

PRRS CAP Goal. The long-term goal of the PRRS CAP is to develop the tools and deliverable knowledge through integrated strategies for producers that will reduce animal suffering, decrease economic losses to producers, and support stakeholder efforts to control and eliminate PRRSV.

Background. PRRSV is a stealthy agent that can efficiently enter a swine unit at any stage of production. As illustrated in Figure 1, PRRSV possesses a complex pattern of transmission, including efficient horizontal and vertical transmission. The virus is transmitted by intranasal, intramuscular, oral, or vaginal routes of exposure. Infected animals shed virus in all bodily secretions. Subclinical, persistent infection in immune competent pigs (carriers) results in the perpetual circulation of virus within herds. Herd immunity, conferred by vaccination or recovery following infection with field virus, is tenuous because continuous mutation, viral recombination, and evolution of several viral genes may allow the virus to persist in a population. These challenges make traditional approaches to disease control and virus elimination less effective. Modified live virus (MLV) vaccines have not fully met expectations and several deficiencies have been noted, including vaccine virus shedding, persistent infection, incomplete protection, inability to distinguish infected from vaccinated pigs, and potential reversion to virulence.

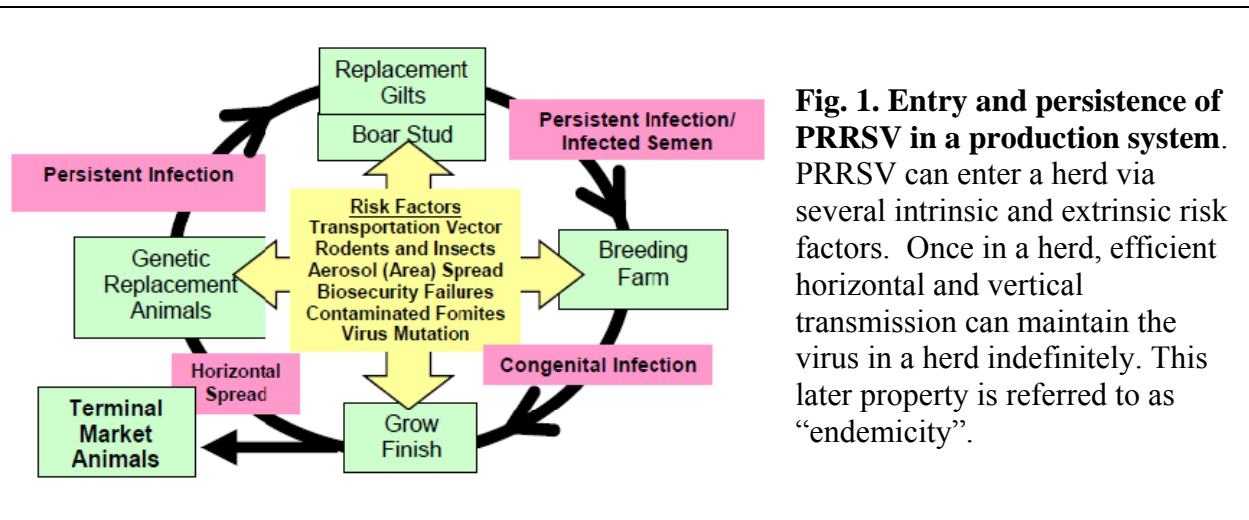


Fig. 1. Entry and persistence of PRRSV in a production system. PRRSV can enter a herd via several intrinsic and extrinsic risk factors. Once in a herd, efficient horizontal and vertical transmission can maintain the virus in a herd indefinitely. This later property is referred to as “endemicity”.

As a result of the complexities and challenges offered by PRRS, the PRRS CAP has taken a global view in developing a strategy to integrate community resources to lessen the impact of PRRS and its eventual elimination. Activities performed by the CAP were identified and prioritized in response to extensive stakeholder input, including meetings with scientists, producers, companies and veterinarians. As a result, activities are divided into three research objectives: Objective 1 (vaccines/immunity), Objective 2 (epidemiology/ecology) and Objective 3 (host genetics). It is important to note that there is no objective specifically devoted to diagnostics; however, improved diagnostics, identified by stakeholders as important, is an outcome embedded within all research and extension objectives. CAP research funding is directed at supporting a small number of large multi-year, multi-institutional projects. This is the same funding approach recently adopted by NIFA. Objective 4 is devoted to extension and includes projects that focus on the control and elimination of PRRSV, including regional elimination projects, standardization of elimination protocols, and novel virus elimination

approaches. Objective 5 is focused on education and outreach, including training fellowships for students from under-represented groups, veterinarians and producers. Dissemination of CAP activities and successes are by way of scientific publications, review publications, stakeholder meetings and workshops, presentations, and the PRRS CAP website (www.PRRS.org). All PRRS CAP activities are performed in cooperation with the National Pork Board (NPB), which represents 20,000 producers in the U.S.

PROGRESS RELATED TO THE RENEWAL (covers Year 1 and partial Year 2 funding).

The principal impact of PRRS CAP is the initiation of several transformations. One example is the beginning of a transformation within the swine industry, which is evident by the initiation of several regional PRRSV elimination projects. Another example is found in the transformation of how PRRS research is conducted: through the creation of large research consortia, such as the PRRS Host Genetics Consortium. The consortium approach provides the mechanism to conduct “Big Science” by coordinating the resources of USDA, the National Pork Board (NPB), universities, and private partners. A third transformation is the increase in public awareness of the impact of infectious diseases on swine health and welfare.

USDA funds for the PRRS CAP became available in August 1, 2008. The first year of the PRRS CAP was primarily devoted to identifying and evaluating projects for funding and initiating what are called the Year One subcontracts, which were completed around July 1, 2009. Currently the PRRS CAP is in Year Two. (A significant delay in the distribution of funding was caused by the USDA re-organization.) PRRS CAP progress described below is primarily the result of a single year of funding, from June 2009 through May 2010. The 2009-2010 report describing the activities and results for the first year of funding (Year One) is presented in the appendix. PRRS CAP activities are “branded” with the logo that appears to the left.



Progress Related to the Funding PRRS CAP Research (Objective 1-3). The funding of PRRS CAP research, extension and activities was initiated in May 2008, with the release of an RFA for PRRS CAP Research, Extension and Education. Each project could be supported for up to \$250,000 of PRRS CAP funds each year for a total of 4 years (up to \$1 million). PRRS CAP participants follow the guiding principles within the PRRS CAP; including the sharing of reagents, clones, proteins, viruses, antibodies, constructs, etc. The RFA and information were distributed through the PRRS listserv, major research universities, minority institutions, and private companies. The closing date for receipt of research proposals was August 20, 2008. A total of nine proposals were received for a total request of \$6,756,492. Participation in proposals included 19 entities (universities, USDA and private companies).

The review of proposals was in two steps. The first review, performed by a scientific review panel, covered the evaluation, scoring and ranking of proposals based on scientific merit. The second step was the PRRS CAP Stakeholder Board (SB) evaluation of the relevance of each proposal. Scientific review was similar to the NIH model as modified by the AI CAP in their review of proposals in 2007. The merit of each proposal was based on (but not limited to) the evaluation of *Competence*, *Completeness*, *Utility*, *Novelty* and *Collaboration*. The scientific review panel was composed of 13 scientific members and headed by Udeni Balasuryia from the University of Kentucky, who is a widely respected arterivirologist and stakeholder board

member. Another member of the panel was Lisa Becton, a PRRS CAP Co-PD and Scientific Director of the National Pork Board Swine Health Committee. Proposals received a final score and ranking. After a second round of reviews by stakeholder board members, the proposals were funded. All CAP research projects have completed the first year of funding.

Progress Related to Funding PRRS CAP Extension (Objective 4, regional elimination and biosecurity). In 2002, Robert Morrison, University of Minnesota and PRRS CAP CoPD, initiated the first collaborative regional effort to control PRRSV in Rice County, MN, followed by the initiation of a second project in Stevens County in 2004. These early efforts identified several challenges related to PRRSV elimination: (1) preventing PRRSV positive pigs from entering the region; (2) achieving and maintaining 100% participation of producers, especially small operations; and (3) documenting the impact of PRRS and PRRSV elimination at the regional level. In several discussions, CAP stakeholders identified several priorities related to regional elimination:

- Continuation and expansion of existing PRRSV control and elimination projects,
- Identification of new elimination projects that present novel ideas and approaches,
- Measurement of producer attitudes regarding on-farm PRRSV control and elimination,
- Assessment of PRRS biosecurity in the field.

Application for regional elimination projects can be initiated at any time during the CAP. Interested parties contact Dr. Morrison and then submit a short proposal containing the following information: (1) The goal(s) of the project; (2) Estimated number, size and location of swine operations; (3) Estimated number of sites introducing pigs from outside the region and the PRRS status of these pigs, (4) Perceived willingness of producers to participate; (5) Suspected PRRS status of sites and recent clinical activity of PRRS; (6) Number of veterinarians servicing the area, including perceived leadership; (7) Description of the proposed program; (8) Timeline; (9) How “success” will be assessed and likelihood of achieving success; (10) Any incorporation of innovative ideas and methods; and (11) Budget, including matching support.

Project applications are evaluated by a committee of experts and a recommendation is forwarded to the stakeholder board which makes the final funding decision. Because of the active interest in initiating projects, there is a \$25,000 limit placed on the funding of new regional elimination projects. Elimination project representatives come together at the Lemn Swine Conference, American Association of Swine Veterinarians meeting and International PRRS Symposium to discuss progress and challenges. Projects are reviewed yearly and funding continued based on progress.

Progress Related to Funding Education. Support for education of students is primarily in the form of mentoring activities of PRRS researchers. The PRRS CAP supports opportunities for undergraduate and veterinary students to participate in summer internship programs and provides support for graduate student fellowships. A special emphasis is placed on the support of veterinarians seeking Ph.D. degrees and students from minority institutions. Funding is in the form of stipends, with matching funds from the mentor. Stipends are approximately \$6,000 for 3-month summer fellowships and \$12,000 per year for graduate fellowships. Fellowship opportunities are open to all those conducting PRRS research/extension activities, regardless of

the level of funding support by the PRRS CAP. Applications can be made at any time and include; (1) a brief statement by the applicant describing the short and long-term career goals, (2) a brief description of the PRRS research to be performed and how it will benefit the student and stakeholders, (3) a two-page biographical sketch, (4) and a letter from the mentor describing support for the student's training activity. Applications to the scholars program are reviewed by a committee headed by Darryl Ragland at the Purdue University.

The following are progress summaries of funded research, extension and education projects.

Project 1, Objective 1, Research-Vaccines/immunity. Immunological consequences of PRRSV diversity. *PI William.W. Laegreid, University of Illinois, CoPI Fernando A. Osorio, University of Nebraska, CoPI Tony L. Goldberg, University of Wisconsin, CoPI Jane Christopher-Hennings, South Dakota State University, CoPI Eric A. Nelson, South Dakota State University, Collaborators: Asit Pattnaik, University of Nebraska, KJ Yoon, Iowa State University, Federico Zuckermann, University of Illinois*

Overview. Failure to develop effective PRRS vaccines is the result of inherent genetic and antigenic variability of PRRSV and presents a major impediment to disease management in production settings. The extent and immunologic consequences of genomic variation in PRRSV are incompletely understood, hindering the development of next generation vaccines capable of effectively protecting against the different PRRSV strains circulating in the field. In order to address these critical impediments to vaccine development, this project addresses two main objectives; define and completely sequence a core set of viruses representing the breadth of PRRSV sequence variation and associate relevant immunologic phenotypes with specific PRRSV genomic variation.

Progress to date. At the University of Wisconsin (Goldberg), substantial progress has been made towards the central goal of objectively defining a "core" set of PRRSV isolates that can form the basis of subsequent cross-neutralization and vaccine development studies. Specifically, PRRSV ORF5 sequences from field isolates in GenBank were downloaded (~12500 sequences) and aligned using FSA (Bradley et al. 2009), with manual correction in Mesquite (Maddison and Maddison, 2009). The aligned sequences underwent a redundancy analysis and identical sequences were removed. Evidence of recombination was detected using RDP3 (Heath et al. 2006) along with sequences that showed evidence of recombination. Phylogenetic trees were constructed using a Bayesian Markov Chain Monte Carlo (MCMC) method implemented in the BEAST package (v.1.5.3, Drummond & Rambaut, 2007). A relaxed molecular clock with an uncorrelated log-normal distribution of rates, a codon based SRD06 model of nucleotide substitution (Shapiro et al. 2006; Vijaykrishna et al. 2008), and a Bayesian skyline coalescent model were used in the analyses. The resulting phylogenetic tree represents a robust presentation of the evolutionary history and geographic 'signal' in PRRSV diversity. The final analysis has yielded a parsimonious set of approximately 50 viruses that objectively reflect the full spectrum of known PRRSV genetic diversity.

At the University of Nebraska (Osorio), work is directed at grouping representative field strains of PRRSV by means of a cross-neutralization. Results to date identify at least 8 putative groups. To link these groups to sequences, Dr. Laegreid (University of Illinois) is performing whole

genome sequencing. The results of neutralizing assays showed that that ISU isolate 19248-01 (herein referred to as “O1”) possessed two unique neutralization phenotypes. First, the O1 isolate was highly reactive in vitro neutralization assay and induces a rapid and robust NA response in pigs during infection. Sequence analysis of O1 identified the loss of two glycosylation sites, one in GP3 and the other in GP5, both of which are normally present in other PRRSV strains. Reverse genetics and an infectious clone are being used to evaluate the role of glycosylation in neutralization. Other immune studies related to cross protection involve the mapping of T cell epitopes contained throughout the non-structural and structural genes of PRRSV. Cell proliferation and ELISPOT analyses of peptide-stimulated lymphocytes from PRRSV-infected pigs have identified epitopes in the N protein (1 epitope), M (1 epitope), GP5 (confirmed 2 epitopes previously described by Vashisht et al (2008)), and NSP9 (2 major and 2 minor epitopes).

With the support of NPB funding, South Dakota State University (Christopher-Hennings) developed a Luminex multiplex swine cytokine assay to measure nine immune-related cytokines simultaneously in pig serum. This assay detects innate (IL-1 β , IL-6, IL-8, IFN α , TNF α); regulatory (IL-10), Th1 (IL-12, IFN γ), and Th2 (IL-4) cytokines (results are reported in Lawson et al., 2010). The cytokine panel is being used as part of the deep phenotyping protocol in Dr. Lunney’s host genetics project.

Project 2. Objective 1, Research-Vaccines/immunity: Innovative approaches to develop a broadly protective and effective vaccine(s) against PRRSV. PI X. J. Meng, Virginia Polytechnic Institute and State University, CoPI Tanja Opriessnig, Iowa State University, CoPI Ying Fang, South Dakota State University

Overview. The current commercially available MLVs and killed vaccines are inadequate for effective PRRSV control and elimination. Despite intensive research on development of an effective PRRSV vaccine over the past 18 years, the traditional approaches for PRRSV vaccine development have not yielded a better product. In this CAP2 PRRSV project, we intended to fill the knowledge gap in this area by developing a candidate multivalent vaccine(s) through molecular breeding and DNA shuffling of known genetically distinct strains of PRRSV. The objective of this proposal is to utilize molecular breeding (DNA shuffling) of PRRSV from major genetic clusters to generate PRRSV chimeric viruses and immunogens as a broadly-protective vaccine candidates. This project will be completed at the end of Year 2.

To facilitate the DNA shuffling/molecular breeding process of PRRSV, a robust reverse genetic system of PRRSV is needed. By introduction of ribozyme elements at both termini of the viral genomic cDNA that were placed under the control of a eukaryotic hybrid promoter (Fig. 1), we developed an improved DNA-launched (plasmid-DNA transfection-based) reverse genetics system for PRRSV with reduced cost and labor.

Based on the phylogenetic analyses of GP5 genes, we initially selected five genetically distinct strains of PRRSV DNA shuffling: VR2385, FL12, MN184B, DQ474837, and JXA1 (Chinese high pathogenic PRRSV strain). The shuffled region included the entire ORF5 gene excluding the 13-bp region that overlaps with ORF6. Shuffling was performed by DNase digestion followed by PCR. Sequence analyses showed that the shuffled products were well represented

from their parental strains, and approximately 20% of the shuffling products have sequences represented from all the five parental GP5 sequences. A library of the shuffled GP5 products has been cloned into the infectious cDNA clone backbone and is being characterized for viability.

Project 3. Objective 1, Research-Vaccines/immunity: Positive prognosticators of immune protection and prophylaxis against PRRSV in swine herds. PI Michael Murtaugh, University of Minnesota, CoPI Renukaradhya Gourapura, Ohio State University

Overview. New vaccines that will solve the problem of PRRS are five to ten years away, if not more. In the meantime, producers and veterinarians need help now to prevent PRRS and reduce its severity. They have few tools to work with: herd closure, biosecurity, and air filtration can eliminate and prevent PRRS, but are not permanent solutions and cannot help in acute outbreaks. Anti-viral therapeutics for acute outbreaks do not exist and are not anticipated in the foreseeable future. A pressing need exists to better understand host factors that favor effective immune prevention and intervention so that immunological control and prevention of PRRS can be improved with currently available tools. The goal of this project is to investigate immunological mechanisms associated with successful prevention and treatment of PRRS by comparing sick and healthy swine in the field. Objective 1 proposes to characterize antibody responses in immune sow herds undergoing a PRRS outbreak. The working hypothesis is that differences in memory B-cell and cross-neutralizing antibody responses distinguish sick and healthy sows. Objective 2 proposes to characterize the effect of vaccine intervention in a naïve finishing herd outbreak. Successful completion of the project will provide the swine industry with 1) knowledge essential for making informed decisions on use of serum inoculation and vaccination for PRRS prevention, 2) tools to facilitate the final stages of regional elimination, and 3) research know-how, field-tested models, and immunological surrogates to help guide vaccine development.

Progress to date. Implementation of the work plan in objective 1 requires extensive logistical preparation for response to an active PRRS outbreak in a swine herd with little or no advance warning. A response team consisting of a senior research associate, laboratory technician, PhD graduate student, and DVM, PhD graduate student was organized. Coordination and communication with the cooperating producer and the veterinarian were carried out, and a mock response was performed, in conjunction with a related research project on PCV2 transmission in farrowing rooms. As part of the immunological assessment of vaccinated pigs, a natural killer (NK) cell (NKC) cytotoxicity assay is being developed by Dr. Gourapura.

Project 4. Objective 2, Research-Epidemiology/ecology: Identifying ecologic and epidemiologic factors in the control of PRRS: A field-based approach. *PI Jeffrey J. Zimmerman, Iowa State University, CoPI Scott A. Dee, University of Minnesota, CoPI Peter R. Davies, University of Minnesota, CoPI Derald J. Holtkamp, Iowa State University, Collaborators: Annette O'Connor, Iowa State University, Steve Pohl, South Dakota State University.*

Overview. PRRS *Epidemiology* is the study of the transmission and control of PRRSV. *Ecology* relates to how the biology of the virus, the pig, infectious disease co-factors, and the production environment interact to maintain PRRSV in herds (endemicity) and promote clinical losses. The introduction of PRRSV into a herd in the absence of any apparent animal or human contact is termed “area spread.” Under most circumstances, the source of the virus responsible for an outbreak is unknown. Other sources for entry of virus into a breeding population include the introduction of infected animals, contaminated fomites, non-porcine hosts, and semen. The goal of this project is to identify ecologically and epidemiologically critical control factors for reducing the impact of PRRS on the farm. The broad goal of this project is to develop and implement tools to identify those critical control factors. Specific objectives are to 1) develop models of PRRSV infection and disease, 2) develop improved time- and cost-effective strategies for conducting herd surveillance, 3) quantify PRRSV mechanisms and patterns of transmission between herds, 4) identify risk factors important in the control of PRRSV and reduction of PRRS, and 5) establish a repository of field samples and data for future investigations. Results from this project are reported in Dee et al. (2009a, 2009b), Hermann et al. (2009), Jacobs et al. (2010), Kittawornrat et al. (2010); Molina et al. (2009).

Progress to date.

- A herd classification system describing the PRRSV status of herds, as well as a standard set of related definitions that is consistent with the biology and ecology of PRRSV has been developed. This outcome was the result of meetings between PRRS CAP researchers, AASV and NPB.
- Improved surveillance by incorporating the analysis of oral fluid samples. Results show that both PRRSV and anti-PRRSV antibodies (IgG, IgA, IgM) are present at diagnostically useful levels in oral fluid specimens collected both under experimental and field conditions.
- To date, 0 (zero) of 5 filtered herds and 17 of the 20 control herds (85%) experienced acute episodes of PRRS secondary to the introduction of new variants. The data support the value of air filtration in the prevention of outbreaks that result from aerial spread.
- PRRS Risk Assessments for the Breeding Herd are currently being completed for sites participating in the *Sow Herd Air Filtration Study*.
- Extensive data and samples have been obtained from field collaborations. These will be helpful for future studies.

Project 5. Objective 3, Research- Host genetics: Characterization of host factors that contribute to PRRS disease resistance and susceptibility. *PI Joan K. Lunney, USDA ARS BARC, CoPI Jack C. M. Dekkers, Iowa State University, CoPI Rohan Fernando, Iowa State University, CoPI Zhihua Jiang, Washington State University, CoPI Roman Pogradichniy, Purdue University, Collaborators: James M. Reecy, Iowa State University, Max Rothschild, Iowa State University, Carolina State University, Juan Pedro Steibel, Michigan State University*

Overview. Continued losses to the pig industry from PRRS make it imperative to search for alternative PRRS control practices. This grant proposes to use state-of-the-art whole genome association analyses to identify the genetic determinants of resistance/susceptibility of commercial U.S. swine to PRRSV infection. The primary objective of this project is to characterize host factors that contribute to PRRS disease resistance and susceptibility (host genetics). The samples to be tested will be those collected through the National Pork Board funded PRRS Host Genomic Consortium (PHGC). DNA samples from PHGC pigs will be genotyped with the newly developed 60K single nucleotide polymorphism (SNP) chip. Extensive whole-genome association analyses will be performed to determine which markers are associated with PRRS susceptibility/resistance traits. Simultaneously, preliminary gene expression analyses are planned to compare PRRS responses that differ in PRRS resistant versus PRRS susceptible PHGC pigs and to dissect pathologic versus protective immune responses in samples collected from PRRSV infected versus vaccinated swine (this work is receiving support from a NIFA grant #2009-03338). The results will be disseminated to swine breeders, genetics companies, and genotyping services so that sets of these recommended genetic markers can be employed in future breeding programs to increase disease resistance.

Progress to date. The principal source of samples to be tested are available through the NPB-funded PHGC (Lunney and Rowland, PIs), a national effort developed with input from PRRS researchers, NC1037/NRSP8 genome researchers, members of the NPB Swine Health and Animal Science Committees, veterinarians, AASV, producers, and commercial partners representing breeders, animal health, feed, and diagnostic companies. The PHGC incorporates a nursery pig model to assess pig responses to acute PRRSV infection (deep phenotyping) and for the study of the relationship between host genes and resistance/susceptibility. Each infection trial includes 200 pigs which are brought into the challenge facility at weaning (14-21 days age), infected a week later with a well characterized PRRSV isolate, and followed for 42 days after infection. Blood and other samples (e.g. oral fluids) and weight measurements are collected regularly for phenotypic data. Tonsil and other samples are collected at the end of the study. Phenotypic measurements include virus load, weight gain, antibody responses, and cytokine levels in serum. All samples are catalogued and distributed to appropriate testing labs and stored for use in later studies. The data are collected into a PHGC relational database housed at Iowa State University. DNA recovered from each pig is genotyped using funding from a separate PRRS CAP grant. Blood samples are collected in Tempus tubes for the purpose of characterizing host and virus gene expression in nucleated blood cells. Oral fluid samples are collected for the purpose of developing improved PRRS surveillance methods. The first milestone was achieved in June 2010 by the infection of 1,500 pigs.

DNA samples from every PHGC pig will be genotyped with Illumina's 60K single nucleotide polymorphism (SNP) chip, the Porcine SNP60 BeadChip. Genomic DNA from 1350 pigs was

prepared at ARS BARC (Lunney) and quality assured via OD and gel analyses, with advice from PIC (Gladney) and Dr. Rothschild at Iowa State University. SNP and whole genome association studies (WGAS) will be initiated in late 2010. A Multivariate Analyses Protocol was developed at MSU (Steibel) to statistically identify pigs at the extremes of weight and viral load. The results identified pigs in different virus/weight categories: HvLg = high virus, low growth = the worst phenotype; HvHg = high virus, high growth; LvLg = low virus, low growth; and LvHg = low virus, high growth = the best phenotype. Data on PHGC 1-4 pigs assigned to the 4 statistical groups will be available as a file on the PHGC database. Results are reported in Lunney et al. (2010).

Project 6. Objective 4, Extension: Regional PRRS Elimination in Michigan. PI Barbara Straw, Michigan State University, CoPI Jerry May, Michigan State University, CoPI Beth Franz, Michigan State University

Allegan and Ottawa counties comprise one of the more intensive swine raising areas of Michigan. Given the intense production in a relatively small geographical area, these farms have struggled with PRRS. Yet this area, because of a unique combination of regional barriers (both natural and manmade) and a history of producer cooperation, holds promise for the elimination of PRRS. Producers, local veterinarians, and MSU Extension are proposing this area take part in a PRRS Regional Elimination Project. The five stages of PRRS Elimination that have been used successfully in other areas (Morrison, MN) will be employed in this project. In Stage 1, MSU Extension personnel will provide leadership and implementation of bookkeeping, communication, and data compilation. Veterinary practitioners have committed to clinical program support; oversight, feedback and encouragement are critical to successful implementation of this program.

Project 7. Objective 4, Extension: Western Illinois tri-county PRRS epidemiology and elimination. PI Dyneah Augsburger, Carthage Veterinary Service, Ltd

Approximately 130 sites are located in the three Western Illinois counties of Hancock, McDonough, and Adams. This project will verify the location of all swine operations within the tri-county area. The status of 20 sites (15% of expected total sites) is known through routine monitoring. Little is known about the PRRSV status of the other sites in the proposed project area. Like many swine producing areas, numerous known unique PRRSV isolates have been introduced that have resulted in clinical disease and costly production losses. Many of the production sites in the tri-county area are affiliated with one of three modern production systems. The goals of the project are: 1) identify swine populations within the three counties of Hancock, McDonough, and Adams, 2) establish PRRS status based on published categories, 3) actively engage multiple stake holders (4-H, FFA, commercial producers), 4) make measurable progress towards PRRS control and elimination.

Project 8. Objective 4, Extension: The elimination of PRRSV from Northern Minnesota. *PI Montse Torremorell, CoPIs Bob Morrison, Peter Davies, Scott Dee, University of Minnesota*

The Stevens Co. PRRS elimination project in Minnesota was initiated in 2004. The purpose of this proposal is to extend PRRSV elimination to all of northern Minnesota by making highway 212 the demarcation line. The result will make more than 1 million pigs PRRSV-free and set the stage for eliminating PRRSV from other northern regions, including North Dakota and South Dakota. Northern MN is rather isolated from the intensive areas of swine production; deriving most of the breeding stock, and purchasing growing pigs from within the region. This situation makes this an ideal project to investigate PRRSV elimination in lower density, isolated regions. There are relatively few veterinarians doing swine work in the area; this deficiency will present new challenges. The project is underway and funding is matched by Swine Disease Elimination Center.

Project 9. Objective 5, Education: Minority research training. *PI Darryl Ragland, Purdue University*

The goal of the project is to develop and provide an inter-institutional, multi-disciplinary, cooperative training experience in swine disease research for promising, under-represented students from historically black institutions (HBI) of higher learning that offer agricultural and related degrees. Dr. Ragland is a veterinarian who graduated from Tuskegee. Outreach efforts are ongoing to establish partnerships with North Carolina Agricultural & Technical State University and Tuskegee University School of Veterinary Medicine. North Carolina A&T State University offers degrees in traditional animal sciences and laboratory animals sciences. Tuskegee University has the distinction of being the only HBI to offer the Doctor of Veterinary Medicine degree as well as an MS degree in Veterinary Science and houses several research centers focused on animal health.

Project 10. Objective 5, Education: PRRS CAP Graduate Scholar Program. *PI Jeffrey Zimmerman, Iowa State University*

One-year fellowships for two graduate students were funded during the first year. Both were doctoral candidates working toward completion of PhD degrees under the direction of Dr. Zimmerman in the Department of Veterinary Microbiology at the College of Veterinary Medicine, Iowa State University. The areas of PRRS research included PRRSV aerobiology, which focused on (A) estimation of the probability of PRRSV transmission to pigs by aerosol exposure (dose-response) and (B) development of cost-effective measures to prevent the transmission of PRRSV in aerosols, e.g., through the use of UV254 irradiation. The second project was related to PRRSV ecology and focused on the development of a real-time, standardized, cost-effective surveillance system that will give producers a cost-effective tool to integrate infectious disease information with assessment, bench-marking, and implementation of interventions. This research involved the analysis of swine oral fluid samples as a tool to monitor PRRSV circulation in commercial swine herds.

Project 10. Objective 5, Outreach: International PRRS Symposium (IPRRSS). 2010 Chair
X. J. Meng, Virginia Polytechnic Institute and State University

The yearly showcasing of PRRS CAP and National Pork Board research and extension activities is in the context of an international PRRS meeting, the IPRRSS (www.prrssymposium.org). The IPRRSS is the only international conference that is totally devoted to PRRS. The IPRRSS precedes the Conference of Workers in Animal Diseases (CRWAD) and receives significant support from Bob Ellis, the organizer for CRWAD. Dr. Ellis reserves the meeting rooms and negotiates with the conference site the lowest possible costs for the IPRRSS meeting.

The IPRRSS grew from the yearly meeting of NC-229 group of PRRS researchers. In conjunction with the NC-229 business meeting, station reports were orally presented by the NC-229 station representatives. The IPRRSS grew out of the request for non-NC-229 PRRS researchers, practitioners and company representatives to attend the NC-229 meeting. In 2004, the station reports were replaced by the first IPRRSS conference. Due to its popularity, the conference grew from 90 participants and a one day format in 2004, to more than 200 registrants the following year. In 2005, the meeting was extended and included poster sessions. For 2009 there were 253 registered attendees from 25 different countries. Ninety-seven abstracts were submitted. Continuing education credits were added in 2008. Travel fellowships were offered to international graduate students in 2009. Two important features of the IPRRSS are: (1) registration is free to all, which encourages attendance by undergraduate and graduate students; and (2) a free lunch is offered during the full-day session, which lessens the cost of the meeting to students and retains the conference attendees onsite for the afternoon sessions. Registration and abstract submission are handled through the symposium website, which is maintained by the NPB. Support for the IPRRSS is through the CAP, NPB, companies and individuals. This level of leveraged support allows the symposium to forgo registration fees, provide a luncheon, and encourage a higher level of attendance. Continuing education credits and international travel fellowships for graduate students are also available. The 2009 program and survey results can be found in the appendix.

Project 11. Objective 4, ExtensionStandardization of regional elimination projects. PI
Derald Holtkamp, Iowa State University.

One means to integrate elimination projects was the creation of a standard set of terminologies and language that could be used to communicate across projects. The process was initiated by series of meetings, organized by Robert Morrison, and located at University of Minnesota (August 18, 2009) and Swine Veterinary Center, St Peter, MN (October 8, 2009). Participants included Bob Rowland, Harry Snelson, Robert Morrison, Max Rodibaugh, Paul Yeske, Montse Torremorell, Derald Holtkamp, Lisa Becton, Dale Polson, Barb Straw, Jeff Zimmerman, Steve Henry, Dyneah Augsburg, and Troy Bigelow. The final document was approved by the AASV Board of Directors (March 9, 2101) and results submitted for publication by the Journal of Swine Health and Production (Holtkamp et al., 2010, Standard Herd Classification and Related Terminology for PRRS Virus). A copy of the manuscript can be found in the appendix material. Future meetings are being held to develop a common set of protocols that can be applied across elimination projects.

Project 12. Objective 5, Outreach: PRRS sponsored meetings and workshops.

In addition to the IPRRSS, the PRRS CAP supported the following meetings and workshops.

- PRRS CAP Workshop, PRRS Diagnostics: Current Developments and Future Needs, December 2008, Chicago
- PRRS CAP Workshop, Europe, United States and China Perspectives on PRRS Research, December 2009, Chicago
- AASV Annual Meeting Workshop on Regional Elimination, March 2009, March 2010
- Allen D. Leman Swine Pre-conference on Regional Elimination, September 2009
- Development and implementation of a multiplex microsphere immunoassay (MIA) platform for swine diagnostics. April 28, 2009, National Pork Board, Des Moines, Iowa
- PRRS Definitions Committee Meeting, University of Minnesota, August 18, 2009
- PRRS Definitions Committee Meeting, Swine Veterinary Center, St Peter, Minnesota, October 8, 2009
- PRRS CAP–NPB PRRS Initiative Joint Conference, Des Moines, Iowa, June 2-3, 2009
- PRRS CAP–NPB PRRS Initiative Joint Conference, Des Moines, Iowa, June 7-8, 2010

Leveraging of PRRS CAP resources. Leveraging USDA funding is an important goal of the CAP. The 2009-2010 year report lists a total of \$3 million of matching funds from universities, companies, other grants, and the National Pork Board (NPB). By far, the largest leveraging partner was the NPB who contributed more than \$1 million for the support of PRRS research, extension and outreach. It is this close association with a commodity group that makes the PRRS CAP unique.

Evaluation PRRS CAP Progress, Outputs and Impacts. The original proposal approved by USDA included a set of measures to evaluate PRRS CAP progress and effectiveness in achieving the goal of PRRSV elimination. The metric is composed of quantitative and qualitative measures. Many of the results described below were derived from the 2009-2010 report (appendix).

1. Evaluation of Research. Number of publications, presentations and patents, outcomes of research, achieving project milestones, and transfer of technologies to the field. The 2009-2010 report (appendix) cites 49 meeting abstracts and 17 publications. All research and extension activities within the CAP are initiated after extensive evaluation, including the identification of specific goals and objectives. These are evaluated yearly as progress reports and presentations to the stakeholder board and colleagues. After a year of funding, most projects have made the indicated progress. Only one research project was considered to have not achieved the indicated milestones and is undergoing subsequent review after six months. Two examples of technology transfer are the filtration of pig barns, which improves the biosecurity for PRRSV and other infectious agents, and the use of oral fluids instead of serum for performing antibody and viral surveillance (Prickett and Zimmerman, 2010). Both projects are performed under Objective 2 (Zimmerman). A unique dissemination activity is the publication of a special issue on PRRS published by the international journal, *Virus Research* (Elsevier Press). The editors, Dr. Rowland and Dr. Lunney, both CAP participants, invited manuscript (original and review articles) for a special issue of *Virus Research* on "Progress in porcine respiratory and reproductive syndrome virus biology and control." The goal of the special issue is to compile

stimulating refereed papers that focus on complex issues related to PRRS control, immunity, vaccine design and virus elimination. Authors have been invited and papers are currently under review. The special issue is set for publication in fall 2010.

2. Evaluation of Extension. Number of projects recruited into the regional elimination program. Number of regional PRRSV elimination successes. Changes in producer awareness. During Year One of CAP funding, three projects were recruited into the regional elimination program (Michigan, Illinois and Minnesota, see above for summaries). The definition of a successful regional elimination project can be found on two levels. The first is installation of process that fosters communication, education and progress among producers. The second is the demonstration that PRRSV has been eliminated (which is expected to take several years). All elimination projects are near the first goal. The publicity from these projects has increased awareness among veterinarians and producers, and has resulted in four requests to fund additional projects. Another change has been the active involvement of private companies, such as Boehringer Ingelheim Vetmedica (BIV). BIV and the CAP are in the process of developing partnerships that will improve funding and coordination of elimination efforts in the field.

3. Evaluation of Education and Outreach. Number of stakeholders attending PRRS CAP sponsored meetings, conferences and workshops. The results of surveys submitted by participants of outreach activities. Dissemination of activities, outputs and impacts to stakeholders. As indicated above, the PRRS CAP sponsors meetings and workshops related to research and extension. Complementary to the IPRRSS, these smaller meetings average about 50 stakeholder participants per meeting. As described above, a web-based survey is used as an instrument to obtain feedback from participants of the IPRRSS. Responding to the survey has led to significant improvements in the overall quality of the conference. Thanks to funding support from the NPB, the PRRS CAP website (www.PRRS.org) was recently overhauled. In addition to standard written information, the website will be used to access recorded presentations, either through WebEx or Camtasia. The PRRS CAP is recording presentations at PRRS meetings, including the PRRS symposium. Research and extension video presentations by PRRS investigators will be made available for download by the public. At present, the presentations are on the private side of the website for review by researchers and the stakeholder board.

RATIONALE AND SIGNIFICANCE

Sixty percent of U.S. herds are estimated to be infected with PRRSV, and according to the NPB, PRRS is “the most economically significant disease facing the industry today.” The \$560 million that PRRS costs U.S. pork producers annually (Neumann et al., 2005) dwarfs annual losses to hog cholera (\$364 million*) and pseudorabies virus (\$36 million*) prior to their eradication (*adjusted to Year 2004 dollars; Hallam et al., 1987; Wise, 1981). The impact of PRRSV translates directly into increased costs to the consumer and unnecessary suffering to animals. Additionally, there is loss of morale and other psychological effects that pig morbidity and mortality have on animal caretakers. Recently, highly pathogenic PRRS has been described in China and Vietnam (Li et al., 2007; Rowland et al., 2007; Tian et al., 2007). The findings and conclusions of Chinese and Vietnamese researchers, presented at the CAP-sponsored International PRRS Symposium (IPRRSS), adds an additional urgency to make sure that the tools are available to keep this disease from affecting the U.S. swine population.

In response to nearly two decades of unrelenting PRRS losses, the “National PRRS Initiative” was created by the NPB in the summer of 2003. Following shortly thereafter, the USDA NC-229 (PRRS) Committee spearheaded the project entitled “*Integrated control and elimination of PRRSV in the U.S.*” or CAP1. The current CAP is often referred to as CAP2 or “CAP”. The CAP integrates the activities of three stakeholder groups, all represented by organizations with national/international reach. Researchers, represented by NC-229 and universities, are focused on developing the new knowledge and technology needed to support PRRSV control and elimination efforts. Approximately 63,000 producers are represented by the National Pork Board (NPB; www.pork.org). Veterinarians, represented by the American Association (AASV; www.aasv.org), include 1300 members involved in practice, industry and academia. All three stakeholder groups are represented on the PRRS CAP Stakeholder Board.

In April 2006, in preparation for the CAP renewal, stakeholder representatives formed the PRRS CAP2 Steering Committee. In a two-day meeting facilitated by the NPB, the Steering Committee formulated stakeholder input on PRRSV control and elimination strategies and developed the broad plan for the PRRS CAP, including (1) the principal research objectives and priorities; (2) the composition, structure, and function of the stakeholder board; (3) identification of the project director and host institution; and (4) guidelines for project management and budget oversight.

Subsequently, several meetings were held to further focus the activities under each CAP objective. For example, CAP stakeholders met in May 2007 at the NPB to organize the PRRS Host Genetics Consortium (PHGC) as the means to conduct long term studies of genetic factors related to host resistance and disease. The consortium was developed with input from PRRS CAP and NC229 disease researchers, NC1037/NRSP8 swine genome researchers, members of the NPB Swine Health and Animal Science committees, veterinarians, producers, and commercial partners representing breeders, animal health, feed, and diagnostic companies. The PHGC incorporates the CAP philosophy by coordinating the complex efforts and tremendous resources needed to address the role of pig genetics in the susceptibility and resistance of pigs to PRRS. For the vaccines/immunity objective, the Department of Veterinary Pathobiology at the University of Illinois hosted a colloquium on the “Past, Present and Future of PRRS Vaccines”. The report was published as an editorial on the AASV website. The NPB hosted a 1½ day meeting in October 2007 to formalize overall CAP planning.

The activities under the CAP are divided into five objectives. The first three objectives focus on the development of tools and knowledge needed to support the efforts of scientists, practitioners and producers. A fourth objective is devoted to extension, which directs some of these new technologies in regional elimination demonstration projects. The fifth objective is education and outreach, which is directed toward the internal community of scientists and veterinarians involved in research, and the external stakeholder groups, including producers, consumers, and the swine industry at large.

The five objectives are:

1. Vaccines/immunity: Develop improved PRRSV vaccines by understanding PRRS viral structure, effects on immunity, and mechanisms of heterologous protection
2. Epidemiology/ecology: Characterize ecologic and epidemiologic factors that will

facilitate the control of PRRS.

3. Host genetics: Characterize host factors that contribute to disease resistance and susceptibility
4. Extension: Develop innovative approaches to on-farm control and elimination of PRRSV and identify factors associated with success and barriers to progress
5. Education/outreach: Develop programs for the education and outreach to scientists, producers and veterinarians.

APPROACH- Year Four of the PRRS CAP

Introduction. The PRRS CAP takes a global approach for the integration of resources and activities that lessen the impact of PRRS. CAP activities are divided into four principal areas: Research, Extension, Education, and Outreach. As described in the logic model, inputs to support these activities include funding and resources from USDA (CAP, ARS, AFRI), NPB and other sources. As described above, an evaluation plan is in place to monitor and assess progress.

The technology and new knowledge that stakeholders have requested are described in three research objectives: Objective 1 (vaccines/immunity), Objective 2 (epidemiology/ecology) and Objective 3 (host genetics). There is no objective specifically devoted to diagnostics; however, improved diagnostic tests, identified by stakeholders as important, are outcomes embedded within each objective. Objectives 1-3 build on the progress made under the previous CAP grant, but with some notable modifications. First, large multi-year and multi-institutional projects are supported, with up to a \$1 million for a single project. Each research project assembles an interactive team that works together in parallel to make rapid progress. Secondly, prior to initiation of funding, all projects are reviewed by a panel of experts and then approved by the CAP Stakeholder Board. And finally, all CAP activities come together by focusing on a single goal: the elimination of PRRSV in the field. Objective 4, Extension, applies new technologies to eliminate PRRSV from farms and larger regions. Objective 5 is education and outreach, including the training of students from minority institutions and support for the International PRRS Symposium (IPRRSS). Year Four activities will be devoted to the completion, or closing out, of some CAP activities, while continuing others through non-CAP funding. For example, after Year Four, the www.PRRS.org website will be turned over to the NPB for continued development and maintenance.

Funding of Research (Objectives 1-3) in Year Four. In Year One, all of the research dollars were committed to long-term, multi-institutional projects. Therefore, Year Four is directed at the continuation of funding for the last year of each research project. Renewal of projects is “asynchronous”, i.e. project PIs can request Year Four funding when appropriate. For example, a project that is making accelerated progress can renew funding prior to the anniversary date, while projects that are delayed can continue beyond the anniversary date. Project renewal is initiated by submission of the following documents by the PI:

- Progress Report
- Plan of work for Year Four, including any deviations from the original proposal
- Detailed budget for each CoPI
- A brief description of how the funding will be leveraged using other resources

The Year Four renewal process is managed by David Benfield, a CAP CoPD. Briefly, renewal materials are distributed to the renewal review panel for comments. The panel consists of stakeholder board members, the CAP CoPDs, the NPB Swine Health Committee, and other experts who might be able to provide insight. The PI presents to the review panel a 20-30 minute Power Point (PP) via WebEx describing progress and plan of work. Virtual conferencing technology provides the opportunity for the panel to ask questions as well as engage the PI in discussion. A copy of the PP presentation is posted on the PRRS CAP website (www.prrs.org). Comments are collected from all of the panel participants and discussed. Only PRRS CAP Stakeholder Board members who do not have a conflict of interest vote on the continuation of funds. It is the obligation of the PI to convey progress to the panel. Failure to do so can result in reduction or loss of funding. At the end, constructive comments and recommendations are forwarded to the PI verbally or in writing.

Funding of Extension (Objective 4) in Year Four. Similar to research, no new regional elimination projects will be initiated in Year Four. The distribution of Year Four funding to ongoing projects follows a format similar to the renewal of research funding. The renewal of funding is managed by Robert Morrison, CoPD.

Funding of Education (Objective 5) in Year Four. Funding for education will follow the same format as previous years. Briefly, support for education is in the form of mentoring activities of PRRS researchers. Opportunities include training for undergraduate and veterinary students to participate in summer internship programs and one year support for graduate students. A special emphasis is placed on the support of veterinarians seeking Ph.D. degrees. Funding will come from within the grant and through matching funds from mentors. Stipends are approximately \$6,000 for three-month summer fellowships and \$12,000 per year for graduate fellowships. Fellowship opportunities will be open to all those conducting PRRS research/extension activities, regardless of the level of funding support by the PRRS CAP. Applications can be submitted at any time and include; (1) a brief statement by the applicant describing the short and long-term career goals of the applicant, (2) a brief description of the PRRS research to be performed and how it will benefit the student and stakeholders, (3) a two-page biographical sketch, (4) and a letter from the mentor describing support for the student's training activity. Scholars are expected to present research progress at the International PRRS Symposium.

Funding of Outreach (Objective 5) in Year Four: International PRRS Symposium (IPRRSS). Year Four operation of the IPRRSS will follow a format similar to previous years. Briefly, the IPRRSS Executive Committee organizes the “nuts and bolts” of the conference, including making the meeting arrangements with the conference site, developing and maintaining the IPRRSS website, editing and compiling the proceedings, contacting meeting sponsors, preparing and distributing the meeting announcement, etc. A separate IPRRSS Program Committee identifies and selects the keynote speakers and selected abstracts for short oral presentations. Members of the program committee are also the chairs and co-chairs of the individual sessions. The meeting is announced through several channels, including the IPRRSS website, CRWAD website, American Association of Swine Veterinarians (AASV) website, NPB website and announcements, and the PRRSV CAP website. Meeting announcements are sent to last year's IPRRSS registrants and distributed through several listservs, including PRRS CAP,

AASV and NPB. Travel fellowships are offered to help support attendance by international graduate students.

PRRS CAP Evaluation Plan. All activities supported by the PRRS CAP are presented in a year-end report for evaluation and feedback by stakeholders and by the public. The report is posted on the PRRS CAP website (www.prrs.org). As described above, all research and extension projects are evaluated on a yearly basis. The outcome of the evaluation process determines the level of funding for the coming year.

The evaluation of the IPRRSS is in the form of an internet survey set up by X.J. Meng, meeting chair. Questions include; 1) the quality of scientific information, 2) the presentation of new and relevant data, 3) the quality of keynote speakers, 4) the overall length of the meeting, 5) the length of short presentations, 6) the length of time for poster viewing, and 7) the availability of time to interact with colleagues. Responses are given on a scale of 1 – 10 where 1 = poor or low value and 10 = excellent or high value. The results are discussed by the executive planning committee and recommendations made for the following meeting.

To aid evaluation by stakeholders, the CAP sponsors two meetings each year. The first is the IPRRSS, which is discussed above. The symposium is geared to the presentation of information and data in the context of an international meeting and focuses on graduate student participation. A second meeting is held six months later (June) in Des Moines, during the week of the World Pork Expo. This is a smaller meeting involving the participation of the project PIs and includes the participation National Pork Board and USDA AFRI PRRS researchers. The one and a half day meeting focuses on: (1) presenting and discussing results from currently funded projects to stakeholders (producers, swine veterinarians, industry representatives and researchers); (2) providing opportunities to foster collaboration and create new working groups between CAP, NPB and AFRI researchers; (3) enhancing outreach and increase awareness of the impact of research, extension and education, and (4) the identification of knowledge gaps. Presentations are video recorded and posted on the CAP website.

Sustaining PRRS CAP Beyond Year 4. An outgrowth of the aggressive leveraging conducted by the PRRS CAP has allowed several PRRS CAP-initiated projects to become self-sustaining. Examples of activities or projects that will become independent of CAP funding are: (1) the PRRS CAP website (www.PRRS.org), (2) the PRRS Host Genetics Consortium, and (3) PRRSV regional elimination. The website is located at the NPB and managed by NPB technical staff. The PRRS CAP develops the content for the site. Since there is no CAP cost associated with the site, it can continue as is. It will only be a matter of developing PRRS-based content, which can be accomplished with minimal funding, including support from the NPB, small grants and private companies. The PHGC lays out a new concept by creating the first-of-its-kind approach to food animal infectious disease research. The NPB, PRRS CAP, ARS, USDA AFRI, private companies, and universities have come together to conduct a multi-year project designed to understand how host genetics influences the outcome of PRRSV infection. The contributions have resulted in a funding package that approaches \$3 million. The first milestone of the project was the experimental infection of almost 1500 pigs and the collection and distribution of almost 80,000 samples. No commodity group possesses this resource. In addition to understanding the genetics of PRRSV infection, the project has yielded several spinoffs, including identifying new

avenues of PRRS research, new diagnostic techniques, new surveillance approaches, and a better understanding of virus ecology. The CAP functions as the leader of the consortium, bringing together the partners, distributing samples, and maintaining a community database. It is likely that a future CAP could function in the same manner. The last CAP activity to achieve independence is regional elimination. Decreased profit margins and increased market instability means that the swine industry can no longer tolerate PRRS, which now affects 60% of herds and costs each affected producer decreases in profits of about 5-10%. As with the PHGC, a consortium is a likely approach for continuing elimination projects. An alternative is the formation of non-profit foundation with financial support coming from the stakeholder community.