production region model

The next logical application was to apply this technology to breeding herds in an effort to consistently produce batches of PRRSV-naïve weaned pigs. In other words, we had to solve the problem of area spread, and develop solutions which would prevent re-infection with new variants of the virus following completion of elimination methods targeting resident isolates. As a side note, we also wanted to do something big, to do something different, to "raise the bar" and forever "change the game" of how applied research projects for PRRSV transmission and biosecurity were conducted

To do so, we devised the "production region model" a working model that mimicked a "neighborhood" of pork production located in a swine-dense region, involving large populations of pigs housed under controlled commercial conditions (Figure 2). We wanted to generate reproducible episodes of airborne transmission of PRRSV through the selection of the proper isolate of PRRSV (MN-184) and operating a continuous flow source population of finishing pigs (n = 300) in order to generate a never-ending supply of infectious bioaerosols to challenge susceptible populations housed "downwind" in treated (filtered) facilities or control (non-filtered) facilities. This source population was later co-infected (year 2) with *Mycoplasma hyopneumoniae* and in year 4 with 2 additional PRRSV isolates, 1-18-2 and 1-26-2. In addition, we

Figure 2



planned to employ innovative air sampling technologies and to apply a highly sensitive PCR-based sampling protocol to accurately track the movement of the virus throughout the model.

From its humble beginning on June 1, 2006 the project has been in constant use and has taken on significant size and scope. On the date of this lecture, September 20, 2010, the study will have been in operation for 1401 days and will have utilized 4714 pigs. A total of 32,207 samples consisting of air samples, insect samples, swabs of incoming fomites and personnel and transport vehicles along with sera and nasal swabs from pigs will have been collected and tested by PCR. Along with the aforementioned new information on PRRSV aerobiology, the following facts regarding the use of air filtration technologies (mechanical filters, antimicrobial filters and electrostatic filters) for reducing the risk of airborne spread of PRRSV (and *M hyo*) have been generated:

A. Mechanical filters with a MERV 16 or a MERV 14 level of efficiency successfully prevent airborne transport and transmission of both PRRSV and *M hyo*.[16,21]

B. Antimicrobial filters successfully prevent airborne transmission of PRRSV and *M hyo* but do not prevent airborne transport.[21]

This information is summarized in greater detail in tables 3 and 4.

Step 4: Application to breeding herds

While these data clearly support the conclusion that air filtration is an effective strategy to reduce airborne risk, they were generated under extremely well controlled conditions where the use of a filter and/or the type of filter used were the only variables. In addition, the setting was a model of a cluster of farms and therefore consisted of small numbers of animals, housed in small facilities with single inlet openings and cared for by a small number of highly educated and goal-oriented professionals. Therefore, the next step was to test the technology in the field. While application was fairly easy and highly successful at the boar stud level, breeding herds were bigger challenges, involving large herds of animals, housed in large facilities that may be 10+ years old, along with an annual personnel turnover rate of approximately 50%. Furthermore, we wanted to test the technology under extremely challenging conditions, i.e. swine-dense regions of southern Minnesota and northwest Iowa. The desire to work under these conditions initiated a wonderful collaboration between the SDEC and 3 outstanding veterinary clinics: Pipestone Veterinary Clinic, Fairmont Veterinary Clinic and the Swine Vet Center. Working with Drs. Gordon Spronk, Paul Ruen and Darwin Reicks, along with the statistical expertise of Dr. Peter Davies, a study was designed that involved a group of filtered (treatment) breeding herds and non-filtered controls. To participate

Table 3: Summary of airborne transmission events of PRRSV and *M hyo* across filter types evaluated as compared to non-filtered control (June 1 2006-July 2010)

Pathogen	Control	MERV 16	MERV 14	Antimicrobial	Electrostatic
PRRSV	31/65[a]	0/39	0/13	0/22	0/9
M hyo	14/35	0/39	0/13	0/22	0/9

a # infections via the airborne route/# replicates

Table 4: Summary of airborne transport events of PRRSV and *M hyo* across filter types evaluated as compared to non-filtered control (June 1 2006-July 2010)

Variable	Control	MERV	*P*	Antimicrobial	*P*
# air samples PRRSV (+)	64/826	0/826	< 0.0005	18/316	0.12
# air samples *M hyo* (+)	23/636	0/636	< 0.0005	5/316	0.19

in the study, herds had to fulfill certain criteria:

1. Have breeding herd inventories of 2400 sows or more.
2. Be surrounded by 4 or more herds within a 4.7 km radius.
3. Have a confirmed history of 3 or more episodes of clinical PRRS secondary to the introduction of an external virus over the past 4 years.
4. Have practiced industry standard biosecurity involving the use of scientifically validated protocols for all known direct and indirect routes of PRRSV introduction in the absence of air filtration yet continued experience re-infection at the frequency described above.

One of the early outcomes of the trial was a publication by Dr. Gordon Spronk and others that described the results of a subset of treated (n = 2) farms and controls (n = 5).[28] Characteristics of selected herds and diagnostic data over the course of the 1-year study period are summarized in tables 5 and 6, respectively. Since this publication, the study has since entered the third year of its proposed 4 year project period. At this time, a total of 10 filtered herds have qualified for the project along with 21 control herds (Dee, unpublished data). While external virus introductions have occurred in 2/10 filtered farms, sources of the infection have not been linked to filter failure but rather to breaches in personnel and transport biosecurity. In contrast, 19/21 non-filtered herds have experience new virus introduction with multiple infections occurring in several of the herds over the 2-year period of time. Although further assessment of air filtration is required involving larger numbers of farms over longer periods of time, the preliminary results from these projects suggest that farms in dense regions of production are at risk of PRRSV airborne challenge and that the filtering of incoming air is an effective means to protect susceptible populations under highly challenging conditions.

In closing, if these 2 innovations prove to be sustainable over time, we may be on the edge of an industry-changing revolution in the areas of surveillance and disease control of pigs, a revolution that will change how we build the next round of facilities of the North American industry and how we monitor populations.

Driver #4: TEAMWORK

Effective **TEAMWORK** is essential for an ARC&E project to succeed. Perhaps the best example of a true team dedicated to the goal of eliminating PRRSV from a region has been Minnesota's own Stevens County Project, headed up by Dr. Bob Morrison. Since Bob will be discussing this project (and others) at another session today, there is no need for me to summarize any results at this time. However, it goes without saying that the success of Stevens County has buoyed producer confidence in the state on Minnesota regarding the feasibility for large-scale PRRSV control and elimination and has been the driver behind other projects currently underway in other states and Canadian provinces. While one can argue that this was not a hog-dense region such as Martin county or Sioux county, it is a "first-of-its-kind proof-of-concept model" that demonstrates that producers and practitioners can work together in a collaborative fashion to accomplish the long-term goal of area elimination.

Table 5: Characteristics of treatment (filtered) and control (non-filtered) sow herds selected for the study

Herd ID[1]	BHI[2]	# sites 4.7km[3]	# new infections/last 4 years[4]
F-1	3128	17	7
F-2	3240	9	4
NF-1	3232	5	4
NF-2	3210	10	5
NF-3	3669	8	4
NF-4	3553	10	3
NF-5	3680	6	3

1 Herds designated as "F" are filtered while those designated as "NF" are non-filtered
2 Breeding herd inventory reported as number of sows
3 The number of growing pig sites located within 4.7 km of the study herds. These facilities were not sourced with pigs from study herds
4 Number of heterologous variants of PRRSV detected in study herds over the four years prior to initiation of the study herds.

Table 6: Summary of the PRRSV status (positive versus negative) in filtered and non-filtered herds over the course of the study

Herd ID[1]	Status 9/08[2]	Status 8/09[3]	Date of new infection[4]	% heterology[5]
F-1	neg	neg	NA[6]	NA
F-2	neg	neg	NA	NA
NF-1	pos	pos	5/09	11
NF-2	pos	pos	7/09	10
NF-3	pos	pos	7/09	5
NF-4	pos	pos	4/09	5
NF-5	pos	pos	5/09	12

1 Herds designated as "F" are filtered while those designated as "NF" are non-filtered
2 PRRSV status at the start of the study
3 PRRSV status at the end of the study
4 The month and year when a new PRRSV variant entered a study herd
5 The difference in the ORF 5 region of the new variant which entered the herd during the 12-month study period when compared to the PRRSV variant that was present.
6 Not applicable

Driver #5: Education

A key component of the **EDUCATION** process is the repeated communication of a clear message. In the case of the elimination of PRRSV, I suggest we start at the beginning and clearly communicate the core principles that we have generated during this lecture:

This is a voluntary effort.
This will be market-driven, not federally mandated.
This will be a strategic, science-based effort.
This will be a team effort.
We have the necessities and innovations to get started.

With this attitude and perspective presented in a calm, collected manner, I find it difficult for even the biggest skeptic to pose much of an argument against getting started. However, with PRRS as the focal point of the discussion, one can never be sure what to expect; therefore, it is now time to "Unite the Clans!"

Chapter 3: Uniting the clans!

The theme of "Uniting the Clans" comes from my favorite movie of all time: "Braveheart". You may recall the scene late in the movie in which William Wallace speaks with

Robert the Bruce, pleading passionately for him to step forward, to lead, to unify his countrymen in an effort to stave off the English forces and at long last, win their freedom. Dr. Spronk gets credit for adapting this concept to unification of the veterinary profession in an effort to deal with PRRS. I loved this analogy and actually used it to develop the theme of the lecture which we will re-visit in greater detail during the keynote address. However, as previously stated the elimination of PRRSV from North America must be a team effort**.** No one can do this alone; we need to build teams of practices, teams of producers and teams of scientists with the spirit of collaboration and philosophy of mutual benefit for all established across the teams. In closing, I am hopeful that the optimism and spirit of collaboration that has been evident over the last 2 years continues to spread across the industry. I am confident that if we unite the clans and follow the road map put forth by the philosophy of the 5 Drivers, the long, strange trip will finally be over.

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Dr. Jeff Zimmerman (ISU)

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